Cyclopropyl Building Blocks in Organic Synthesis, 57[‡]

Convenient Syntheses and Biological Activity of Novel ω-*trans*-(Bicyclopropyl)- and ω-(Bicyclopropylidenyl)-Substituted Fatty Acids and Their Derivatives

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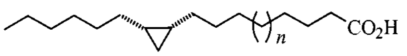
A series of ω-*trans*-(bicyclopropyl)-substituted fatty acids **9** has been synthesized from bicyclopropylidene (**5**) starting by deprotonation with *n*-butyllithium. Electrophilic substitution of lithiobicyclopropylidene with THP-protected ω-iodoalkanols **6** gave the THP-protected (bicyclopropylidenyl)alkanols **7** in 63–88% yield. A reasonably diastereoselective reduction of the bicyclopropylidene moiety in **7** was achieved with lithium in liquid ammonia, and deprotection of the resulting *trans*-(bicyclopropyl)alkanol derivatives **8** followed by Jones oxidation provided the fatty acids **9** in yields ranging from 59 to 75%. ω-Bicyclopropylidenyl-substituted fatty acids **11** were prepared by deprotection and oxidation of the THP-protected bicyclopropylidenylalkanols **7** in 34–43% yield. Subsequent transformation of the acids **11** into the amides **12** proceeded in 68–73% yield. Preliminary biological studies show that bicyclopropyl-substituted fatty acids **9** inhibit the growth of fungi (*Aspergillus nidulans* and *Aspergillus niger*) and are degraded by microbial enrichment cultures following a β-oxidation pathway to yield bicyclopropanecarboxylic and bicyclopropylacetic acid from odd- and even-numbered ω-bicyclopropylalkanoic acids, respectively. Selected bacteria of the genus *Rhodococcus* are able to fully degrade these fatty acids, including the bicyclopropyl units.

Introduction

Although the cyclopropane ring is a highly strained entity, cyclopropyl derivatives are easily formed, are often remarkably stable and also frequently occur as substructures in natural products. Many terpenes, steroids and fatty acids with cyclopropyl moieties exhibit interesting biological activities.[1,2] Fatty acids containing a single cyclopropyl group were isolated in the 1960s from bacterial membranes. This first example, *cis*-10-(2-hexylcyclopropyl)decanoic acid (**1**)[3] isolated from *Lactobacillius arabinosus*, apparently plays an important role in transmembrane transport. However, very little is known about how cyclopropyl-containing fatty acids function and are degraded in nature.[4] Even less is known about the function of the oligocyclopropyl units in the two more recently discovered natural products FR-900848 (**2**)[5] and U-106308 (**3**).[6] Compound FR-900848 (**2**) with its fatty acid side-chain containing a total of five cyclopropyl units, four of which are contiguous, showed activity against filamentous fungi which was not immediately related to the peculiar fatty acid moiety. The discovery of the amide U-106308 (**3**) with five contiguous cyclopropyl rings in the fatty acid side-chain, which proved to be a good cholesteryl ester transfer protein inhibitor, showed that these oligocyclopropyl chains were much more than ‘‘accidents of nature’’. In the meantime, the absolute configuration of **2**[7] and the total syntheses of **2** and **3**[8] have been reported.

In order to be able to study the minimal structure requirements for biological activities of oligocyclopropyl fatty acids, we have set out to prepare fatty acids **9** with bicyclopropyl end groups. In addition, ω-bicyclopropylidenyl-sub-



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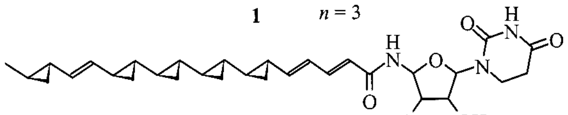

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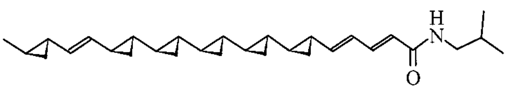

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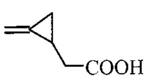

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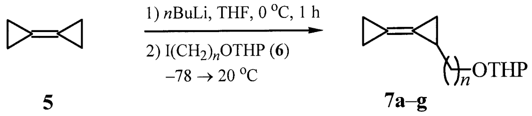
stituted fatty acids **11** and their *N*-isopropyl amides **12** appeared to be interesting targets for synthesis, since (methylenecyclopropyl)acetic acid (**4**) had been shown to be formed by enzymatic degradation of hypoglycine A and to play the essential role in the strong hypoglycemic effect revealed by the latter.[9]

Results and Discussion

Bicyclopropylidene (**5**), a unique tetrasubstituted alkene and a versatile C_6 building block,[10] has been shown to be a suitable precursor for a variety of functionally monosubstituted bicyclopropylidenes. The latter, which could easily be prepared directly in moderate to excellent yields by deprotonation of **5** with *n*-butyllithium in THF at 0 °C, followed by electrophilic substitution with appropriate reagents.[11] Substitution of lithiobicyclopropylidene with THP-protected ω-iodoalkanols **6** should thus yield THP-protected bicyclopropylidenylalkanols as potential precursors to fatty acids **9** with bicyclopropyl end groups. Indeed, alkylation of lithiobicyclopropylidene with THP-protected ω-iodoalkanols **6** was successful, but only with iodides **6** with $n \geq 3$ (Scheme 1, Table 1).

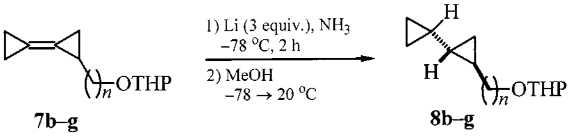


Scheme 1. For details see Table 1

Table 1. THP-protected bicyclopropylidenylalkanols **7** from bicyclopropylidene (**5**)

Iodide	*n*	Product	Yield (%)
6a	2	**7a**	0
6b	3	**7b**	63
6c	4	**7c**	85
6d	5	**7d**	82
6e	6	**7e**	88
6f	7	**7f**	68
6g	8	**7g**	65

The *trans*-diastereoselective reduction of the double bond in bicyclopropylidene derivatives **7** was apparently the central problem in our synthetic strategy to attain *trans*-bicyclopropyl-terminated fatty acids **9**. *cis*-Bicyclopropylalkanes could be prepared from alkylbicyclopropylidenes by catalytic hydrogenation with palladium on $BaSO_4$ (Lindlar catalyst), albeit in moderate yields (40−45%),[12] and this could also be applied to bicyclopropylidenylalkanols.[13] With dissolved lithium in ammonia or primary amines (Birch[14a] or Benkeser conditions[14b]), bicyclopropylidenylalkanes[15] and -alkanol derivatives **7** were found to yield *cis*- and *trans*-bicyclopropylalkanes[15] and -alkanol derivatives **8** quantitatively in most cases, and the stereoselectivity of these reductions was strongly dependent on the solvent and on the temperature.[15] For example, reduction of **7c** and **7e** with lithium in ethylamine afforded the desired bicyclopropyl derivatives **8c** and **8e** each in 72% yield but only as 1:2 mixtures of *cis* and *trans* isomers. However, the reduction of *n*-butylbicyclopropylidene was found to be highly *trans*-diastereoselective in liquid ammonia at −78 °C.[16] Using this protocol, the THP-protected bicyclopropylidenylalkanols **7b−g** were reduced to the *trans*-bicyclopropyl derivatives **8b−g** in 63−88% yield and with stereoselectivities of ≥ 95% (Scheme 2 and Table 2).



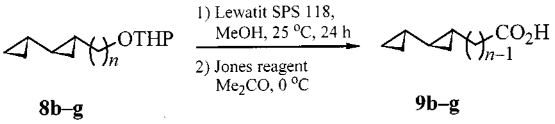
Scheme 2. For details see Table 2

Table 2. ω-[(1'',1'''-Bicycloprop-2''-yl)alkoxy]tetrahydropyrans **8** from THP-protected bicyclopropylidenylalkanols **7**

Entry	Starting material	*n*	Conditions[a]	Product	Yield (%)	d.r.[b] (*cis*/*trans*)
1	**7b**	3	B	**8b**	63	1:19
2	**7c**	4	A	**8c**	72	1:2
3	**7c**	4	B	**8c**	88	1:19
4	**7d**	5	B	**8d**	82	1:19
5	**7e**	6	A	**8e**	72	1:2
6	**7e**	6	B	**8e**	87	1:19
7	**7f**	7	B	**8f**	67	1:19
8	**7g**	8	B	**8g**	75	1:19

[a] A: 1) Li (3 equiv.), $EtNH_2$, −78 °C, 2 h, 2) MeOH, −78 → 20 °C; B: 1) Li (3 equiv.), NH_3, −78 °C, 2 h, 2) MeOH, −78 → 20 °C. − [b] Proved by GC.

The ω-(*trans*-bicyclopropyl)alkanol derivatives **8b−g** were deprotected under mild conditions (Lewatit SPS118, methanol), and the resulting alcohols (without further purification) were subsequently oxidized with Jones reagent to give the corresponding ω-(*trans*-bicyclopropyl)-substituted fatty acids **9b−g** in 59−75% yield over the two steps (Scheme 3, Table 3).

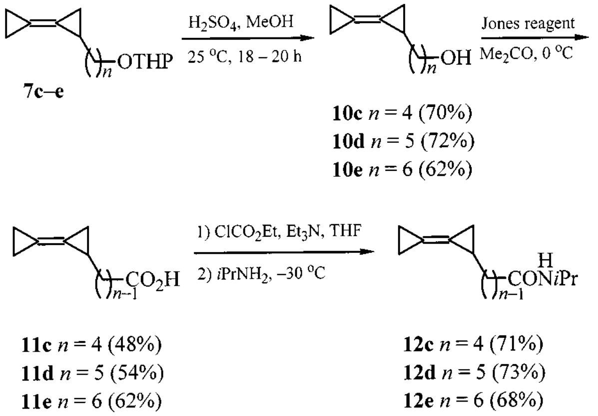


Scheme 3. For details see Table 3

Table 3. ω-(1',1''-Bicycloprop-2'-yl)alkanoic acids **9** from ω-[(1',1''-bicycloprop-2''-yl)alkoxy]tetrahydropyrans **8**

Starting material	*n*	Product	Yield (%)
8b	3	**9b**	62
8c	4	**9c**	72
8d	5	**9d**	75
8e	6	**9e**	67
8f	7	**9f**	59
8g	8	**9g**	69

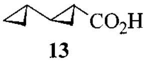
In view of the known biological activity of (methylenecyclopropyl)acetic acid (**4**),[9] the facile access to the THP-protected bicyclopropylidenylalkanols **7c−e** makes them ideal reagents in the syntheses of ω-bicyclopropylidenyl-substituted fatty acids **11** and their *N*-isopropyl amides **12**. Deprotection of compounds **7c−e** gave the ω-bicyclopropylidenylalkanols **10c−e** (62−72%). Subsequent Jones oxidation lead to the ω-bicyclopropylidenylalkanoic acids **11** (48−62%), which were transformed into the *N*-isopropyl-substituted amides (68−73% yield)[17] via mixed anhydrides generated by treatment with ethyl chloroformate and triethylamine[18] (Scheme 4).



