Pair-Wise Interactions by Gas Chromatography; Part III:[1,2] Synthesis of Isosteric Stationary Phases for Gas Chromatography

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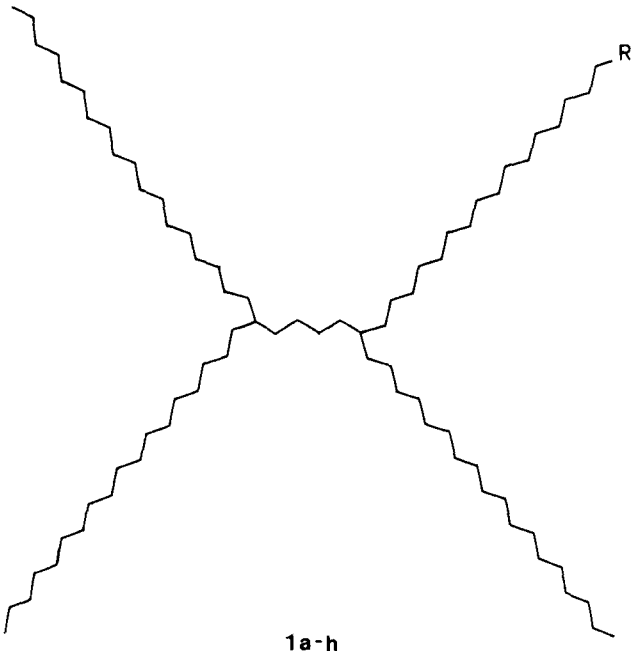
Received 17 November 1992

Retention in gas/liquid partition chromatography depends on the size and, to a lesser extent, on the form of the solvent used as stationary phase. How the measurement of interaction free enthalpies between a functional group and a solute free of size and form effects synthesis and properties of seven high molecular weight solvents is described. The monofunctional paraffin derivatives have the same form and nearly the same molar volume as that of their parent alkane 19,24-dioctadecyldotetracontane.

A first design of the synthesis of compounds **1b–i** (Figure 1) was based on the reported successful preparation of the branched paraffin **1a**.[3] Reaction of the Grignard reagent of 1-bromooctadecane with dimethyl adipate afforded the corresponding diol. The paraffin **1a** was obtained in moderate yield by dehydration of the diol and hydrogenation of the resulting diene mixture. Based on this reaction sequence it was planned to prepare the ketone **4** containing the first three octadecyl side chains and to introduce the fourth functionalized substituent of eighteen heavy atoms by Grignard reaction.

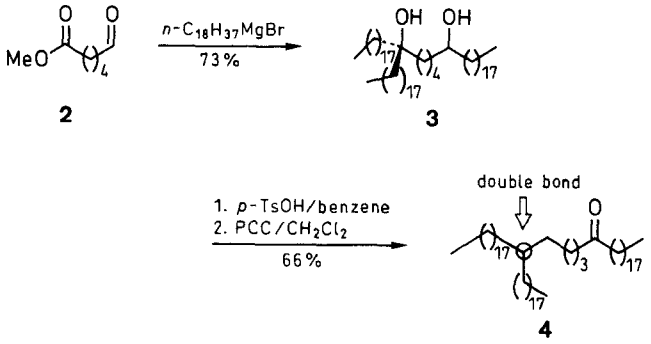


1a-h

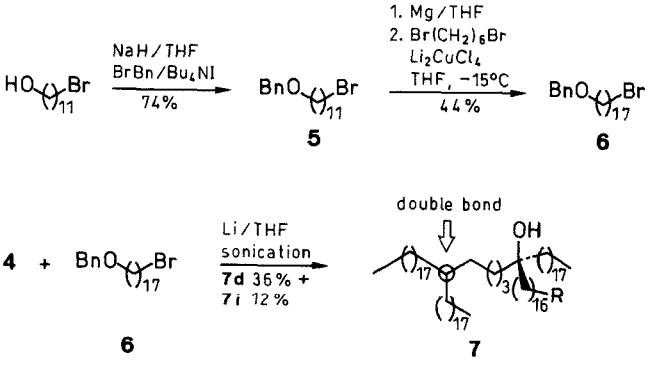
1, (7)	R	Acronym of **1x**	1, (7)	R	Acronym of **1x**
a	Et	C78	**f**	CH_2Cl	PCL
b	CH_2CF_3	MTF	**g**	CH_2Br	PBR
c	OMe	MMx	**h**	CH_2CN	PCN
d	CH_2OH	POH	**i**	CH_2OBn	
e	CH_2OMs				

Figure 1. Structure of the target compounds **1b–i** designated by their acronyms. Intermediates **7** having the same group R are designated by the same small letters **b–i**.

The ketone **4** is readily available from methyl 6-oxohexanoate **(2)**[4] following reaction scheme **2** → **4** by reaction with excess octadecylmagnesium bromide, dehydration of the diol **3** and oxidation of the secondary alcohol with pyridinium chlorochromate.

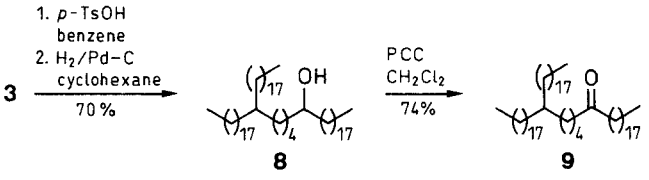


In a first attempt for the synthesis of 18,23-dioctadecyl-1-hentetracontanol **(1d)**, 1-benzyl-17-bromoheptadecane **(6)** was chosen as starting material. This protected alcohol was obtained by the copper(I) catalyzed coupling of the Grignard reagent of 1-benzyloxy-11-bromoundecane **(5)** with 1,6-dibromohexane.[5,6] The ether **5** was prepared by benzylation of 11-bromo-1-undecanol with benzyl bromide and sodium hydride in tetrahydrofuran with tetrabutylammonium iodide as phase transfer catalyst.[7] Surprisingly, when ketone **4** was added to the Grignard reagent of 1-benzyloxy-17-bromoheptadecane **(6)** it remained unchanged and was quantitatively recovered. The unsaturated ketone, **4**, showed a complete lack of reactivity toward normal nucleophiles such as Grignard or Wittig reagents. Cerium(III) chloride[8] promoted addition of the same Grignard reagent was also unsuccessful. The Wittig–Horner reaction[9] of the same ketone with the corresponding phosphonate gave the same negative results. The only way to get addition products with bromide **6** as reaction partner was with lithium sand in tetrahydrofuran at 50 °C under sonication.[10,11] The major compound obtained was the deprotected alcohol **7d** (36%) accompanied by small quantities of the expected benzyl