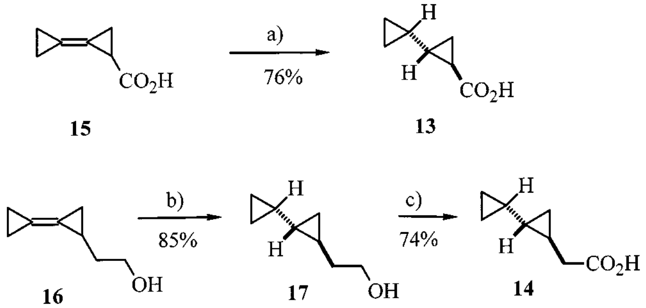
Scheme 4. Syntheses of ω-(1′,1′′-bicyclopropyliden-2′-yl)alkanoic acids **11c−e** and *N*-isopropyl-substituted ω-(1′,1′′-bicyclopropyliden-2′′-yl)alkanamides **12c−e**

In order to learn at least something about the biological degradability of ω-bicyclopropyl-substituted fatty acids of type **9** by microorganisms, bacterial enrichment cultures from soil samples were grown on media containing ω-bicyclopropyl-substituted fatty acids **9b−e** as an additional carbon source. Chemical workup of these cultures and isolation of the degradation products revealed that these cultures only degraded the side-chains of compounds **9b−e** by the usual β-oxidation pathway[4,19] to yield either *trans*-2-bicyclopropanecarboxylic acid (**13**) from **9b,d** with odd-numbered or *trans*-2-bicyclopropylacetic acid (**14**) from **9c**,**e** with even-numbered carbon side-chains (Table 4). Thus, the bicyclopropyl groups in the starting materials were left untouched in all cases.

Table 4. Degradation products of ω-bicyclopropyl-substituted fatty acids **9b−e** formed by microbial enrichment cultures

Starting Material	Chain Length in Starting Material	Product
9b,d	odd-numbered	 **13**
9c,e	even-numbered	 **14**

An authentic sample of *trans*-2-bicyclopropanecarboxylic acid[20] (**13**) was obtained in 76% yield by the reduction of the bicyclopropylidenecarboxylic acid[11] (**15**) using lithium (4 equiv.) in liquid ammonia at −78 °C (Scheme 5). The 2-[*trans*-(1′,1′′-bicycloprop-2′-yl)]acetic acid (**14**) was easily available from 2-(1′,1′′-bicyclopropyliden-2′-yl)ethanol (**16**) which had previously been prepared by the reaction of lithiobicyclopropylidene with ethylene oxide.[21] Subsequent reduction of **16** under the same Birch conditions applied to **7b−g** gave the corresponding 2-(1′,1′′-bicycloprop-2′-yl)ethanol (**17**) in 85% yield, but only with 85% *trans* diastereoselectivity. Finally, Jones oxidation of **17** gave 2-[*trans*-(1′,1′′-bicycloprop-2′-yl)]acetic acid (**14**) in 74% yield (Scheme 5).



Scheme 5. Syntheses of *trans*-bicyclopropanecarboxylic acid (**13**) and 2-[*trans*-(1′,1′′-bicycloprop-2′-yl)]acetic acid (**14**); a) 1) Li (4 equiv.), NH_3, −78 °C, 2 h, 2) MeOH, −78 → 20 °C, 3) 2 N HCl; b) 1) Li (4 equiv.), NH_3, −78 °C, 2 h, 2) MeOH, −78 → 20 °C, c) Jones reagent, Me_2CO, 0 °C

Further experiments with a variety of bacteria strains[22] showed that at least one strain of the genus *Rhodococcus*, *Rhodococcus ruber* P-IV-B-11,[23] was able to grow on media containing acids **9b**,**c** or **13** as one or even the sole carbon source, and to completely degrade them. The fact that in no case could any distinct degradation product be detected, suggested that the *Rhodococcus* species had actually used the acids as a carbon source for growth. However, in order to obtain reliable information about the metabolic pathway, it will be essential to carry out further investigations with ^{13}C-labelled substrates of type **9**.

In order to examine the minimum structural requirements for the antibiotic activities of oligocyclopropyl fatty acids, the antimicrobial spectrum of **9b**,**c** and **13** was determined as shown in Table 5.

The acids **9b** and **9c** have a specific activity in the range of 5 to 50 mM against the tested Gram-positive bacteria *Bacillus subtilis* and *Rhodococcus ruber*, against the tested yeasts *Kluyveromyces marxianum* and *Saccharomyces cerevisiae* as well as the filamentous fungi *Aspergillus nidulans* and *Aspergillus niger*. No growth inhibitory property could be observed against Gram-negative bacteria like *E.coli* and *Pseudomonas* sp. The acid **13** hardly showed any antibiotic activity against any of the tested organisms. The result that the acids **9b** and **9c** exhibit growth inhibitory activity against filamentous fungi could already be observed in enrichment experiments, in which after inoculation with soil samples no growth of fungi appeared in cultures containing **9b** or **9c** (data not shown in Table 4). Finally, it is noteworthy that ω-bicyclopropyl-substituted fatty acids **9** as reported here, were used as side-chains for unprecedented types of liquid crystalline compounds.[13]

Table 5. Antimicrobial spectrum of ω-bicyclopropyl-substituted fatty acids **9b**,**c** and **13**

Test organisms	Group	**13** MIC[a] [mM]	**9b** MIC [mM]	**9c** MIC [mM]
E. coli K12	Gram-negative bacteria	–[b]	–	–
Pseudomonas sp.	Gram-negative bacteria	–	–	–
Bacillus subtilis	Gram-positive bacteria	–	10	20
Rhodococcus ruber	Gram-positive bacteria	–	20	50
Kluyveromyce marxianium	Yeast	5	50	50
Saccharomyces cerevisiae	Yeast	–	50	20
Aspergillus nidulans	Filamentous fungi	–	50	10
Asperigillus niger	Filamentous fungi	–	5	5

[a] MIC = minimum inhibitory concentration. − [b] – = not inhibitory.

Experimental Section

General: ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker AM 250 spectrometer (250 MHz for ^{1}H, 62.9 MHz for ^{13}C) at ambient temperature in $CDCl_3$ using $CHCl_3$ ($\delta = 7.26$) and $CDCl_3$ ($\delta = 77.0$) as internal standards. Chemical shifts (δ) are quoted in ppm and coupling constants (J) in Hertz to the nearest 0.1 Hz. The following abbreviations are used: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet) and br. (broad). Multiplicities of ^{13}C NMR signals were determined by the DEPT sequence and are reported as follows: + for CH or CH_3, − for CH_2, and C_{quat} for C. For signals which could not be assigned unambiguously, all atoms concerned are marked with an asterisk (*). − IR spectra were recorded with a Bruker FT-IR spectrometer IFS 66. − Mass spectra were recorded using electron impact ionization at 70 eV or direct chemical ionization with NH_3 as the reactant gas. High-resolution mass data (HRMS) were obtained with a Varian MAT 311 using preselected ion peak matching at $R \approx 10000$ to be within ±2 ppm. − Elemental analyses were performed by the Mikroanalytisches Labor des Instituts für Organische Chemie der Universität Göttingen, Germany. − All solvents were distilled before use (DE = diethyl ether. The light petroleum (petroleum ether, PE) used for the chromatographic elution was the fraction boiling between 35 and 65 °C. − Chromatography: Merck silica gel 60 (230−400 mesh). Whenever necessary, the stationary phase was deactivated with 3% NEt_3, and the eluents contained 3% NEt_3. − Unless otherwise specified, solutions of NH_4Cl, $NaHCO_3$ and NaCl were saturated aqueous solutions. − Starting materials: Compounds **6b**,[24] **6c**,[25] **6d**,[26] **6e**,[27] **6f**[24] and **6g**[28] were prepared according to published procedures. The strongly acidic ion exchange resin Lewatit SPS118 was kindly provided by the Bayer AG. All other chemicals were used as commercially available.

General Procedure for the Preparation of THP-Protected Bicyclopropylidenylalkanols 7 (GP 1): To a solution of *n*-butyllithium (12.5 mmol) in THF (25.0 mL, 0.500 M) was added bicyclopropylidene (**5**) (12.5 mmol) at −30 °C. The solution was stirred at 0 °C for an additional 1 h. A solution of the respective iodide **6b−g** (12.4 mmol) in THF (5−20 mL) was then added at −78 °C. After stirring at 0 °C for 1 h, the solution was warmed to room temperature. The mixture was poured into a suspension of H_2O/Et_2O (1:3). The aqueous phase was extracted with Et_2O (3 × 30 mL), the combined organic phases were washed with brine (60 mL), dried with $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by column chromatography on deactivated silica gel.

General Procedure for the Preparation of 2-[ω-(1′,1′′-Bicycloprop-2′-yl)alkoxy]tetrahydro-2*H*-pyran (8) (GP 2): To a blue solution of lithium (15.0 mmol, 3 equiv.) in liquid ammonia (50 mL), was added a mixture of the respective THP-protected bicyclopropylidenylalkanol **7b−g** (5.00 mmol) in THF (10 mL) over 1 h at −78 °C. The reaction mixture was stirred at −78 °C for 2−4 h. A mixture of methanol (5 mL) and Et_2O (20 mL) was then added at −78 °C, and the ammonia was evaporated at room temperature overnight. The residue was dissolved in H_2O (20 mL) at 5 °C. The aqueous layer was extracted with Et_2O (3 × 20 mL), the combined organic phases were washed with brine (20 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel.

General Procedure for the Preparation of ω-(1′,1′′-Bicycloprop-2′-yl)alkanoic Acids 9 (GP 3): To a solution of the respective 2-[ω-(1′,1′′-bicycloprop-2′-yl)alkoxy]tetrahydro-2*H*-pyran **8b−g** (5.00 mmol) in methanol (15 mL) was added the strongly acidic ion exchange resin Lewatit SPS118 (0.10 g). The mixture was stirred at room temperature for 24 h. After filtration, the solvent was removed under reduced pressure and acetone (30 mL) was added to the residue. After having cooled the solution to 0 °C, Jones reagent (ca. 1.7 mL, 3 M) was added. The addition was continued until the characteristic orange color of the reagent persisted for about 15 min. After stirring at 0 °C for 3−5 h, *i*PrOH (5 mL) was added. The aqueous layer was extracted with Et_2O (5 × 20 mL), the combined organic phases were washed with brine (30 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.

General Procedure for the Preparation of ω-(1′,1′′-Bicyclopropyliden-2′-yl)alkanols 10 (GP 4): To a solution of the respective THP-protected compound **7c−e** (8.00 mmol) in methanol (45 mL) were added a few drops of conc. sulfuric acid, and the solution was stirred at room temperature for 18−20 h. To the mixture was added a solution of $NaHCO_3$ (2 mL). The aqueous layer was extracted with Et_2O (3 × 40 mL) and the combined organic phases were dried with $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel.

General Procedure for the Preparation of ω-(1′,1′′-Bicyclopropyliden-2′-yl)alkanoic Acids 11 (GP 5): To a solution of the respective ω-(1′,1′′-bicyclopropyliden-2′-yl)alkanol **10c−e** (0.540 mmol) in acetone (20 mL), was added Jones reagent (ca. 180 µL, 3 M) at 0 °C. The addition was continued until the characteristic orange color of the reagent persisted for about 15 min. After stirring at 0 °C for 1 h, a mixture of *i*PrOH and H_2O (5 mL: 10 mL) was added. The aqueous layer was extracted with Et_2O (5 × 15 mL), the combined organic phase was washed with brine (25 mL), dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.

General Procedure for the Preparation of ω-(1′,1′′-Bicyclopropyliden-2′-yl)-*N*-isopropylalkanamides 12 (GP 6): To a solution of the respective ω-(1′,1′′-bicyclopropyliden-2′-yl)alkanoic acid **11c−e** (3.0 mmol) in THF (15 mL) was added at −20 °C NEt_3 (4.5 mmol, 1.5 equiv.), and the solution was stirred for 15 min $ClCO_2Et$ (3.6 mmol, 1.2 equiv.) was then added at this temp., and the mixture was stirred for an additional 30 min. Subsequently, *i*PrNH_2 (3.3 mmol, 1.1 equiv.) was added, and the mixture was stirred at 0 °C for 1 h. The mixture was poured into $NaHCO_3$ (0.5 N, 15 mL), and the aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic phase was washed with Na_2CO_3 solution (2 × 15 mL), HCl (2 N, 2 × 15 mL), Na_2CO_3 solution (2 × 15 mL), NaCl solution (20 mL), and then dried with $MgSO_4$. The solvent was evaporated under reduced pressure, and the residue purified by filtration on silica gel.

2-[3′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)propyloxy]tetrahydro-2*H*-pyran (7b): According to GP 1, bicyclopropylidene (**5**) (1.00 g, 12.5 mmol) was treated with *n*-butyllithium (7.70 mL, 12.3 mmol, 1.60 M in hexane) in THF (25 mL) and 2-(3′-iodopropyloxy)tetrahydro-2*H*-pyran (**6b**) (3.34 g, 12.4 mmol). Chromatography on deactivated silica gel (120 g, column 2 × 30 cm, PE/DE = 15:1, R_f = 0.61) gave 1.74 g (63%) of **7b** as a colorless oil. − IR (film): ν = 3042 cm^{-1} (*c*Pr−H), 2940, 2859, 1121 (CH−O), 1077 (CH_2−O), 1033 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.85−0.95 (m, 1 H, *c*Pr−H), 1.15−1.30 (m, 2 H, *c*Pr−H), 1.30−1.95 (m, 14 H, THP−H, 2′,3′-H, *c*Pr−H), 3.35−3.48 (m, 1 H, 1′-H), 3.48−3.55 (m, 1 H, THP−H), 3.65−3.80 (m, 1 H, 1′-H), 3.80−3.90 (m, 1 H, THP−H), 4.65 (t, *J* = 3.6 Hz, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.7 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.7 (−, *c*Pr−C), 16.0 (+, *c*Pr−C), 19.6 (−, THP−C), 25.4 (−, THP−C), 29.3 (−, C-3′*), 30.7 (−, C-2′*), 33.5 (−, THP−C), 62.2 (−, C-1′), 66.9 (−, C-6), 98.8 (+, C-2), 110.0 (C_{quat}, *c*Pr−C), 116.0 (C_{quat}, *c*Pr−C).

2-[4′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)butoxy]tetrahydro-2*H*-pyran (7c): According to GP 1, bicyclopropylidene (**5**) (2.00 g, 25.0 mmol) was treated with *n*-butyllithium (15.4 mL, 24.7 mmol, 1.60 M in hexane) in THF (50 mL) and 2-(4′-iodobutoxy)tetrahydro-2*H*-pyran (**6c**) (7.10 g, 25.0 mmol). Chromatography on deactivated silica gel (300 g, column 3 × 45 cm, PE/DE = 15:1, R_f = 0.57) gave 4.95 g (85%) of **7c** as a colorless oil. − IR (film): ν = 3048 cm^{-1} (*c*Pr−H), 2938, 2868, 1120 (CH−O), 1078 (CH_2−O), 1034 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.80−0.90 (m, 1 H, *c*Pr−H), 1.10−1.20 (m, 2 H, *c*Pr−H), 1.20−1.96 (m, 16 H, THP−H, 2′,3′,4′-H, *c*Pr−H), 3.40−3.45 (m, 1 H, 1′-H), 3.45−3.55 (m, 1 H, THP−H), 3.75−3.85 (m, 1 H, 1′-H), 3.85−3.95 (m, 1 H, THP−H), 4.60 (t, *J* = 3.5 Hz, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.7 (−, *c*Pr−C), 16.0 (+, *c*Pr−C), 19.6 (−, THP−C), 25.5 (−, THP−C), 26.2 (−, C-4′*), 29.4 (−, C-3′*), 30.7 (−, C-2′*), 33.0 (−, THP−C), 62.2 (−, C-1′), 67.5 (−, C-6), 98.7 (+, C-2), 109.5 (C_{quat}, *c*Pr−C), 116.0 (C_{quat}, *c*Pr−C). − DCI-MS (200 eV, NH_3), *m/z* (%): 254 (62) [M + NH_4^+], 153 (5), 119 (38) [$C_5H_9O_2$ + NH_4^+], 102 (100) [C_5H_8O + NH_4^+]. − $C_{15}H_{24}O_2$ (236.4): calcd. C 76.23, H 10.23; found C 76.42, H 10.10.

2-[5′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)pentyloxy]tetrahydro-2*H*-pyran (7d): According to GP 1, bicyclopropylidene (**5**) (2.00 g, 25.0 mmol) was treated with *n*-butyllithium (15.4 mL, 24.7 mmol, 1.60 M in hexane) in THF (50 mL) and 2-(5′-iodopentyloxy)tetrahydro-2*H*-pyran (**6d**) (7.36 g, 24.7 mmol). Chromatography on deactivated silica gel (340 g, column 5 × 35 cm, PE/DE = 15:1, R_f = 0.54) gave 5.06 g (82%) of **7d** as a colorless oil. − IR (film): ν = 3049 cm^{-1} (*c*Pr−H), 2927, 2855, 1184 (CH−O), 1079 (CH_2−O), 1035 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.80−0.90 (m, 1 H, *c*Pr−H), 1.10−1.20 (m, 2 H, *c*Pr−H), 1.20−1.95 (m, 18 H, THP−H, 2′,3′,4′,5′-H, *c*Pr−H), 3.32−3.46 (m, 1 H, 1′-H), 3.46−3.52 (m, 1 H, THP−H), 3.68−3.72 (m, 1 H, 1′-H), 3.72−3.95 (m, 1 H, THP−H), 4.60 (t, *J* = 3.5 Hz, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 16.0 (+, *c*Pr−C), 19.6 (−, THP−C), 25.4 (−, THP−C), 25.9 (−, C-5′*), 26.2 (−, C-4′*), 28.4 (−, C-3′*), 30.7 (−, C-2′*), 33.1 (−, THP−C), 62.3 (−, C-1′), 67.6 (−, C-6), 98.8 (+, C-2), 109.4 (C_{quat}, *c*Pr−C), 116.1 (C_{quat}, *c*Pr−C). − DCI-MS (200 eV, NH_3), *m/z* (%): 268 (98) [M + NH_4^+], 246 (38), 216 (8), 184 (8), 119 (48) [$C_5H_9O_2$ + NH_4^+], 102 (100) [C_5H_8O + NH_4^+]. − $C_{16}H_{26}O_2$ (250.4): calcd. C 76.75, H 10.47; found C 76.56, H 10.57.

2-[6′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)hexyloxy]tetrahydro-2*H*-pyran (7e): According to GP 1, bicyclopropylidene (**5**) (4.00 g, 49.9 mmol) was treated with *n*-butyllithium (30.9 mL, 49.4 mmol, 1.60 M in hexane) in THF (100 mL) and 2-(6′-iodohexyloxy)tetrahydro-2*H*-pyran (**6e**) (15.4 g, 49.3 mmol). Chromatography on deactivated silica gel (650 g, column 5 × 80 cm, PE/DE = 15:1, R_f = 0.64) gave 11.47 g (88%) of **7e** as a colorless oil. − IR (film): ν = 3051 cm^{-1} (*c*Pr−H), 2925, 2854, 1121 (CH−O), 1078 (CH_2−O), 1034 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.80−0.90 (m, 1 H, *c*Pr−H), 1.10−1.20 (m, 2 H, *c*Pr−H), 1.20−1.95 (m, 20 H, THP−H, 2′,3′,4′,5′,6′-H, *c*Pr−H), 3.32−3.40 (m, 1 H, 1′-H), 3.40−3.55 (m, 1 H, THP−H), 3.60−3.75 (m, 1 H, 1′-H), 3.75−3.95 (m, 1 H, THP−H), 4.60 (t, ^3J = 3.5 Hz, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 16.1 (+, *c*Pr−C), 19.7 (−, THP−C), 25.5 (−, THP−C), 29.3 (−, C-6′*), 29.5, 29.4 (−, C-5′*), 29.6 (−, C-4′*), 29.7 (−, C-3′*), 31.8 (−, C-2′*), 33.2 (−, THP−C), 62.3 (−, C-1′), 67.6 (−, C-6), 98.8 (+, C-2), 109.4 (C_{quat}, *c*Pr−C), 116.2 (C_{quat}, *c*Pr−C). − DCI-MS (200 eV, NH_3); *m/z* (%): 282 (33) [M + NH_4^+], 226 (8), 119 (30) [$C_5H_9O_2$ + NH_4^+], 102 (100) [C_5H_8O + NH_4^+]. − $C_{17}H_{28}O_2$ (264.4): calcd. C 77.22, H 10.67; found C 77.55, H 10.61.

2-[7′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)heptyloxy]tetrahydro-2*H*-pyran (7f): According to GP 1, bicyclopropylidene (**5**) (2.00 g, 25.0 mmol) was treated with *n*-butyllithium (16.0 mL, 24.7 mmol, 1.54 M in hexane) in THF (50 mL) and 2-(7′-iodoheptyloxy)tetrahydro-2*H*-pyran (**6f**) (8.06 g, 24.7 mmol). Chromatography on deactivated silica gel (360 g, column 5 × 40 cm, PE/DE = 15:1, R_f = 0.60) gave 4.71 g (68%) of **7f** as a colorless oil. − IR (film): ν = 3050 cm^{-1} (*c*Pr−H), 2925, 2854, 1121 (CH−O), 1079 (CH_2−O), 1034 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.80−0.90 (m, 1 H, *c*Pr−H), 1.10−1.20 (m, 2 H, *c*Pr−H), 1.20−1.95 (m, 22 H, THP−H, 2′,3′,4′,5′,6′,7′-H, *c*Pr−H), 3.37 (dt, ^2J = 13.2, *J* = 6.8 Hz, 1 H, 1′-H), 3.44−3.53 (m, 1 H, THP−H), 3.73 (dt, ^2J = 13.2, *J* = 6.8 Hz, 1 H, 1′-H), 3.81−3.90 (m, 1 H, THP−H), 4.60 (t, *J* = 3.8 Hz, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 14.1, 16.1 (+, *c*Pr−C), 19.7 (−, THP−C), 22.6 (−, C-7′*), 25.6 (−, THP−C), 29.4 (−, C-6′*), 29.6 (−, C-5′*), 29.7 (−, C-4′*), 30.7 (−, C-3′*), 31.9 (−, C-2′*), 33.2 (−, THP−C), 62.3 (−, C-1′), 67.6 (−, C-6), 98.8 (+, C-2), 109.4 (C_{quat}, *c*Pr−C), 116.2 (C_{quat}, *c*Pr−C). − DCI-MS (200 eV, NH_3); *m/z* (%): 296 (62)

$[M + NH_4^+]$, 274 (11), 251 (5), 218 (8), 182 (5) $[M - C_6H_{10}O_2 + NH_4^+]$, 119 (28) $[C_5H_9O_2 + NH_4^+]$, 102 (100) $[C_5H_8O + NH_4^+]$. − $C_{18}H_{30}O_2$ (278.4): calcd. C 77.65, H 10.86; found C 77.40, H 10.88.