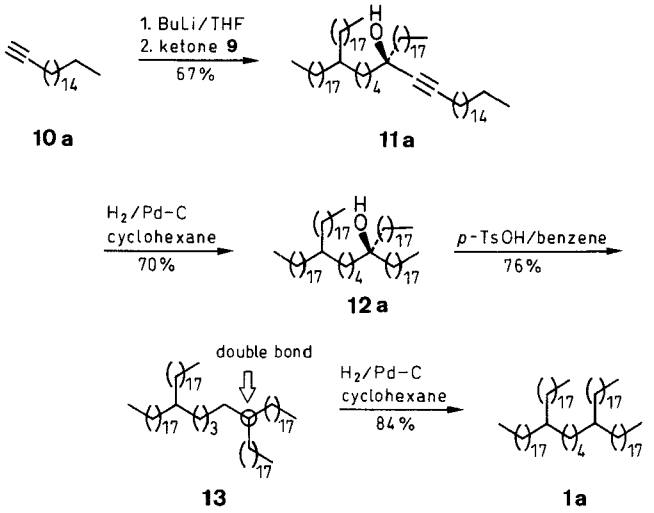
ether, **7i** (12%). Isolation of small quantities (~ 300 mg) of the desired compound was difficult because of the presence of many side products arising from Wittig rearrangement of the protected alcohol. Nevertheless, in this way some 3 g of POH was prepared and used as stationary phase in gas chromatography.

For consecutive experiments the unsaturated ketone **4**, (mixture of three regio- and stereoisomers) was replaced by the pure, recrystallized saturated ketone, **9**, prepared by hydrogenation of the unsaturated intermediate from the dehydration of diol **3** and oxidation of the resulting secondary alcohol, **8**, by pyridinium chlorochromate following reaction scheme **3** → **9**. The reactivity of the ketone **9** was in every respect similar to that of its unsaturated precursor. A re-examination of the reactivity of the ketones with Grignard reagents prepared with a new quality of magnesium ("magnesium for Grignard" from Fluka) showed that the saturated ketone **9** did react with this reagent, at least in tetrahydrofuran, when the mixture was refluxed for a minimum of 15 hours. Conversion was less than 70% and there was about 15–20% secondary alcohol **8** formed by the reduction of the ketone with the primary Grignard reagent used indicating a steric congestion at the electrophilic center. These findings are in agreement with the observation that dimethyl adipate and Grignard reagents gave the diols in poor yields[3] (41–60%). It was then preferred to use metal acetylides, more nucleophilic and less sensitive to steric hindrance than Grignard reagents, that gave the desired addition products on ketone **9** in a smooth reaction and in excellent yields.

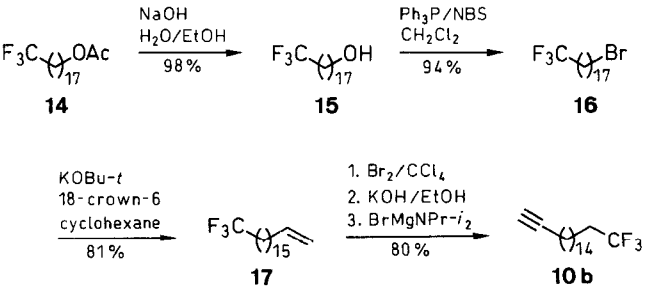


In a first reaction sequence, **10a** → **1a**, it was proven in a "classical" way that ketone **9** gave with 1-octadecyne, after the necessary transformations, the same branched paraffin, **1a**, as that obtained from dimethyl adipate and 1-octadecylmagnesium bromide. Ketone **9**, poorly soluble in tetrahydrofuran, was added to a solution of 1-lithio-1-octadecyne. After hydrolysis, the desired propargylic alcohol, **11a**, was obtained. Its catalytic hydrogenation gave the tertiary alcohol **12a**. The acid-catalyzed dehydration of **12a** in benzene led to the expected alkene mixture, **13** that gave after catalytic hydrogenation 19,24-dioctadecyldotetracontane **(1a)** (in the reaction schemes all yields refer to isolated pure compounds). The branched paraffin, **1a**, was in every respect identical to the alkane previously prepared from octadecylmagnesium bromide and dimethyl adipate.[3] Yields in the reaction schemes were good showing the viability of this approach for the preparation of monosubstituted alkanes **1b–h**.

The necessary acetylene derivatives, **10b**, **10c** and **10i**, for the preparation of the compounds **1b–h** were synthesized as follows.



18,18,18-Trifluorooctadecyl acetate **(14)**, accessible from 15-hexadecenyl acetate by trifluoroethylation,[12] was hydrolyzed with sodium hydroxide in ethanol to give the fluorinated alcohol **15**. Bromation of the product with *N*-bromosuccinimide and triphenylphosphine in dichloromethane at 0°C gave the bromide **16**. The base promoted elimination of hydrobromic acid from compound **16** was made with potassium *tert*-butoxide in cyclohexane with 18-crown-6 as phase transfer catalyst.[13] The alkene, **17**, was separated by silica gel column chromatography from the *tert*-butyl trifluorooctadecyl ether (18%) formed by the nucleophilic substitution of the bromide by the base. Bromination of the alkene **17** and subsequent biselimination of hydrobromic acid by potassium hydroxide in refluxing ethanol gave a mixture of the desired alkyne **10b** and 24% of (*E*)-18-bromo-1,1,1-trifluoro-17-octadecene. In fact the *trans*-bromoalkene eliminated only very slowly under these conditions by *syn*-mechanism and it was necessary to find another base to complete the reaction. Lithium diisopropylamide and in general all lithium bases could not be applied as they reacted with the trifluoromethyl group. Bromomagnesium diisopropylamide, mainly used as a weak base for Claisen condensation of esters[14] or for selective enolization of unsymmetrical ketones,[15] successfully dehydrobrominated the *trans*-bromoalkene in refluxing tetrahydrofuran and the alkyne **10b** was obtained in 80% yield. It is important to note that this base was not applicable to produce the alkyne directly from the 1,2-dibromo compound because it gave the starting alkene by debromination.