2-[8′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)octyloxy]tetrahydro-2*H*-pyran (7g): According to GP 1, bicyclopropylidene (**5**) (3.00 g, 37.4 mmol) was treated with *n*-butyllithium (24.1 mL, 37.1 mmol, 1.54 M in hexane) in THF (80 mL) and 2-(8′-iodoctyloxy)tetrahydro-2*H*-pyran (**6g**) (12.6 g, 37.0 mmol). Chromatography on deactivated silica gel (600 g, column 5 × 70 cm, PE/DE = 10:1, R_f = 0.54) gave 7.04 g (65%) of **7g** as a colorless oil. − IR (film): ν = 3051 cm^{-1} (*c*Pr−H), 2926, 2854, 1137 (CH−O), 1078 (CH_2−O), 1033 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.80−0.90 (m, 1 H, *c*Pr−H), 1.10−1.20 (m, 2 H, *c*Pr−H), 1.20−1.95 (m, 24 H, THP−H, 2′,3′,4′,5′,6′,7′,8′-H, *c*Pr−H), 3.41 (dt, ^2J = 13.6, *J* = 7.0 Hz, 1 H, 1′-H), 3.48−3.55 (m, 1 H, 6−H), 3.71 (dt, ^2J = 13.6, *J* = 7.0 Hz 1 H, 1′-H), 3.85−3.93 (m, 1 H, 6-H), 4.57 (t, *J* = 3.5 Hz, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 14.1, 16.1 (+, *c*Pr−C), 19.7 (−, THP−C), 22.7 (−, C-8′*), 26.2 (−, THP−C), 29.3 (−, C-7′*), 29.5 (−, C-6′*), 29.5 (−, C-5′*), 29.7 (−, C-4′*), 30.7 (−, C-3′*), 31.9 (−, C-2′*), 33.2 (−, THP−C), 62.3 (−, C-1′), 67.7 (−, C-6), 98.8 (+, C-2), 109.4 (C_{quat}, *c*Pr−C), 116.3 (C_{quat}, *c*Pr−C). − DCI-MS (200 eV, NH_3), *m/z* (%): 310 (80) $[M + NH_4^+]$, 288 (6), 232 (4), 135 (5), 119 (38) $[C_5H_9O_2 + NH_4^+]$, 102 (100) $[C_5H_8O + NH_4^+]$.

2-[3′-(1′′,1′′′-Bicycloprop-2′′-yl)propyloxy]tetrahydro-2*H*-pyran (8b): 2-[3′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)propyloxy]tetrahydro-2*H*-pyran (**7b**) (1.50 g, 6.75 mmol) in THF (20 mL) was treated with lithium (0.140 g, 20.2 mmol) in ammonia (250 mL) according to GP 2. After column chromatography on silica gel (150 g, column 3 × 34 cm, PE/DE = 8:1, R_f = 0.67), 0.954 g (63%) of **8b** (colorless oil) was obtained as a 95:5 *trans/cis* isomeric mixture, proved by GC. − IR (film): ν = 3079 cm^{-1} (*c*Pr−H), 2987, 2925, 2847, 1065 (CH−O), 1030 (CH_2−O), 1001 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.05−0.15 (m, 1 H, *c*Pr−H), 0.15−0.25 (m, 1 H, *c*Pr−H), 0.25−0.35 (m, 1 H, *c*Pr−H), 0.36−0.50 (m, 2 H, *c*Pr−H), 0.52−1.00 (m, 2 H, *c*Pr−H), 1.05−1.40 (m, 2 H, *c*Pr−H), 1.41−1.85 (m, 10 H, THP−H, 1′,2′-H), 3.35−3.40 (m, 1 H, 3′-H), 3.40−3.60 (m, 1 H, 6-H), 3.65−3.78 (m, 1 H, 3′-H), 3.78−3.85 (m, 1 H, 6-H), 4.60 (t, *J* = 7.3 Hz, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.8 (−, *c*Pr−C), 3.0 (−, *c*Pr−C), 9.9 (−, *c*Pr−C), 12.2 (+, *c*Pr−C), 16.5 (+, *c*Pr−C), 19.7 (−, THP−C), 20.5 (+, *c*Pr−C), 25.5 (−, THP−C), 29.3 (−, C-1′*), 30.7 (−, C-2′*), 30.8 (−, THP−C), 62.3 (−, C-3′**), 67.3 (−, C-6**), 98.8 (+, C-2). − DCI-MS (200 eV, NH_3); *m/z* (%): 242 (50) $[M + NH_4^+]$, 203 (5), 186 (18), 169 (24), 119 (25) $[C_5H_9O_2 + NH_4^+]$, 102 (100) $[C_5H_8O + NH_4^+]$.

2-[4′-(1′′,1′′′-Bicycloprop-2′′-yl)butoxy]tetrahydro-2*H*-pyran (8c): 2-[4′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)butoxy]tetrahydro-2*H*-pyran (**7c**) (6.81 g, 28.8 mmol) in THF (25 mL) was treated with lithium (0.599 g, 86.3 mmol) in ammonia (350 mL) according to GP 2. After column chromatography on silica gel (400 g, column 5 × 42 cm, PE/DE = 8:1, R_f = 0.60), 6.03 g (88%) of **8c** (colorless oil) was obtained as a 95:5 *trans/cis* isomeric mixture, proved by GC. − IR (film): ν = 3076 cm^{-1} (*c*Pr−H), 2937, 2870, 1124 (CH−O), 1079 (CH_2−O), 1035 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = −0.05 to +0.55 (m, 4 H, *c*Pr−H), 0.60−0.98 (m, 3 H, *c*Pr−H), 1.05−1.90 (m, 14 H, *c*Pr−H, THP−H, 1′,2′,3′-H), 3.38−3.42 (m, 1 H, 4′-H), 3.42−3.50 (m, 1 H, 6-H), 3.65−3.78 (m, 1 H, 4′-H), 3.78−3.85 (m, 1 H, 6-H), 4.52−4.60 (m, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 12.2 (+, *c*Pr−C), 16.0 (+, *c*Pr−C), 19.6 (−, THP−C), 20.3 (+, *c*Pr−C), 25.4 (−, THP−C), 29.2, 29.3 (−, C-1′*), 29.4, 29.5 (−, C-2′*), 30.0, 30.2 (−, C-3′*), 33.5 (−, THP−C), 62.3 (−, C-4′**), 67.6, 67.7 (−, C-6**), 98.8 (+, C-2). − DCI-MS (200 eV, NH_3); *m/z* (%): 256 (17) $[M + NH_4^+]$, 232 (4), 214 (2), 176 (3), 135 (8), 119 (23) $[C_5H_9O_2 + NH_4^+]$, 102 (100) $[C_5H_8O + NH_4^+]$. − $C_{15}H_{26}O_2$ (238.4): calcd. C 75.58, H 10.99; found C 75.48, H 11.20.

2-[5′-(1′′,1′′′-Bicycloprop-2′′-yl)pentyloxy]tetrahydro-2*H*-pyran (8d): 2-[5′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)pentyloxy]tetrahydro-2*H*-pyran (**7d**) (3.83 g, 15.3 mmol) in THF (15 mL) was treated with lithium (0.319 g, 46.0 mmol) in ammonia (250 mL) according to GP 2. After column chromatography on silica gel (230 g, column 4.5 × 25 cm, PE/DE = 10:1, R_f = 0.82), 3.16 g (82%) of **8d** (colorless oil) was obtained as a 95:5 *trans/cis* isomeric mixture, proved by GC. − IR (film): ν = 3070 cm^{-1} (*c*Pr−H), 2926, 2855, 1109 (CH−O), 1016 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = −0.02 to +0.65 (m, 4 H, *c*Pr−H), 0.68−1.10 (m, 3 H, *c*Pr−H), 1.15−1.90 (m, 16 H, *c*Pr−H, THP−H, 1′,2′,3′,4′-H), 3.32−3.42 (m, 1 H, 5′-H), 3.42−3.52 (m, 1 H, 6-H), 3.60−3.70 (m, 1 H, 5′-H), 3.70−3.92 (m, 1 H, 6-H), 4.52−4.60 (m, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.9 (−, *c*Pr−C), 3.0 (−, *c*Pr−C), 9.5 (−, *c*Pr−C), 12.2 (+, *c*Pr−C), 16.4 (+, *c*Pr−C), 19.7 (−, THP−C), 22.7 (−, THP−C), 25.4 (−, THP−C), 26.9 (−, C-1′*), 29.5 (−, C-2′*), 29.7 (−, C-3′*), 30.7 (−, C-4′*), 33.0 (−, THP−C), 62.2 (−, C-5′**), 67.6 (−, C-6**), 98.7 (+, C-2). $C_{16}H_{28}O_2$ (252.4): calcd. C 76.14, H 11.18; found C 75.99, H 11.06.

2-[6′-(1′′,1′′′-Bicycloprop-2′′-yl)hexyloxy]tetrahydro-2*H*-pyran (8e): 2-[6′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)hexyloxy]tetrahydro-2*H*-pyran (**7e**) (3.94 g, 14.9 mmol) in THF (25 mL) was treated with lithium (0.310 g, 44.7 mmol) in ammonia (300 mL) according to GP 2. After column chromatography on silica gel (220 g, column 4.5 × 25 cm, PE/DE = 15:1, R_f = 0.53), 3.44 g (87%) of **8e** (colorless oil) was obtained as a 95:5 *trans/cis* isomeric mixture, proved by GC. − IR (film): ν = 3077 cm^{-1} (*c*Pr−H), 2925, 2853, 1121 (CH−O), 1079 (CH_2−O), 1034 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = −0.02 to +0.60 (m, 4 H, *c*Pr−H), 0.60−1.00 (m, 3 H, *c*Pr−H), 1.00−1.95 (m, 18 H, *c*Pr−H, THP−H, 1′,2′,3′,4′,5′-H), 3.38−3.45 (m, 1 H, 6′-H), 3.45−3.52 (m, 1 H, 6-H), 3.68−3.77 (m, 1 H, 6′-H), 3.77−3.85 (m, 1 H, 6-H), 4.52−4.60 (m, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.5 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.8 (−, *c*Pr−C), 12.3 (+, *c*Pr−C), 16.7 (+, *c*Pr−C), 19.7 (−, THP−C), 20.4 (+, *c*Pr−C), 25.5 (−, THP−C), 26.9 (−, C-1′*), 29.5 (−, C-2′*), 29.6 (−, C-3′*), 29.7 (−, C-4′*), 30.8 (−, C-5′*), 34.1 (−, THP−C), 62.3 (−, C-6′**), 67.7 (−, C-6**), 98.8 (+, C-2). − DCI-MS (200 eV, NH_3), *m/z* (%): 284 (16) $[M + NH_4^+]$ 260 (4), 232 (13), 204 (19), 164 (2), 119 (15) $[C_5H_9O_2 + NH_4^+]$, 102 (100) $[C_5H_8O + NH_4^+]$. − $C_{17}H_{30}O_2$ (266.4): calcd. C 76.64, H 11.35; found C 76.60, H 11.00.

2-[7′-(1′′,1′′′-Bicycloprop-2′′-yl)heptyloxy]tetrahydro-2*H*-pyran (8f): 2-[7′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)heptyloxy]tetrahydro-2*H*-pyran (**7f**) (4.01 g, 14.4 mmol) in THF (30 mL) was treated with lithium (0.299 g, 43.1 mmol) in ammonia (220 mL) according to GP 2. After column chromatography on silica gel (240 g, column 4.5 × 30 cm, PE/DE = 15:1, R_f = 0.48), 2.71 g (67%) of **8f** (colorless oil) was obtained as a 95:5 *trans/cis* isomeric mixture, proved by GC. − IR (film): ν = 3060 cm^{-1} (*c*Pr−H), 2925, 2854, 1127 (CH−O), 1079 (CH_2−O), 1034 (CH_2−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = −0.02 to +0.60 (m, 4 H, *c*Pr−H), 0.60−1.00 (m, 3 H, *c*Pr−H), 1.00−1.95 (m, 20 H, *c*Pr−H, THP−H, 1′,2′,3′,4′,5′,6′-H), 3.32−3.45 (m, 1 H, 7′-H), 3.45−3.52 (m, 1 H, 6-H), 3.70−3.79 (m, 1 H, 7′-H), 3.79−3.92 (m, 1 H, 6-H), 4.52−4.60 (m, 1 H, 2-H).

− ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.7 (−, *c*Pr−C), 2.8 (−, *c*Pr−C), 9.8 (−, *c*Pr−C), 12.2 (+, *c*Pr−C), 16.7 (+, *c*Pr−C), 19.6 (−, THP−C), 20.3 (+, *c*Pr−C), 22.7 (−, C-1′*), 25.4 (−, THP−C), 26.2 (−, C-2′*), 29.3 (−, C-3′*), 29.5 (−, C-4′*), 29.7 (−, C-5′*), 31.9 (−, C-6′*), 34.0 (−, THP−C), 62.3 (−, C-7′**), 67.7 (−, C-6**), 98.8 (+, C-2). − DCI-MS (200 eV, NH_3), *m/z* (%): 298 (19) [M + NH_4^+], 274 (8), 208 (6), 158 (4), 119 (23) [$C_5H_9O_2$ + NH_4^+], 102 (100) [C_5H_8O + NH_4^+].

2-[8′-(1′′,1′′′-Bicycloprop-2′′-yl)octyloxy]tetrahydro-2*H*-pyran (8g): 2-[8′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)octyloxy]tetrahydro-2*H*-pyran (**7g**) (6.87 g, 23.5 mmol) in THF (30 mL) was treated with lithium (0.491 g, 70.7 mmol) in ammonia (300 mL) according to GP 2. After column chromatography on silica gel (400 g, column 5.0 × 42 cm, PE/DE = 15:1, R_f = 0.45), 1.21 g of **7g** and 5.18 g (75%) of **8g** (colorless oil) was obtained as a 95:5 *trans/cis* isomeric mixture, proved by GC. − IR (film): ν = 3056 cm^{-1}, 2925, 2853, 1121 (CH−O), 1079 (CH_2−O), 1034 (CH_2−O). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.02 to +0.60 (m, 4 H, *c*Pr−H), 0.60−1.00 (m, 3 H, *c*Pr−H), 1.02−1.98 (m, 22 H, *c*Pr−H, THP−H, 1′,2′,3′,4′,5′,6′,7′-H), 3.38−3.45 (m, 1 H, 8′-H), 3.45−3.52 (m, 1 H, 6H), 3.70−3.82 (m, 1 H, 8′-H), 3.82−3.90 (m, 1 H, 6-H), 4.52−4.60 (m, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.8 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.5 (−, *c*Pr−C), 12.3 (+, *c*Pr−C), 16.7 (+, *c*Pr−C), 19.7 (−, THP−C), 20.6 (−, C-1′*), 25.4 (−, THP−C), 26.5 (−, C-2′*), 28.7 (−, C-3′*), 29.3 (+, *c*Pr−C), 29.5 (−, C-4′*), 29.7 (−, C-5′*), 30.7 (−, C-6′*), 33.9 (−, C-7′*), 34.6 (−, THP−C), 62.3 (−, C-8′**), 67.3 (−, C-6**), 98.8 (+, C-2). − DCI-MS (200 eV, NH_3), *m/z* (%): 312 (28) [M + NH_4^+], 310 (46) [M + NH_4^+ − 2 H], 288 (12), 242 (6), 226 (2), 119 (24) [$C_5H_9O_2$ + NH_4^+], 102 (100) [C_5H_8O + NH_4^+].

3-(1′,1′′-Bicycloprop-2′-yl)propanoic Acid (9b): 2-[3′-(1′′,1′′′-Bicycloprop-2′′-yl)propyloxy]tetrahydro-2*H*-pyran (**8b**) (1.60 g, 7.13 mmol) in methanol (25 mL) was stirred with Lewatit SPS118 (80.0 mg) at room temperature for 24 h. After filtration and evaporation of the solvent, the residue was treated with Jones reagent in acetone (35 mL) at 0 °C according to GP 3. Chromatography on silica gel (90 g, column 3.0 × 30 cm, PE/DE = 3:1, R_f = 0.61) gave 0.682 g (62%) of **9b** as a colorless oil. − IR (film): ν = 3078 cm^{-1} (*c*Pr−H), 2999, 2927, 2665 (COOH), 1709 (C=O), 937 (OH). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.05 to +0.25 (m, 5 H, *c*Pr−H), 0.30−0.55 (m, 2 H, *c*Pr−H), 0.60−0.90 (m, 2 H, *c*Pr−H), 1.20−1.52 (m, 2 H, 3−H), 2.32 (t, *J* = 7.2 Hz, 2 H, 2-H), 11.60 (br. s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.7 (−, *c*Pr−C), 2.8 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 11.9 (+, *c*Pr−C), 16.0 (+, *c*Pr−C), 20.2 (+, *c*Pr−C), 29.2 (−, C-3), 34.0 (−, C-2), 177.0 (C_{quat}, C-1). − MS (70 eV), *m/z* (%): 154 (2) [M$^+$], 136 (4) [M$^+$ − H_2O], 126 (6), 109 (7) [M$^+$ − CO_2H], 94 (100) [M$^+$ − $C_2H_4O_2$], 93 (16), 81 (64) [M$^+$ − $C_3H_5O_2$], 79 (85), 71 (38), 67 (63), 55 (29), 54 (34), 41 (62). − $C_9H_{14}O_2$ (154.2): calcd. C 70.10, H 9.15; found C 70.27, H 9.44; 154.0993 (correct HRMS).

4-(1′,1′′-Bicycloprop-2′-yl)butanoic Acid (9c): 2-[4′-(1′′,1′′′-Bicycloprop-2′′-yl)butoxy]tetrahydro-2*H*-pyran (**8c**) (0.982 g, 4.12 mmol) in methanol (25 mL) was stirred with Lewatit SPS118 (90.0 mg) at room temperature for 24 h. After filtration and evaporation of the solvent, the residue was treated with Jones reagent in acetone (30 mL) according to GP 3. Chromatography on silica gel (40 g, column 1.5 × 35 cm, PE/DE = 3:1, R_f = 0.48) yielded 0.499 g (72%) of **9c** as a colorless oil. − IR (film): ν = 3078 cm^{-1} (*c*Pr−H), 2980, 2931, 2659 (COOH), 1710 (C=O), 1457 (CH_2), 1413 (CH_2), 937 (OH). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.05 to +0.07 (m, 2 H, *c*Pr−H), 0.07−0.50 (m, 2 H, *c*Pr−H), 0.50−1.00 (m, 3 H, *c*Pr−H), 1.00−1.40 (m, 4 H, 3-H, *c*Pr−H), 1.50−1.68 (m, 2 H, 4-H), 2.12−2.20 (m, 2 H, 2-H), 10.90 (br. s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.7 (−, *c*Pr−C), 9.5 (−, *c*Pr−C), 11.9 (+, *c*Pr−C), 16.1 (+, *c*Pr−C), 20.1 (+, *c*Pr−C), 22.3 (−, C-4), 31.3 (−, C-3), 33.2 (−, C-2), 176.1 (C_{quat}, C-1). − MS (70 eV), *m/z* (%): 168 (3) [M$^+$], 144 (5), 126 (2), 115 (8), 108 (21), 101 (17), 95 (16), 85 (22), 81 (45), 73 (57), 67 (36), 60 (100), 55 (31), 43 (24), 41 (43). − $C_{10}H_{16}O_2$ (168.2): 168.1150 (correct HRMS).

5-(1′,1′′-Bicycloprop-2′-yl)pentanoic Acid (9d): 2-[5′-(1′′,1′′′-Bicycloprop-2′′-yl)pentyloxy]tetrahydro-2*H*-pyran (**8d**) (0.674 g, 2.67 mmol) in methanol (25 mL) was stirred with Lewatit SPS118 (60.0 mg) at room temperature for 24 h. After filtration and evaporation of the solvent, the residue was treated with Jones reagent in acetone (25 mL) according to GP 3. Chromatography on silica gel (30 g, column 1.5 × 28 cm, PE/DE = 3:1, R_f = 0.41) yielded 0.364 g (75%) of **9d** as a colorless oil. − IR (film): ν = 3078 cm^{-1} (*c*Pr−H), 2999, 2927, 2660 (COOH), 1709 (C=O), 937 (OH). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.05 to +0.50 (m, 4 H, *c*Pr−H), 0.68−1.00 (m, 3 H, *c*Pr−H), 1.00−1.45 (m, 6 H, 3,4-H, *c*Pr−H), 1.46−1.70 (m, 2 H, 5-H), 2.12−2.20 (m, 2 H, 2-H), 11.70 (br. s., 1 H, COOH). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.9 (−, *c*Pr−C), 3.0 (−, *c*Pr−C), 9.8 (−, *c*Pr−C), 12.2 (+, *c*Pr−C), 14.1, 16.5 (+, *c*Pr−C), 20.4 (+, *c*Pr−C), 24.4, 24.6 (−, C-5), 29.0, 29.1 (−, C-4), 29.2 (−, C-3), 33.1, 34.0 (−, C-2), 180.2 (C_{quat}, C-1) . − MS (70 eV), *m/z* (%): 182 (2) [M$^+$], 158 (8), 129 (29), 115 (33), 98 (20), 87 (16), 81 (24), 73 (83), 67 (21), 60 (100), 57 (54), 43 (36), 41 (43). − $C_{11}H_{18}O_2$ (182.3): calcd. C 72.49, H 9.95; found C 72.81, H 9.86.

6-(1′,1′′-Bicycloprop-2′-yl)]hexanoic Acid (9e): 2-[6′-(1′′,1′′′-Bicycloprop-2′′-yl)hexyloxy]tetrahydro-2*H*-pyran (**8e**) (0.863 g, 3.24 mmol) in methanol (35 mL) was stirred with Lewatit SPS118 (80.0 mg) at room temperature for 24 h. After filtration and evaporation of the solvent, the residue was treated with Jones reagent in acetone (30 mL) according to GP 3. Chromatography on silica gel (40 g, column 1.5 × 35 cm, PE/DE = 2:1, R_f = 0.71) yielded 0.426 g (67%) of **9e** as a colorless oil. − IR (film): ν = 3073 cm^{-1} (*c*Pr−H), 3000, 2958 (O−H), 2926, 1711 (C=O), 937 (OH). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.05 to +0.10 (m, 2 H, *c*Pr−H), 0.10−0.50 (m, 2 H, *c*Pr−H), 0.52−0.95 (m, 3 H, *c*Pr−H), 0.95−1.45 (m, 8 H, 3,4,5-H, *c*Pr−H), 1.45−1.60 (m, 2 H, 6-H), 2.22 (t, *J* = 7.3 Hz, 2 H, 2-H), 10.45 (br. s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.7 (−, *c*Pr−C), 2.8 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 12.1 (+, *c*Pr−C), 16.4 (+, *c*Pr−C), 20.2 (+, *c*Pr−C), 24.7 (−, C-6), 28.7, 28.9 (−, C-5), 29.0, 29.1 (−, C-4), 29.2, 29.3 (−, C-3), 33.7, 33.8 (−, C-2), 176.6 (C_{quat}, C-1). − MS (70 eV), *m/z* (%): 196 (5) [M$^+$], 172 (17), 157 (7), 129 (39), 101 (19), 95 (53), 81 (82), 73 (94), 60 (100), 55 (78), 43 (43), 41 (86). − $C_{12}H_{20}O_2$ (196.3): calcd. C 73.43, H 10.27; found C 73.49, H 10.32.