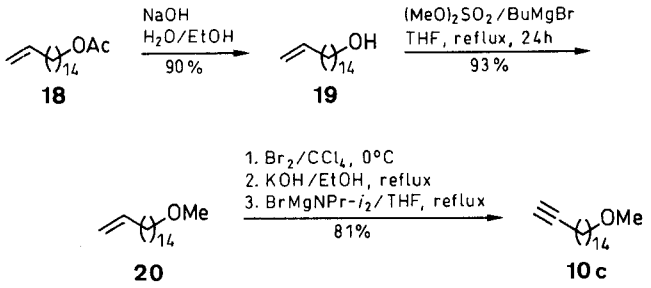
The alkenol **19** obtained by hydrolysis of the acetate **18**[12] gave with dimethyl sulfate and butylmagnesium bromide

Table 1. Spectroscopic Data of the Synthesized Compounds

Product	IR (CCl_4/CS_2) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ, J (Hz)
1a	2920, 2850, 1465, 1380, 720	0.89 (t, 12H, J = 6.5), 1.26 (m, 146H)	14.08, 22.71, 26.80, 27.22, 29.39, 29.75, 30.21, 31.96, 33.84, 37.50
1b	2930, 2850, 1465, 1255, 1145, 720, 655	0.89 (t, 9H, J = 6.4), 1.27 (m, 142H), 1.55 (m, 2H), 2.06 (m, 2H)	14.08, 21.88 (q, J = 2.8), 22.70, 26.80, 27.23, 28.75, 29.21, 29.39, 29.59, 29.75, 30.21, 31.96, 33.80 (q, J = 28), 33.84, 37.51, 127.32 (q, J = 276)
1c	2920, 2850, 1465, 1380, 1370, 1120, 720	0.89 (t, 9H, J = 6.5), 1.26 (m, 140H), 1.58 (m, 2H), 3.34 (s, 3H), 3.37 (t, 2H, J = 6.6)	14.07, 22.69, 26.18, 26.79, 27.22, 29.37, 29.54, 29.73, 30.19, 31.95, 33.84, 37.50, 58.48, 73.02
1d	3640, 2930, 2850, 1465, 1380, 1370, 1050, 720	0.89 (t, 9H, J = 6.4), 1.40 (m, 145H), 3.65 (t, 2H, J = 6.5)	14.07, 22.69, 25.78, 26.79, 27.21, 29.37, 29.47, 29.64, 29.73, 30.19, 31.95, 32.88, 33.83, 37.49, 63.11
1e	2920, 2850, 1465, 1370, 1345, 1175, 970, 950, 810, 720, 530	0.89 (t, 9H, J = 6.4), 1.27 (m, 142H), 1.76 (quint., 2H, J = 7.0), 3.01 (s, 3H), 4.23 (t, 2H, J = 6.6)	14.07, 22.69, 25.46, 26.78, 27.21, 29.06, 29.19, 29.36, 29.44, 29.55, 29.73, 30.18, 31.94, 33.82, 37.42, 37.49, 70.10
1f	2920, 2850, 1465, 1380, 1370, 720, 655	0.89 (t, 9H, J = 6.4), 1.27 (m, 142H), 1.78 (quint., 2H, J = 6.9), 3.54 (t, 2H, J = 6.9)	14.08, 22.71, 26.80, 26.95, 27.23, 28.94, 29.39, 29.51, 29.59, 29.75, 30.21, 31.96, 32.73, 33.84, 37.51, 45.07
1g	2920, 2850, 1465, 1380, 1370, 720, 650	0.89 (t, 9H, J = 6.4), 1.26 (m, 142H), 1.87 (quint., 2H, J = 7.0), 3.42 (t, 2H, J = 6.9)	14.09, 22.71, 26.80, 27.23, 28.24, 28.82, 29.39, 29.48, 29.59, 29.75, 30.21, 31.96, 32.92, 33.84, 37.51
1h	2920, 2850, 2250, 1465, 1380, 1370, 720	0.89 (t, 9H, J = 6.4), 1.27 (m, 142H), 1.67 (quint., 2H, J = 7.2), 2.34 (t, 2H, J = 7.0)	14.07, 17.11, 22.69, 25.44, 26.79, 27.21, 28.70, 28.78, 29.37, 29.53, 29.73, 30.19, 31.95, 33.83, 37.49, 119.68
3	3620, 2920, 2850, 1465, 1380, 720	0.89 (t, 9H, J = 6.4), 1.26 (m, 102H), 1.57 (m, 10H), 3.60 (m, 1H)	14.07, 22.69, 23.53, 25.69, 26.31, 29.36, 29.71, 30.32, 31.94, 37.46, 37.61, 39.32, 71.96, 74.41
8	3630, 2920, 2850, 1465, 1380, 720	0.89 (t, 9H, J = 6.6), 1.26 (m, 112H), 3.59 (m, 1H)	14.07, 22.69, 25.69, 26.14, 26.76, 26.84, 29.36, 29.72, 30.17, 31.94, 33.77, 37.46, 37.57, 72.04
9	2920, 2850, 1715, 1465, 1380, 720	0.89 (t, 9H, J = 6.5), 1.26 (m, 103H), 1.55 (m, 4H), 2.39 (t, 4H, J = 7.4)	14.03, 22.68, 23.99, 24.47, 26.54, 26.79, 29.36, 29.45, 29.51, 29.68, 29.73, 30.17, 31.95, 33.65, 33.81, 37.45, 42.84, 42.88, 211.25
11a	3620, 2920, 2850, 1465, 1380, 720	0.89 (t, 12H, J = 6.4), 1.26 (m, 140H), 2.20 (t, 2H, J = 6.7)	14.07, 18.66, 22.69, 24.38, 24.84, 26.78, 27.02, 28.86, 29.18, 29.37, 29.73, 30.20, 31.95, 33.78, 37.48, 42.44, 71.42, 83.40, 84.72
11b	3620, 2930, 2850, 1465, 1255, 1140, 720, 655	0.89 (t, 9H, J = 6.5), 1.26 (m, 138H), 2.07 (m, 2H), 2.20 (t, 2H, J = 6.7)	14.07, 18.66, 21.88 (q, J = 2.8), 22.70, 24.39, 24.85, 26.79, 27.03, 28.76, 28.86, 29.19, 29.21, 29.38, 29.74, 29.91, 30.21, 31.96, 33.80 (q, J = 28), 33.80, 37.50, 42.45, 42.84, 71.42, 83.44, 84.71, 127.31 (q, J = 276)
11c	3620, 2930, 2850, 1465, 1380, 1370, 1120, 720	0.89 (t, 9H, J = 6.5), 1.26 (m, 135H), 1.50 (m, 4H), 1.80 (br s, 1H), 2.20 (t, 2H, J = 6.8), 3.34 (s, 3H), 3.37 (t, 2H, J = 6.5)	14.07, 18.65, 22.68, 24.37, 24.84, 26.18, 26.77, 27.02, 28.86, 29.17, 29.36, 29.54, 29.72, 29,84, 30.20, 31.94, 33.79, 37.48, 42.44, 58.46, 71.41, 73.00, 83.41, 84.71
11i	3620, 3090, 3070, 3030, 2920, 2850, 1465, 1365, 1100, 785, 735, 720, 695	0.89 (t, 9H, J = 6.5), 1.26 (m, 141H), 1.57 (m, 6H), 2.20 (t, 2H, J = 6.7), 3.47 (t, 2H, J = 6.6), 4.51 (s, 2H), 7.34 (m, 5H)	14.08, 18.66, 22.69, 24.38, 24.84, 26.25, 26.78, 27.03, 28.86, 29.18, 29.37, 29.53, 29.73, 29.90, 30.20, 31.95, 33.79, 37.49, 42.44, 70.59, 71.41, 72.88, 83.42, 84.72, 127.42, 127.58, 128.31, 138.84
12a	3620, 2920, 2850, 1465, 1380, 720	0.89 (t, 12H, J = 6.4), 1.26 (m, 146H)	14.07, 22.69, 23.51, 23.94, 26.78, 27.44, 29.37, 29.72, 30.19, 30.33, 31.95, 33.79, 37.47, 39.37, 74.44
12b	3620, 2920, 2850, 1465, 1255, 1145, 725, 655	0.89 (t, 9H, J = 6.5), 1.26 (m, 144H), 2.07 (m, 2H)	14.07, 21.87 (q, J = 2.8), 22.70, 23.52, 23.97, 26.79, 27.45, 28.74, 29.20, 29.38, 29.58. 29.69, 29.73, 30.20, 30.35, 31.96, 33.80 (q, J = 28), 33.80, 37.49, 39.39, 74.45, 127.32 (q, J = 276)
12c	3620, 2930, 2850, 1465, 1380, 1370, 1120, 720	0.89 (t, 9H, J = 6.5), 1.26 (m, 136H), 1.57 (m, 6H), 3.34 (s, 3H), 3.37 (t, 2H, J = 6.6)	14.07, 22.69, 23.51, 23.95, 26.17, 26.77, 27.43, 29.36, 29.72, 30.18, 30.34, 31.94, 33.78, 37.46, 39.38, 58.47, 73.01, 74.46
12d	3620, 2930, 2860, 1465, 1380, 1050, 720	0.89 (t, 9H, J = 6.6), 1.26 (m, 137H), 1.54 (m, 8H), 3.65 (t, 2H, J = 6.5)	14.07, 22.68, 23.51, 23.95, 25.78, 26.78, 27.44, 29.36, 29.46, 29.72, 30.18, 30.33, 31.94, 32.87, 33.79, 37.47, 39.38, 63.07, 74.46
13	2920, 2850, 1465, 1380, 720	0.89 (t, 12H, J = 6.4), 1.26 (m, 137H), 1.97 (m, 6H), 5.09 (t, 1H, J = 7.1)	14.09, 22.71, 26.51, 26.80, 26.97, 27.31, 27.78, 28.18, 28.39, 28.58, 28.77, 28.98, 29.39, 29.53, 29.75, 30.21, 31.61, 31.96, 33.48, 33.82, 37.00, 37.49, 124.82, 139.59, 139.66

in refluxing tetrahydrofuran the methoxyalkene **20** in 93% yield. Bromination of the double bond in carbon tetrachloride followed by potassium hydroxide elimination in refluxing ethanol and successive treatment with bromomagnesium diisopropylamide resulted the methyl ether **10c** in 81% isolated yield.

The coupling of the Grignard reagent of 1-bromo-10-undecene **(21)** with 6-iodohexyl acetate, catalyzed by copper(I), followed by saponification with sodium hydroxide in aqueous ethanol gave the alcohol **22**. Bromination and subsequent dehydrobromination by potassium hydroxide in anhydrous ethanol then by bromomagnesium diiso-



propylamide in tetrahydrofuran afforded the 16-heptadecyn-1-ol (**23**). Benzylation with sodium hydride and benzyl bromide in dimethylformamide[16] led to the isomerized alkyne, **24** that was converted again to the terminal acetylenic compound, **10i**, by the use of the zipper reagent, potassium 1,3-aminopropylamide (KAPA).[17]

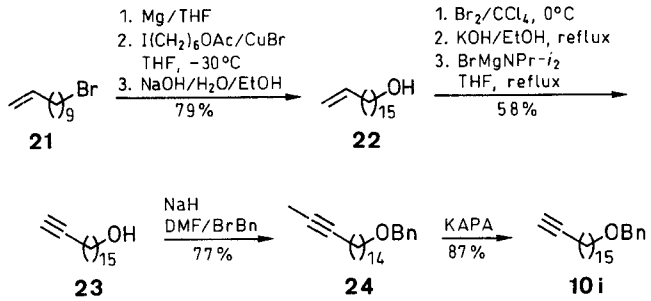


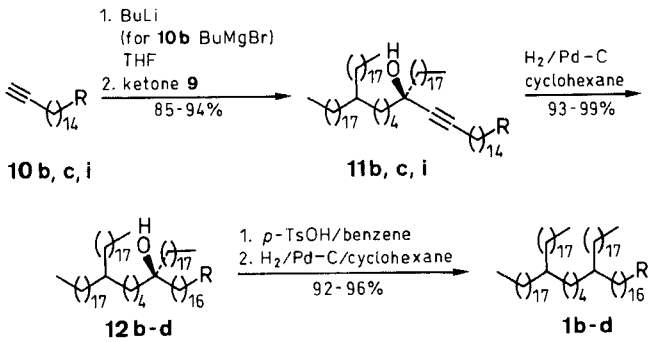
Table 2. Physical Properties of the Synthetic Intermediates

Compound	Purity (%)[a]	bp (°C)/mbar mp (°C)	$d^{20,b}$ (g cm^{-3})	n_D^{20c}
10b	99.2	–	0.933	1.4247
10c	98.4	108–110/0.014	0.845	1.4501
10i	99.4	34.0–34.5	–	–
15	99.6	65–65.5	–	–
16	99.4	29.5–30.0	–	–
17	98.7	–	0.914	1.4220
19	98.7	37–38	–	–
20	98.5	–	0.829	1.4459
22	98.5	44.5–45.5	–	–
23	99.9	56–57	–	–
24	99.5	33.5–34.0	–	–

[a] Determined by GC.
[b] Confidence limit at the 95% confidence level $\Delta_{95} = 0.002$ g cm^{-3}.
[c] $\Delta_{95} = 0.0005$.