7-(1′,1′′-Bicycloprop-2′-yl)heptanoic Acid (9f): 2-[7′-(1′′,1′′′-Bicycloprop-2′′-yl)heptyloxy]tetrahydro-2*H*-pyran (**8f**) (0.653 g, 2.33 mmol) in methanol (30 mL) was stirred with Lewatit SPS118 (60.0 mg) at room temperature for 24 h. After filtration and evaporation of the solvent, the residue was treated with Jones reagent in acetone (20 mL) according to GP 3. Chromatography on silica gel (20 g, column 1.5 × 30 cm, PE/DE = 2:1, R_f = 0.68) yielded 0.288 g (59%) of **9f** as a colorless oil. − IR (film): ν = 3071 cm^{-1} (*c*Pr−H), 2965 (O−H), 2926, 1712 (C=O), 939 (OH). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.05 to +0.10 (m, 2 H, *c*Pr−H), 0.10−0.52 (m, 2 H, *c*Pr−H), 0.54−0.99 (m, 3 H, *c*Pr−H), 0.99−1.51 (m, 10 H, 3,4,5,6-H, *c*Pr−H), 1.51−1.64 (m, 2 H, 7-H), 2.36 (t, *J* = 7.0 Hz, 2 H, 2-H), 10.55 (br. s, 1 H, COOH). −

^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.9 (−, *c*Pr−C), 3.0 (−, *c*Pr−C), 9.8 (−, *c*Pr−C), 12.2 (+, *c*Pr−C), 14.1, 16.0 (+, *c*Pr−C), 20.4 (+, *c*Pr−C), 22.4 (−, C-7), 24.6 (−, C-6), 28.7 (−, C-5), 29.2 (−, C-4), 29.4 (−, C-3), 33.3 (−, C-2), 176.5 (C_{quat}, C-1). − MS (70 eV), *m/z* (%): 210 (9) [M^+], 193 (2), 157 (7), 129 (39), 101 (19), 87 (34), 60 (80), 58 (5), 43 (48), 41 (75). − $C_{13}H_{22}O_2$ (210.3): calcd. C 74.24, H 10.54; found C 74.54, H 10.85.

8-(1′,1′′-Bicycloprop-2′-yl)octanoic Acid (9g): 2-[8′-(1′′,1′′′-Bicycloprop-2′′-yl)octyloxy]tetrahydro-2*H*-pyran (**8g**) (1.20 g, 4.08 mmol) in methanol (50 mL) was stirred with Lewatit SPS118 (99.0 mg) at room temperature for 24 h. After filtration and evaporation of the solvent, the residue was treated with Jones reagent in acetone (40 mL) according to GP 3. Chromatography on silica gel (40 g, column 1.5 × 35 cm, PE/DE = 2:1, R_f = 0.61) yielded 0.631 g (69%) of **9g** as a colorless oil. − IR (film): ν = 3078 cm^{-1} (*c*Pr−H), 3000, 2665 (O−H), 1711 (C=O), 938 (OH). − ^1H NMR (250 MHz, $CDCl_3$): δ = −0.02 to +0.22 (m, 2 H, *c*Pr−H), 0.22−0.52 (m, 2 H, *c*Pr−H), 0.78−1.00 (m, 3 H, *c*Pr−H), 1.00−1.50 (m, 12 H, 3,4,5,6,7-H, *c*Pr−H), 1.50−1.70 (m, 2 H, 8-H), 2.32 (t, *J* = 7.6 Hz, 2 H, 2-H), 10.48 (br. s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.9 (−, *c*Pr−C), 3.0 (−, *c*Pr−C), 9.8 (−, *c*Pr−C), 12.2 (+, *c*Pr−C), 14.1, 16.5 (+, *c*Pr−C), 20.4 (+, *c*Pr−C), 22.6 (−, C-8), 29.2 (−, C-7), 29.3 (−, C-6), 29.5 (−, C-5), 29.7 (−, C-4), 31.9 (−, C-3), 34.1 (−, C-2), 180.5 (C_{quat}, C-1). − MS (70 eV), *m/z* (%): 224 (9) [M^+], 200 (38), 144 (5), 115 (11), 101 (26), 85 (34), 73 (64), 60 (100), 55 (37), 41 (39).

2-(1′,1′′-Bicycloprop-2′-yl)ethanol (17): 2-(1′,1′′-Bicyclopropyliden-2′-yl)ethanol (**16**) (0.500 g, 4.03 mmol) in THF (10 mL) was treated with lithium (0.112 g, 16.1 mmol) in ammonia (150 mL) according to GP 2. After column chromatography on silica gel (25 g, column 1.5 × 25 cm, PE/DE = 8:1, R_f = 0.69), 0.431 g (85%) of **17** (colorless oil) was obtained as a 95:5 *trans/cis* isomeric mixture, proved by GC. − IR (film): ν = 3354 cm^{-1} (OH), 3058 (*c*Pr−H), 2937, 2870, 1145 (C−O). − ^1H NMR (250 MHz, $CDCl_3$): δ = −0.05 to +0.05 (m, 1 H, *c*Pr−H), 0.20−0.40 (m, 2 H, *c*Pr−H), 0.40−0.60 (m, 2 H, *c*Pr−H), 0.65−0.90 (m, 2 H, *c*Pr−H), 1.38−1.48 (m, 4 H, *c*Pr−H, 2-H), 2.25 (br. s, 1 H, OH), 3.64 (t, *J* = 7.0 Hz, 2 H, 1-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.8 (−, *c*Pr−C), 3.0 (−, *c*Pr−C), 9.3 (−, *c*Pr−C), 12.1 (+, *c*Pr−C), 13.2 (+, *c*Pr−C), 20.0 (+, *c*Pr−C), 32.2 (−, C-2), 63.3 (−, C-1). − MS (70 eV), *m/z* (%): 126 (10) [M^+], 108 (11), 97 (15) [$M^+ - C_2H_5$], 95 (30) [$M^+ - CH_3O$], 93 (82), 82 (13) [$M^+ - C_2H_4O$], 80 (42), 79 (78), 68 (50) [$C_5H_8^+$], 67 (100) [$C_5H_7^+$], 55 (70) [$C_4H_7^+$], 54 (40) [$C_4H_6^+$], 53 (36) [$C_4H_5^+$], 41 (78) [$C_3H_5^+$]. − $C_8H_{14}O$ (126.2): calcd. C 76.14, H 11.18; found C 76.40, H 11.20; 126.1044 (correct HRMS).

2-(1′,1′′-Bicycloprop-2′-yl)acetic Acid (14): A solution of 2-(1′,1′′-bicycloprop-2′-yl)ethanol (**17**, 1.23 g, 9.75 mmol) in acetone (35 mL) was treated with Jones reagent at 0 °C according to GP 3. Chromatography on silica gel (90 g, column 3.0 × 30 cm, PE/DE = 3:1, R_f = 0.61) gave 1.01 g (74%) of **14** as a colorless oil. − IR (film): ν = 3074 cm^{-1} (*c*Pr−H), 3002, 2938, 2685 (O−H), 1710 (C=O), 1415, 1303, 1225, 1109, 1018, 936, 875, 818. − ^1H NMR (250 MHz, $CDCl_3$): δ = −0.05 to +0.07 (m, 2 H, *c*Pr−H), 0.07−0.80 (m, 4 H, *c*Pr−H), 0.85−1.42 (m, 3 H, *c*Pr−H), 2.15 (d, *J* = 7.4 Hz, 2 H, 2-H), 11.50 (s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.8 (−, *c*Pr−C), 9.5 (−, *c*Pr−C), 11.6 (+, *c*Pr−C), 12.1 (+, *c*Pr−C), 20.0 (+, *c*Pr−C), 38.6 (−, C-2), 177.1 (C_{quat}, C-1). − MS (70 eV), *m/z* (%): 140 (6) [M^+], 122 (3) [$M^+ - H_2O$], 95 (22) [$M^+ - CO_2H$], 94 (11), 81 (62) [$M^+ - CH_3CO_2$], 80 (100) [$M^+ - CH_3CO_2H$], 79 (41), 77 (16), 70 (9), 67 (38), 60 (17), 57 (23), 54 (44), 43 (19), 41 (48) [$C_3H_5^+$]. − $C_8H_{12}O_2$ (140.2): calcd. C 68.55, H 8.63; found C 68.36, H 8.67; 140.0837 (correct HRMS).

2-Bicyclopropanecarboxylic Acid (13): Bicyclopropylidenecarboxylic acid (**15**) (2.00 g, 16.1 mmol) in THF (25 mL) was treated with lithium (447 mg, 64.4 mmol, 4 equiv.) in ammonia (300 mL) according to GP 2. After column chromatography on silica gel (150 g, column 3 × 38 cm, PE/DE = 3:1, R_f = 0.64), 1.55 g (76%) of **13** (colorless oil) was obtained as a 95:5 *trans/cis* isomeric mixture, proved by GC. − IR (film): ν = 3007 cm^{-1} (*c*Pr−H), 2676 (O−H), 1694 (C=O), 925 (OH), 891. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.00−0.23 (m, 2 H, *c*Pr−H), 0.25−0.50 (m, 2 H, *c*Pr−H), 0.51−0.87 (m, 2 H, *c*Pr−H), 1.05−1.22 (m, 1 H, *c*Pr−H), 1.25−1.65 (m, 1 H, *c*Pr−H), 1.70−1.85 (m, 1 H, *c*Pr−H), 10.60 (s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 3.7 (−, *c*Pr−C), 11.5 (−, *c*Pr−C), 14.2 (+, *c*Pr−C), 19.2 (+, *c*Pr−C), 25.9 (+, *c*Pr−C), 180.9 (C_{quat}, COOH). − For other spectral data see ref.[20]

4-(1′,1′′-Bicyclopropyliden-2′-yl)butan-1-ol (10c): 2-[4′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)butyloxy]tetrahydro-2*H*-pyran (**7c**) (2.00 g, 8.46 mmol) in methanol (50 mL) was treated with a few drops of sulfuric acid and stirred at room temperature for 18 h according to GP 4. After column chromatography on silica gel (80 g, column 2.0 × 40 cm, PE/DE = 1:1, R_f = 0.59), 900 mg (70%) of **10c** was obtained as a colorless solid (m.p. 37 °C). − IR (KBr): ν = 3319 cm^{-1} (OH), 3040 (*c*Pr−H), 2937, 1058. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.90−0.95 (m, 1 H, *c*Pr−H), 1.15−1.21 (m, 2 H, *c*Pr−H), 1.22−1.40 (m, 2 H, *c*Pr−H), 1.41−1.75 (m, 8 H, 2,3,4-H, *c*Pr−H), 1.80 (s, 1 H, OH), 3.71 (t, *J* = 7.2 Hz, 2 H, 1-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.7 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 15.9 (+, *c*Pr−C), 25.6 (−, C-3*), 32.4 (−, C-2*), 32.9 (−, C-4*), 63.0 (−, C-1), 109.6 (C_{quat}, *c*Pr−C), 115.94 (C_{quat}, *c*Pr−C). − DCI-MS (200 eV, NH_3), *m/z* (%): 170 (100) [$M + NH_4^+$], 153 (72) [$M + H^+$], 135 (60), 112 (20), 102 (19), 100 (12). − $C_{10}H_{16}O_1$ (152.2): calcd. C 78.90, H 10.59; found C 78.75, H 10.37.