With the necessary acetylene derivatives at hand the introduction of the functionalized side chain in ketone **9** was made with the corresponding acetylides prepared by reaction with butyllithium with the exception of trifluoroalkyne **10b**. For the latter side chain the bromomagnesium acetylide had to be used because, as already mentioned, trifluoromethyl groups are attacked by organolithium reagents. The bromomagnesium acetylide was prepared by reacting a simple Grignard reagent with the acetylene **10b** where it was necessary to work under reflux to get complete transmetalation.

The acetylides obtained from the alkynes **10b, c, i** reacted very smoothly with ketone **9** to give the propargylic alcohols **11b, c, i** in yields of 85–94%. Catalytic hydrogenation of the triple bond has been found to be advantageously accomplished before the dehydration of the tertiary alcohol to give the alcohols **12b–d** from ynols **11b, c, i** with 10% palladium on activated carbon. Dehydration of the tertiary alcohols **12b–d** by azeotropic distillation in benzene with *p*-toluenesulfonic acid as catalyst using a Dean-Stark trap gave the corresponding alkene mixture. Hydrogenation led to the compounds **1b–d** in yields of 92–96%.

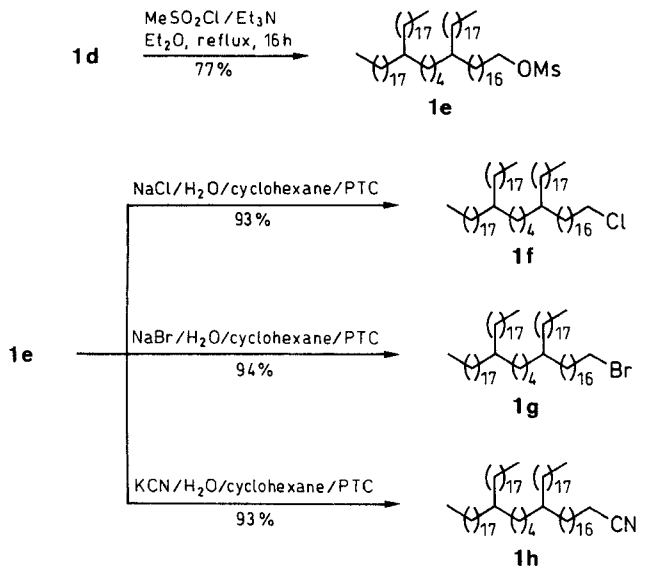


The mesylate of alcohol **1d** was the common starting product for the preparation of the halogenated stationary phases **1f, g** and nitrile **1h**. The derivatives were prepared by phase-transfer catalyzed nucleophilic substitution. The chloride **1f** was obtained by refluxing the ester **1e** in cyclohexane for 18 hours with excess aqueous sodium chloride in the presence of 3 mol% hexadecyltributylphosphonium bromide.[18] In similar reactions the bromi-

Table 3. Regression Coefficients of Equation 1 for the Calculation of the Logarithm of the Density (Corrected for Vacuum) of the Stationary Phases **1a–d, f–h** and **12a** as a Function of the Temperature. Experimental Points Determined in the Temperature Range Indicated. Densities and Molar Volumes at the Standard Temperature $T^\dagger = 130$ °C are Also Given. Note that $\kappa(T) = \kappa^\dagger + \Delta T\alpha$ ($\Delta T = T - T^\dagger$)

			Regression Coefficients				
		Temp. Range (°C)	$\ln d^\dagger$	$\kappa^\dagger$ x 10^4	α x 10^7	$d^\dagger$ (g cm^{-3})	$v^\dagger$ (cm^3 mol^{-1})
1a	(C78)	85–193	−0.25970	7.63	2.27	0.7713	1421.2
1b	(MTF)	85–195	−0.23299	7.74	2.57	0.7922	1451.8
1c	(MMX)	86–196	−0.25157	7.82	3.72	0.7776	1412.2
1d	(POH)	83–197	−0.24589	7.80	1.50	0.7820	1404.2
1f	(PCL)	82–178	−0.23644	7.60	2.51	0.7894	1414.4
1g	(PBR)	84–169	−0.20088	7.77	1.70	0.8180	1419.3
1h	(PCN)	84–196	−0.24513	7.64	3.27	0.7826	1414.7
12a	(TOH)	82–195	−0.24650	7.81	2.20	0.7815	1423.0

de, **1g**, and the cyano compound, **1h**, were obtained in excellent yields with aqueous sodium bromide and potassium cyanide, respectively.



The final products, C78, MTF (for monotrifluoro), MMX (monomethoxy), POH (primary alcohol), PCL (primary chloride), PBR (primary bromide), PCN (primary cyanide) as well as compound **12a** (TOH, for tertiary alcohol) were designed to be used as stationary phases for gas chromatography. Therefore, during synthesis great care was taken to arrive at pure final products. All starting materials were research grade and all intermediates were carefully purified by column chromatography and crystallization. The control of the purity of materials of such high molecular weight is difficult. High temperature gas chromatography of the paraffin, C78, showed the presence of about 4% of another isomer probably of the same molecular weight and similar shape as the target alkane. In fact, the purity of all high molecular weight intermediates and products was controlled by accumulating high resolution FT-NMR spectra during 20–40 hours in order to detect signals of possible impurities. In these experiments the presence of the rearranged byproduct in C78 could not be detected, hence it should also be a paraffin with two tertiary carbons and four methyl groups. Based on NMR measurements all compounds had a purity greater than 99.5%. The characterization of this minor byproduct of the C78 paraffin is still under way. For hydrogenation palladium on activated carbon was used as catalyst. Possible palladium traces were controlled by X-ray fluorescence on discs pressed from the crystalline compounds and were found to be less than 15 ppm. These "solvents" were designed to have about the same molar volume as that of the paraffin C78. The experimental molar volume of the individual compounds relative to that of C78 between 80 and 200 °C is shown in Figure 2.

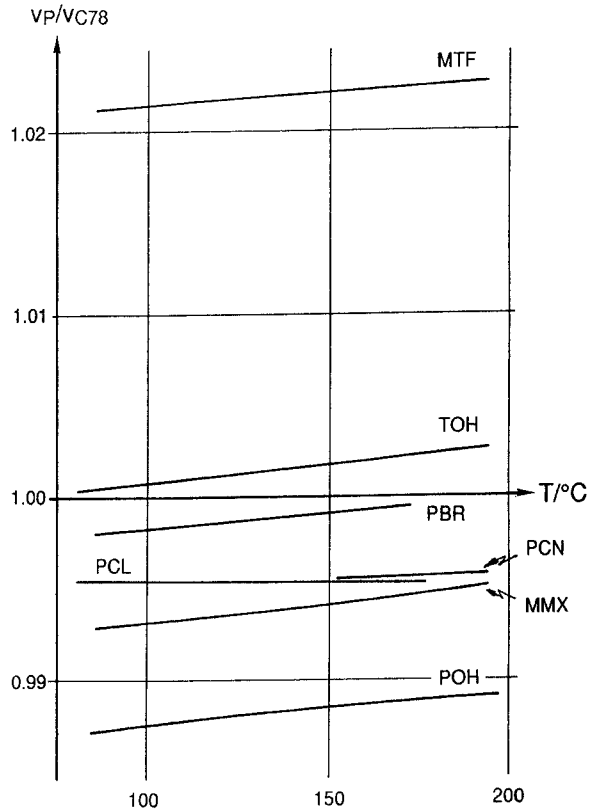


Figure 2. Relative molar volume of the compounds designated in Figure 1 by acronyms as well as that of compound **12a** (TOH) with reference to the molar volume of the paraffin, C78, as a function of the temperature.

Research grade 1,2-dibromoethane, *p*-TsOH, pyridinium chlorochromate (PCC), BuLi 1.6 M in hexane, Ph_3P, NBS, KOBu-*t*, 18-crown-6, 1-bromobutane, anhydr. THF, *i*-Pr_2NH, $(MeO)_2SO_2$, Br_2, 10-undecen-1-ol, AcCl, 11-bromo-1-undecanol, 1,5-dibromopentane, 1,6-dibromohexane, Bu_4NI, LiCl, $CuCl_2$, KCN, hexadecyltributylphosphonium bromide, 20% NaH in mineral oil, anhydr. DMF, BnBr, 10% Pd–C, 1,3-diaminopropane and 20% KH in mineral oil were purchased from Fluka (Buchs, Switzerland) and used as received. Research grade oxepane and silica gel 60 were purchased from Merck AG (Darmstadt, Germany). 1-Bromooctadecane from Fluka was purified in the laboratories of Chemie Uetikon (Uetikon am See, Switzerland) to a purity of 99.9% by fractional distillation. Methyl 6-oxohexanoate **(2)**, was prepared according to Bosone et al. from ε-caprolactone.[4] 6-Iodohexyl acetate was prepared from oxepane and acetyl chloride in the presence of catalytic amounts of $ZnCl_2$ and subsequent substitution of the chloride by NaI in acetone according to Williams et al.[19] 1-Bromo-10-undecene was prepared according to Chen et al.[20] by reacting 10-undecene-1-ol in CH_2Cl_2 with Ph_3P and (instead of CBr_4) NBS. 1-Octadecyne **(10a)** was prepared from 1,2-dibromooctadecane and ethanolic KOH according to Majima et al.[21] 18,18,18-Trifluorooctadecyl acetate **(14)** was prepared according to Ref. 12 from trifluoroethyl iodide and 15-hexadecenyl acetate.

GC analyses were performed on a Hewlett-Packard (model 5890A) instrument equipped with a fused silica macrobore capillary column (i.d. = 0.30 mm; length = 25.0 m) with crosslinked methylsilicone as stationary phase. Retention indexes I_T were calculated from isothermal chromatograms made at the temperature T/°C. IR spectra were recorded on a Perkin-Elmer (model 684) spectrophotometer. Elemental analyses were made with an instrument from Leco Corp. (St. Joseph MI, USA; model CHN-900). ^1H NMR spectra were recorded at 200 MHz and ^{13}C NMR spectra were measured at 50 MHz on a spectrometer from Bruker (Spectrospin, Fällanden, Switzerland; model AC-P 200). Coupling constants are reported in *J* (Hz). Melting points were determined on a Büchi-Tottoli apparatus and are uncorrected. All densities are corrected for vacuum. Density of the final products was determined on samples with a 2.0 mL pycnometer from Schmizo AG (Zofingen, Switzerland) at almost equidistant temperatures (ca. every 10 °C) between 80–200 °C in an oil bath. Densities can be calculated at any temperature by using the following expression:[22]

$$\ln d_T = \ln d^\dagger - \kappa^\dagger \cdot \Delta T - \frac{\alpha}{2} \cdot \Delta T^2 \qquad \text{(eq 1)}$$

where $\Delta T = T - T^\dagger$ with $T^\dagger = 130\,^\circ C$ and the coefficents $\kappa^\dagger$, α and $\ln d^\dagger$, determined by fitting equation 1 on the experimental points, are listed in Table 3. Densities of all other liquids were determined on samples of 100–200 mg at $20.0 \pm 0.1\,^\circ C$ with a precision of $\pm 0.002\,g\,cm^{-3}$. Satisfactory microanalyses were obtained for **1a, c–h, 3, 4, 6, 7d, i, 8, 9, 10c, i, 11a, c, i, 12a, c, d, 13, 19–24** and for 16,17-dibromo-1-heptadecanol: C ± 0.27, H ± 0.30.

As observed earlier[12] the trifluoromethyl derivatives failed to give correct and reproducible microanalyses, therefore they were omitted. (Syntheses are reported in the order of the numbering of the compounds in the discussion).

19,24-Dioctadecyldotetracontane (1a):
In a 100 mL stainless steel autoclave, equipped with a magnetic stirrer, a solution of alkenes **13** (1.2 g, 1.12 mmol) in cyclohexane (70 mL) was hydrogenated at 40 °C under 10 bar H_2 pressure for 20 h in the presence of 10 % Pd–C (0.13 g) as catalyst. The mixture was then cooled to r.t., the catalyst was removed by filtration on a silica gel column (20 g) with cyclohexane (250 mL) as mobile phase. The solvent was evaporated (rotary evaporator) and the solid residue (1.20 g) was recrystallized from PrOH/hexane/EtOH (7:17:1) (25 mL) to give the pure alkane **1a** (1.03 g, 84 %); mp 70–74.5 °C.

Final Products 1b–d; General Procedure:
In a round-bottom flask equipped with a Dean-Stark trap, alcohol **12b–d** and *p*-TsOH (20–64 mol-%) were dissolved in benzene (10–45 mL/mmol). The mixture was heated to reflux for 5 h, allowed to cool to r.t. where it was washed successively with H_2O (2 × 10–20 mL/mmol), sat. aq $NaHCO_3$ (10–20 mL/mmol) and dried (Na_2SO_4). The solvent was removed on a rotary evaporator. The residue was hydrogenated in cyclohexane (40–80 mL/mmol) with 10 % Pd–C (0.05 g/mmol) as catalyst at 40 °C under 10–13 bar H_2 pressure for 16–20 h. The catalyst was filtered on a silica gel column (10–20 g/g starting alcohol **12b–d**). Elution with cyclohexane or cyclohexane/benzene or even cyclohexane/Et_2O afforded the pure alkane **1b–d** that was recrystallized according to the following procedures.