5-(1′,1′′-Bicyclopropyliden-2′-yl)pentan-1-ol (10d): 2-[5′-(1′′,1′′′-Bicyclopropyliden-2′′-yl)pentyloxy)tetrahydro-2*H*-pyran (**7d**) (2.00 g, 7.99 mmol) in methanol (50 mL) was treated with sulfuric acid and stirred at room temperature for 20 h according to GP 4. After column chromatography on silica gel (82 g, column 2.0 × 41 cm, PE/DE = 1:1, R_f = 0.52), 0.956 g (72%) of **10d** was obtained as a colorless solid (m.p. 36.5 °C). − IR (KBr): ν = 3352 cm^{-1} (OH), 3051 (*c*Pr−H), 2929, 2855, 1456, 1411. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.80−0.95 (m, 1 H, *c*Pr−H), 1.10−1.22 (m, 2 H, *c*Pr−H), 1.25−1.65 (m, 12 H, 2,3,4,5-H, *c*Pr−H), 1.75 (s, 1 H, OH), 3.65 (t, *J* = 7.5 Hz, 2 H, 1-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.7 (−, *c*Pr−C), 16.0 (+, *c*Pr−C), 25.4 (−, C-3*), 29.3 (−, C-4*), 32.7 (−, C-5*), 33.1 (−, C-2*), 63.0 (−, C-1), 109.5 (C_{quat}, *c*Pr−C), 116.1 (C_{quat}, *c*Pr−C). − DCI-MS (200 eV, NH_3), *m/z* (%):184 (100) [$M + NH_4^+$], 167 (30) [$M + H^+$], 153 (6), 132 (10) 102 (4), 100 (17). − $C_{11}H_{18}O_1$ (166.3): calcd. C 79.46, H 10.91; found C 79.41, H 11.00.

6-(1′,1′′-Bicyclopropyliden-2′-yl)hexan-1-ol (10e): 2-[6′-(1′,1′′-Bicyclopropyliden-2′-yl)hexyloxy)tetrahydro-2*H*-pyran (**7e**) (2.00 g, 7.56 mmol) in methanol (50 mL) was treated with sulfuric acid and stirred at room temperature for 19 h according to GP 4. After column chromatography on silica gel (72 g, column 2.0 × 36 cm, PE/DE = 3:1, R_f = 0.32), 845 mg (62%) of **10e** was obtained as a colorless solid (m.p. 37 °C). − IR (KBr): ν = 3341 cm^{-1} (OH), 3038 (*c*Pr−H), 2852, 1480, 1361. − ^{1}H NMR (250 MHz, CDCl$_3$, plus DEPT): δ = 0.80−0.91 (m, 1 H, *c*Pr−H), 1.05−1.20 (m, 2 H, *c*Pr−H), 1.35−1.80 (m, 14 H, 6,5,4,3,2-H, *c*Pr−H), 1.85 (s, 1 H, OH), 3.65 (t, *J* = 7.4 Hz, 2 H, 1-H). − ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 16.0 (+, *c*Pr−C), 25.7 (−, C-4*), 29.1 (−, C-5*), 29.4 (−, C-3*), 32.7 (−, C-6*), 33.1 (−, C-2*), 63.0 (−, C-1), 109.6 (C$_{quat}$, *c*Pr−C), 115.9 (C$_{quat}$, *c*Pr−C). − DCI-MS (200 eV, NH$_3$), *m/z* (%): 198 (100) [M + NH$_4^+$], 196 (21), 182 (17), 181 (58) [M + H$^+$], 163 (50), 152 (19), 130 (20). − C$_{12}$H$_{20}$O$_1$ (180.3): calcd. C 79.94, H 11.18; found C 79.99, H 10.89.

4-(1′,1′′-Bicyclopropyliden-2′-yl)butanoic Acid (11c): According to GP 5, 4-(1′,1′′-bicyclopropyliden-2′-yl)butan-1-ol (**10c**) (1.00 g, 6.58 mmol) in acetone (20 mL) was treated with Jones reagent at 0 °C. After column chromatography on silica gel (60 g, column 1.5 × 22 cm, PE/DE = 2:1, R_f = 0.50) 524 mg (48%) of **11c** was obtained as a colorless solid (m.p. 44.5 °C). − IR (film): ν = 3045 cm^{-1} (*c*Pr−H), 2688 (O−H), 1709 (C=O), 964 (OH). − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.80−1.00 (m, 1 H, *c*Pr−H), 1.05−1.12 (m, 2 H, *c*Pr−H), 1.20−1.40 (m, 4 H, 3-H*, *c*Pr−H), 1.40−1.70 (m, 4 H, 4-H*, *c*Pr−H), 2.30 (t, *J* = 7.0 Hz, 2 H, 2-H), 11.15 (br. s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, CDCl$_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.8 (−, *c*Pr−C), 9.5 (−, *c*Pr−C), 15.4 (+, *c*Pr−C), 24.6 (−, C-3*), 32.4 (−, C-4*), 33.6 (−, C-2*), 110.00 (C$_{quat}$, *c*Pr−C), 115.4 (C$_{quat}$, *c*Pr−C), 180.3 (C$_{quat}$, C-1). − DCI-MS (200 eV, NH$_3$), *m/z* (%): 350 (9) [2 M + NH$_4^+$], 201 (22) [M + NH$_4^+$ + NH$_3$], 184 (100) [M + NH$_4^+$], 167 (12) [M + H$^+$], 149 (8), 133 (5), 121 (6), 119 (15), 107 (13). − C$_{10}$H$_{14}$O$_2$ (166.2): calcd. C 72.26, H 8.49; found C 72.20, H 8.71.

5-(1′,1′′-Bicyclopropyliden-2′-yl)pentanoic Acid (11d): According to GP 5, 5-(1′,1′′-bicyclopropyliden-2′-yl)pentan-1-ol (**10d**) (1.00 g, 6.02 mmol) in acetone (20 mL) was treated with Jones reagent at 0 °C. After column chromatography on silica gel (56 g, column 1.5 × 21 cm, PE/DE = 2:1, R_f = 0.52), 585 mg (54%) of **11d** was obtained as a colorless solid (m.p. 44−45 °C). − IR (film): ν = 3050 cm^{-1} (*c*Pr−H), 2680 (O−H), 1710 (C=O), 1412, 960 (OH). − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.80−0.95 (m, 1 H, *c*Pr−H), 1.00−1.22 (m, 2 H, *c*Pr−H), 1.23−1.80 (m, 10 H, 5,4,3-H, *c*Pr−H), 2.20 (t, *J* = 7.2 Hz, 2 H, 2-H), 11.08 (br. s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, CDCl$_3$, plus DEPT): δ = 2.7 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 15.7 (+, *c*Pr−C), 24.3 (−, C-3*), 28.9 (−, C-5*), 32.4 (−, C-4*), 33.7 (−, C-2*), 110.1 (C$_{quat}$, *c*Pr−C), 115.5 (C$_{quat}$, *c*Pr−C), 180.49 (C$_{quart}$, C-1). − DCI-MS (200 eV, NH$_3$); *m/z* (%): 215 (12) [M + NH$_4^+$ + NH$_3$], 210 (15), 198 (100) [M + NH$_4^+$], 181 [M + H$^+$], 163 (8), 135 (3), 121 (9), 107 (5). − C$_{11}$H$_{16}$O$_2$ (180.3): calcd. C 73.30, H 8.95; found C 73.07, H 9.14.

6-(1′,1′′-Bicyclopropyliden-2′-yl)hexanoic Acid (11e): According to GP 5, 6-(1′,1′′-bicyclopropyliden-2′-yl)hexan-1-ol (**10e**) (1.00 g, 5.55 mmol) in acetone (21 mL) was treated with Jones reagent at 0 °C. After column chromatography on silica gel (50 g, column 1.5 × 20 cm, PE/DE = 2:1, R_f = 0.46), 668 mg (62%) of **11e** was obtained as a colorless solid (m.p. 35 °C). − IR (KBr): ν = 3042 cm^{-1} (*c*Pr−H), 2919, 2890 (O−H), 1700 (C=O), 1462, 963 (OH). − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.80−0.91 (m, 1 H, *c*Pr−H), 1.05−1.20 (m, 2 H, *c*Pr−H), 1.35−1.85 (m, 12 H, 3,4,5,6-H, *c*Pr−H), 2.20 (t, *J* = 7.0 Hz, 2 H, 2-H), 11.45 (br. s, 1 H, COOH). − ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 2.6 (−, *c*Pr−C), 2.8 (−, *c*Pr−C), 9.5 (−, *c*Pr−C), 15.8 (+, *c*Pr−C), 24.6 (−, C-4*), 28.6 (−, C-5*), 29.0 (−, C-3*), 32.9 (−, C-6*), 34.0 (−, C-2*), 109.6 (C$_{quat}$, *c*Pr−C), 115.9 (C$_{quat}$, *c*Pr−C), 180.5 (C$_{quat}$, C-1). − DCI-MS (200 eV, NH$_3$); *m/z* (%): 212 (100) [M + NH$_4^+$], 195 (18) [M + H$^+$], 177 (12), 149 (10), 135 (5), 119 (10), 106 (15), 100 (5). − C$_{12}$H$_{18}$O$_2$ (194.3): calcd. C 74.19, H 9.34; found C 74.20, H 9.04.

4-(1′,1′′-Bicyclopropyliden-2′-yl)-*N*-isopropylbutanamide (12c): 4-(1′,1′′-Bicyclopropyliden-2′-yl)butanoic acid (**11c**) (0.50 g, 3.0 mmol) in THF (12 mL) was treated with NEt$_3$ (0.63 mL, 4.5 mmol), ClCO$_2$Et (0.34 mL, 3.6 mmol) and H$_2$N*i*Pr (0.28 mL, 3.3 mmol) according to GP 6. After filtration through silica gel (5 g, EtOAc), 442 mg (71%) of **12c** was obtained as a colorless solid (m.p. 61 °C). − IR (KBr): ν = 3301 cm^{-1} (CONH), 3240 (CONH), 3050 (*c*Pr−H), 2970, 1636 (C=O), 1540, 1456. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.85−0.95 (m, 1 H, *c*Pr−H), 1.10−1.16 (m, 2 H, *c*Pr−H), 1.16−1.22 [m, 8 H, CH(C*H*$_3$)$_2$, cPr−H], 1.23−1.38 (m, 4 H, *c*Pr−H, 3*-H), 1.40−1.58 (m, 1 H, 4*-H), 1.62−1.80 (m, 1 H, 4*-H), 2.20 (t, *J* = 7.0 Hz, 2 H, 2-H), 4.00 [sept, *J* = 7.8 Hz, 1 H, C*H*(CH$_3$)$_2$], 5.30 (s, 1 H, NH). − ^{13}C NMR (62.9 MHz, CDCl$_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 15.9 (+, *c*Pr−C), 22.8 [+, 2 C, CH(*C*H$_3$)$_2$], 25.7 (−, C-4*), 29.2 (−, C-3*), 32.9 (−, C-2), 41.2 [+, C−CH(CH$_3$)$_2$], 109.48 (C$_{quat}$, *c*Pr−C), 116.0 (C$_{quat}$, *c*Pr−C), 173.4 (C$_{quat}$, C-1). − DCI-MS (200 eV, NH$_3$), *m/z* (%): 415 (20) [2 M + H$^+$], 227 (10), 225 (18) [M + NH$_4^+$], 208 (100) [M + H$^+$], 186 (4), 138 (3), 107 (5). − C$_{13}$H$_{21}$ON.(207.3): calcd. C 75.32, H 10.21; found C 75.11, H 10.37.

5-(1′,1′′-Bicyclopropyliden-2′-yl)-*N*-isopropylpentanamide (12d): 5-(1′,1′′-Bicyclopropyliden-2′-yl)pentanoic acid (**11d**) (0.50 g, 2.8 mmol) in THF (12 mL) was treated with NEt$_3$ (0.59 mL, 4.2 mmol), ClCO$_2$Et (0.31 mL, 3.3 mmol) and H$_2$N*i*Pr (0.27 mL, 3.1 mmol) according to GP 6. After filtration through silica gel (5 g, Et$_2$O), 443 mg (73%) of **12d** was obtained as a colorless solid (m.p. 62 °C). − IR (KBr): ν = 3289 cm^{-1} (CONH), 3075 (*c*Pr−H), 2970, 1641 (C=O), 1549. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.82−0.97 (m, 1 H, *c*Pr−H), 0.95−1.10 (m, 10 H, CH(C*H*$_3$)$_2$, *c*Pr−H), 1.10−1.45 (m, 6 H 4*,5*-H, *c*Pr−H), 1.45−1.65 (m, 2 H, 3*-H), 2.10 (t, *J* = 7.0 Hz, 2 H, 2-H), 3.95 [sept, *J* = 7.5 Hz, 1 H, C*H*(CH$_3$)$_2$], 6.00 (s, 1 H, NH). − ^{13}C NMR (62.9 MHz, CDCl$_3$, plus DEPT): δ = 2.5 (−, *c*Pr−C), 2.8 (−, *c*Pr−C), 9.5 (−, *c*Pr−C), 15.7 (+, *c*Pr−C), 22.7 [+, 2 C, CH(*C*H$_3$)$_2$], 25.4 (−, C-5*), 29.1 (−, C-4*), 32.8 (−, C-3*), 36.8 (−, C-2), 41.0 [+, *C*H(CH$_3$)$_2$], 109.5 (C$_{quat}$, *c*Pr−C), 115.8 (C$_{quat}$, *c*Pr−C), 172.1 (C$_{quat}$, C-1). − DCI-MS (200 eV, NH$_3$), *m/z* (%): 443 (19) [2 M + H$^+$], 222 (80) [M + H$^+$], 217 (40), 163 (5), 134 (5), 104 (10). − C$_{14}$H$_{23}$ON.(221.3): calcd. C 75.97, H 10.47; found C 75.98, H 10.18.

6-(1′,1′′-Bicyclopropyliden-2′-yl)-*N*-isopropylhexanamide (12e): 6-(1′,1′′-Bicyclopropyliden-2′-yl)hexanoic acid (**11e**) (0.51 g, 2.6 mmol) in THF (12 mL) was treated with NEt$_3$ (0.54 mL, 3.9 mmol), ClCO$_2$Et (0.30 mL, 3.1 mmol) and H$_2$N*i*Pr (0.24 mL, 2.8 mmol) according to GP 6. After filtration through silica gel (5 g, Et$_2$O), 418 mg (68%) of **12e** was obtained as a colorless solid (m.p. 63 °C). − IR (KBr): ν = 3307 cm^{-1} (CONH), 3048 (*c*Pr−H), 2927, 1634 (C=O), 1540, 1470. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.80−0.95 (m, 1 H, *c*Pr−H), 1.10−1.20 [m, 10 H, CH(C*H*$_3$)$_2$, *c*Pr−H], 1.20−1.52 (m, 8 H, 4*,5*,6*-H, *c*Pr−H), 1.55−1.65 (m, 2 H, 3*−H), 2.20 (t, *J* = 7.1 Hz, 2 H, 2-H), 4.05 [sept, *J* = 7.6 Hz, 1 H, C*H*(CH$_3$)$_2$], 5.25 (s, 1 H, NH). − ^{13}C NMR (62.9 MHz, CDCl$_3$, plus DEPT): δ = 2.6 (−, *c*Pr−C), 2.9 (−, *c*Pr−C), 9.6 (−, *c*Pr−C), 15.9 (+, *c*Pr−C), 22.8 [+, 2 C, CH(*C*H$_3$)$_2$], 25.8 (−, C-4*), 28.9 (−, C-3*), 29.2 (−, C-5*), 33.0 (−, C-6*), 36.9 (−, C-2), 40.9 [+, *C*H(CH$_3$)$_2$], 109.5 (C$_{quat}$, *c*Pr−C), 116.0 (C$_{quat}$, *c*Pr−C), 172.1 (C$_{quat}$, C-1). − DCI-MS (200 eV, NH$_3$), *m/z* (%): 488 (10) [2 M + NH$_4^+$], 471 (18) [2 M + H$^+$], 318 (5), 270 (10), 253 (100) [M + NH$_4^+$], 236 (75) [M + H$^+$], 201 (5), 175 (5), 118 (3). −

$C_{15}H_{25}ON$.(235.4): calcd. C 76.55, H 10.71; found C 76.80, H 10.41.

Biological Degradation of Fatty Acids 9

General Procedure for the Degradation of Fatty Acids by Enrichment Cultures (GP 7): For the enrichment of bacterial strains able to degrade ω-bicyclopropyl-substituted fatty acids, soil samples were added to an M1 mineral medium[29] (1000 mL) containing 1.00 g [0.1% (w/v)] of the ω-bicyclopropyl-substituted fatty acids. The cultures were incubated on a shaker (130 rpm) at 30 °C. Bacterial growth was detected by measurement of the optical density for several days. For the isolation of degradation products the cell suspensions were centrifuged. After the addition of an HCl solution (2 N, 200 mL), the aqueous phase was extracted with CH_2Cl_2 (7 × 100 mL). The combined organic phases were washed with brine (250 mL), dried with $MgSO_4$, and concentrated under reduced pressure.

Degradation of 9b: 3-(1′,1′′-Bicycloprop-2′-yl)propanoic acid (**9b**) (1.00 g) in M1 mineral medium was subjected to GP 7. After chromatography on silica gel (50 g, 2 × 2.5 cm, PE/DE = 3:1, R_f = 0.64), 398 mg of **13** was obtained.

Degradation of 9c: 4-(1′,1′′-Bicycloprop-2′-yl)butanoic acid (**9c**) (1.00 g) in M1 mineral medium was subjected to GP 7. After chromatography on silica gel (60 g, 2 × 2.9 cm, PE/DE = 3:1, R_f = 0.61), 352 mg of **14** was obtained.

Degradation of 9d: 5-(1′,1′′-Bicycloprop-2′-yl)pentanoic acid (**9d**) (1.00 g) in M1 mineral medium was subjected to GP 7. After chromatography on silica gel (55 g, 2 × 2.7 cm, PE/DE = 3:1, R_f = 0.64), 386 mg of **13** was obtained.

Degradation of 9e: 6-(1′,1′′Bicycloprop-2′-yl)hexanoic acid (**9e**) (1.00 g) in M1 mineral medium was subjected to GP 7. After chromatography on silica gel (52 g, 2 × 2.5 cm, PE/DE = 3:1, R_f = 0.61), 402 mg of **14** was obtained.

Degradation of Fatty Acids by Bacteria Strains: Several strains[22] were tested for their ability to grow on media containing ω-bicyclopropyl-substituted fatty acids. Thus, 100 μL of an overnight culture was added to 10 mL of the M3 mineral medium[30] containing 10 mM, of ω-bicyclopropyl-substituted fatty acid **9b**,**c** or **13**. Incubation and growth detection were performed as described above.

Degradation of 9b by *Rhodococcus ruber* P-IV-B-11: 3-(1′,1′′-Bicycloprop-2′-yl)]propanoic acid (**9b**) (250 mg) in M3 mineral medium (137 mL) was added to *Rhodococcus ruber* P-IV-B-11. The culture was incubated for 3 d on a shaker (130 rpm) at 30 °C. For the isolation of degradation products the cell suspensions were centrifuged. After the addition of HCl (2 N, 80 mL), the aqueous phase was extracted with CH_2Cl_2 (7 × 50 mL). The combined organic phases were washed with brine (100 mL), dried with $MgSO_4$, and concentrated under reduced pressure. After chromatography on silica gel (50 g, 2 × 2.5 cm, PE/DE = 3:1, R_f = 0.61), 57 mg of **9b** was recovered.

Degradation of 9c by *Rhodococcus ruber* P-IV-B-11: 4-(1′,1′′-Bicycloprop-2′-yl)]butanoic acid (**9c**) (250 mg) in M3 mineral medium (125 mL) was added to *Rhodococcus ruber* P-IV-B-11. The culture was incubated for 3 d on a shaker (130 rpm) at 30 °C. For the isolation of degradation products the cell suspensions were centrifuged. After addition of HCl (2 N, 80 mL), the aqueous phase was extracted with CH_2Cl_2 (7 × 50 mL). The combined organic phases were washed with brine (100 mL), dried with $MgSO_4$, and concentrated under reduced pressure. After chromatography on silica gel (45 g, 2 × 2.3 cm, PE/DE = 3:1, R_f = 0.48) 70 mg of **9c** was recovered.

Degradation of 13 by *Rhodococcus ruber* P-IV-B-11: 2-Bicyclopropanecarboxylic acid (**13**) (250 mg) in M3 mineral medium (161 mL) was added to *Rhodococcus ruber* P-IV-B-11. The culture was incubated for 3 d on a shaker (130 rpm) at 30 °C. For the isolation of degradation products the cell suspensions were centrifuged. After addition of HCl (2 N, 80 mL), the aqueous phase was extracted with CH_2Cl_2 (7 × 60 mL). The combined organic phases were washed with brine (100 mL), dried with $MgSO_4$, and concentrated under reduced pressure. After chromatography on silica gel (60 g, 2 × 2.8 cm, PE/DE = 3:1, R_f = 0.64), 80 mg of **13** was recovered.

Tests for Antimicrobial Activities of ω-Bicyclopropyl-Substituted Fatty Acids 9: To investigate the antimicrobial activity of ω-bicyclopropyl-substituted fatty acids **9** against bacteria, yeasts and fungi, the MIC (minimum inhibitory concentration) values for the acids **9b**,**c** and **13** were determined. MIC is defined as the lowest antibiotic concentration that inhibits the growth of a specific organism. Tubes with 5 mL of liquid growth media, containing graded doses of ω-bicyclopropyl-substituted fatty acids **9b**,**c** and **13**, were inoculated with the test organisms from overnight cultures and incubated for up to 2 d at a suitable temperature on a shaker. The visible bacteria growth in each tube was compared with a reference tube containing growth medium only. The tube with the lowest concentration, that showed no growth was taken to be the minimum inhibitory concentration (MIC).

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