1,1,1-Trifluoro-19,24-dioctadecyldotetracontane **(1b)**:
Alcohol **12b** (6.69 g, 5.74 mmol) was dehydrated with *p*-TsOH (0.22 g, 1.16 mmol) in benzene (100 mL). The crude product (6.58 g) was hydrogenated at 40 °C in cyclohexane (400 mL) with 10 % Pd–C (0.30 g) as catalyst under 11.5 bar H_2 pressure for 16 h. After filtration of the catalyst, silica gel (50 g) and cyclohexane as eluent, and evaporation of the solvent the residue (6.15 g) was recrystallized from EtOH/hexane (5:3) (240 mL) at 0 °C to give 6.08 g (92 %) of pure trifluoroalkane **1b**; mp 69–74 °C.

1-Methoxy-17,22-dioctadecyltetracontane **(1c)**:
Alcohol **12c** (11.14 g, 10.0 mmol) was dehydrated with *p*-TsOH (0.39 g, 2.0 mmol) in benzene (100 mL). The crude product (11.0 g) was hydrogenated at 40 °C in cyclohexane (400 mL) with 10 % Pd–C (0.52 g) as catalyst under 10 bar H_2 pressure for 18 h. After removal of the catalyst, silica gel (100 g) with cyclohexane/Et_2O (90:10) as eluent, and evaporation of the solvent the residue (10.61 g) was treated with $NaBH_4$ (0.37 g, 10 mmol) in a mixture of 94 % EtOH (20 mL) and cyclohexane (20 mL) at 50 °C for 30 min (reduction of trace amounts of unreacted ketone **9**). The solvent was removed on a rotary evaporator and the residue was filtered on silica gel (50 g). Elution with cyclohexane/benzene (85:15) (200 mL) afforded 10.65 g of ether **1c** that was recrystallized from EtOH/hexane (55:45) (360 mL) to give 10.56 g (96 %) of pure methoxyalkane **1c**; mp 65.5–71.5 °C.

18,23-Dioctadecyl-1-hentetracontanol **(1d)**:
Alcohol **12d** (24.8 g, 22.3 mmol) was dehydrated with *p*-TsOH (2.70 g, 14.2 mmol) in benzene (1000 mL). The crude product (24.5 g) was hydrogenated at 40 °C in cyclohexane (850 mL) with 10 % Pd–C (2.45 g) as catalyst under 13 bar H_2 pressure for 20 h. After filtration of the catalyst the residue (23.9 g) was recrystallized from EtOH/MeOH (3:2) to give 23.5 g (96 %) of pure primary alcohol **1d**; mp 70–74.5 °C.

Final Products from Alcohol 1d:
18,23-Dioctadecylhentetracontanyl methanesulfonate **(1e)**:
In a 1 L 3-necked round-bottom flask a solution of alcohol **1d** (17.5 g, 16.0 mmol) in anhydr. Et_2O (700 mL) and Et_3N (3.1 g, 31 mmol) was heated to reflux then MsCl (2.90 g, 25.0 mmol) was added dropwise within 10 min. The mixture was refluxed overnight, cooled to r.t. and H_2O (150 mL) was added. The organic phase was washed with 10 % aq NaOH (100 mL), 3 % aq H_2SO_4 (2 × 100 mL), sat. aq $NaHCO_3$ (2 × 100 mL) and dried (Na_2SO_4). Distillation of the solvent on a rotary evaporator gave 20.1 g of a pale yellow solid which was filtered on silica gel (100 g) with Et_2O/cyclohexane (1:1) (600 mL) as mobile phase. The solid obtained (18.4 g) was recrystallized from Et_2O to give 14.5 g (77 %) of pure mesylate **1e** as a white powder; mp 77–79.5 °C.

1-Chloro-18,23-dioctadecylhentetracontane **(1f)**:
In a 1 L 3-necked round-bottom flask equipped with a magnetic stirrer, a thermometer and a reflux condenser was introduced a solution of NaCl (25.0 g, 428 mmol) in H_2O (100 mL) and a solution of mesylate **1e** (8.52 g, 7.24 mmol) and hexadecyltributylphosphonium bromide (0.11 g, 0.20 mmol) in cyclohexane (360 mL). After heating to reflux for 18 h the content was cooled to r.t., the organic phase was washed with H_2O (2 × 50 mL) and dried (Na_2SO_4). The solvent was removed on a rotary evaporator and the white solid residue (8.26 g) was filtered on silica gel (80 g) with cyclohexane (900 mL) as mobile phase. After distillation of the solvent, the residue was recrystallized from PrOH/EtOH/cyclohexane (6:1:13) to give 7.45 g (93 %) of pure chloro compound **1f**; mp 72.5–75.5 °C.

1-Bromo-18,23-dioctadecylhentetracontane **(1g)**
In a 1 L 2-necked round-bottom flask equipped with a magnetic stirrer, thermometer and reflux condenser was introduced a solution of NaBr (27 g, 0.26 mol) in H_2O (100 mL) and a solution of mesylate **1e** (8.57 g, 7.29 mmol) and hexadecyltributylphosphonium bromide (0.12 g, 0.20 mmol) in cyclohexane (380 mL). After heating at reflux for 18 h the mixture was cooled to r.t., the organic phase was washed with H_2O (2 × 50 mL) and dried (Na_2SO_4). After distillation of the solvent in a rotary evaporator the residue (8.76 g) was chromatographed on silica gel (150 g) with cyclohexane as mobile phase (700 mL). The solid obtained after removal of the solvent was recrystallized from PrOH/EtOH/cyclohexane (6:1:13) to give 8.24 g (94 %) of pure bromo compound **1g**; mp 73–76 °C.

1-Cyano-18,23-dioctadecylhentetracontane **(1h)**:
In a 1 L 3-necked round-bottom flask equipped with a magnetic stirrer, thermometer and reflux condenser was introduced a solution of KCN (9.60 g, 147 mmol) in H_2O (100 mL) and a solution of mesylate **1e** (8.68 g, 7.38 mmol) and hexadecyltributylphosphonium bromide (0.13 g, 0.30 mmol) in cyclohexane (400 mL). After heating at reflux for 21 h the content was cooled to r.t., the organic layer was washed with 2 M aq NaOH (2 × 150 mL), sat. aq $NaHCO_3$ (2 × 100 mL) and dried (Na_2SO_4). Distillation of the solvent afforded 9.29 g of a yellow solid which was filtered on silica gel (190 g) successively with cyclohexane (800 mL) and benzene/cyclohexane (1:9, 2.0 L) as mobile phases. The cyclohexane fraction gave after evaporation of the solvent 0.25 g of white wax that was not identified. The benzene fraction gave 7.81 g of solid that was recrystallized from EtOAc to afford 7.57 g (93 %) of pure cyano compound **1h** as a white powder; mp 66–68 °C.

19-Octadecyl-19,24-dotetracontanediol (3):
In a 1 L flask, equipped with a mechanical stirrer, thermometer, reflux condenser and a dropping funnel, Mg (25.0 g, 1.03 mol) was covered with THF (170 mL) and activated with 1,2-dibromoethane (1.8 g, 10 mmol). After evolution of ethylene had stopped a solution of 1-bromooctadecane (198.3 g, 0.590 mol) in THF (250 mL) was added at a rate as to maintain a gentle reflux (ca. 1.5 h). The mixture was kept under reflux for an additional 2 h then cooled to r.t. and decanted from excess Mg into another 2 L round-bottom flask. To

this Grignard reagent a solution of methyl 6-oxohexanoate (**2**; 24.6 g, 0.170 mol) in THF (100 mL) was added at r.t., then the mixture was heated to reflux for 5 h and allowed to cool to r.t. After hydrolysis with sat. aq NH_4Cl (150 mL) the aqueous phase was extracted with a mixture of Et_2O/hexane (2:1) (6 × 200 mL). The combined organic phase was washed with brine (100 mL), dried (Na_2SO_4) and the solvent was evaporated (rotary evaporator). The white residue (175.1 g) was dissolved in cyclohexane (500 mL) and filtered on a silica gel column (525 g). Elution with cyclohexane (2.0 L) afforded 46.3 g of a white solid (mixture of octadecane and hexatriacontane). Elution with a mixture of Et_2O/cyclohexane (1:1) (2.0 L) gave 123.6 g of a solid that was recrystallized twice from EtOAc to afford 109.2 g (73%) of pure diol **3**; mp 69–70°C.

24-Octadecyl-X-dotetraconten-19-one (Mixture of X = 23 and 24) (4):

In a 500 mL round-bottom flask equipped with a Dean-Stark trap, a solution of *p*-TsOH · H_2O (1.2 g, 6.3 mmol) in benzene (50 mL) was heated to reflux for 20 min then a solution of 19-octadecyl-19,24-dotetracontanediol (**3**; 43.8 g, 50.0 mmol) in benzene (250 mL) was added and the mixture was refluxed for 2 h. The mixture was then cooled to r.t., diluted with Et_2O (150 mL) and the resulting solution was washed successively with sat. aq $NaHCO_3$ (2 × 50 mL), H_2O (3 × 100 mL) then dried (Na_2SO_4). After elimination of the solvent (rotary evaporator) the pale yellow residue (39.7 g) was recrystallized twice from acetone to give 34.3 g of unsaturated alcohol as a white powder; mp 57–59°C. The unsaturated alcohol (39.7 g, 46.3 mmol) was dissolved in CH_2Cl_2 (1000 mL) and the solution was added dropwise at r.t. to a well-stirred suspension of PCC (24.9 g, 120 mmol) in CH_2Cl_2 (150 mL). The black mixture was stirred for an additional period of 5 h, then it was diluted with Et_2O (500 mL) and cyclohexane (200 mL). The black tar that separated was removed by filtration and the filtrate was concentrated on a rotary evaporator. The dark brown residue was dissolved in hexane (700 mL) and filtered on Florisil (30–60 mesh, 30 g). After removal of the solvent, the residue was recrystallized twice from EtOAc to give 32.9 g (66%) of pure ketone **4**; mp 57–58°C.

1-Benzyloxy-11-bromoundecane (5):

In a 500 mL 3-necked round-bottom flask equipped with a magnetic stirrer, thermometer and a reflux condenser fitted with a gas inlet, a solution of 11-bromo-1-undecanol (25.1 g, 100 mmol) in THF (225 mL) was cooled to −10°C (ice/salt bath) under an Ar atmosphere. At this temperature a 55% dispersion of NaH in mineral oil (4.8 g, 0.11 mol) was added within 30 min. The mixture was stirred for an additional 2 h, allowed to warm to r.t., then Bu_4NI (3.7 g, 10 mmol) was added. After dropwise addition of BnBr (25.7 g, 150 mmol) the mixture was stirred for 2 h at r.t. It was heated to reflux for 2 h then cooled to r.t. and poured over ice-water (300 mL). The aqueous phase was extracted with Et_2O (3 × 100 mL), the combined organic phase was dried (Na_2SO_4) and the solvent was removed on a rotary evaporator. The residue was distilled at 175°C/1.33 × 10^{-2} mbar to give 25.4 g (74%) of pure **5** as a colorless liquid.

1-Benzyloxy-17-bromoheptadecane (6):

In a 500 mL round-bottom flask equipped with a mechanical stirrer, thermometer, reflux condenser, gas inlet and a dropping funnel, Mg (2.4 g, 100 mmol) was covered with anhydr. THF (200 mL) and activated with 1,2-dibromoethane (0.2 g, 1.0 mmol). After evolution of ethylene had stopped, a solution of 1-benzyloxy-11-bromoundecane (**5**; 17.1 g, 50.0 mmol) in anhydr. THF (40 mL) was added dropwise at a rate as to maintain a gentle reflux (ca. 30 min). The mixture was heated to reflux for 2 h then cooled to r.t. and decanted from excess Mg into a dropping funnel under Ar atmosphere. In another 500 mL round-bottom flask a solution of 1,6-dibromohexane (18.3 g, 75.0 mmol) in anhydr. THF (30 mL) was cooled to −15°C (ice/salt bath) and a solution of $CuCl_2$ (100 mg, 0.75 mmol) and LiCl (64 mg, 1.5 mmol) in anhydr. THF (5 mL) was added. To this cold, well-stirred mixture the previously prepared Grignard reagent was added dropwise within 1 h and the mixture was stirred at the same temperature for an additional 5 h period and overnight at r.t. It was then hydrolyzed with sat. aq NH_4Cl (100 mL) and the aqueous phase was extracted with Et_2O (3 × 100 mL). The combined organic phase was washed with H_2O (100 mL), dried (Na_2SO_4) and the solvent was evaporated. The excess 1,6-dibromohexane was distilled at 45°C/2.7 × 10^{-2} mbar. The oily residue contained the ether **6** together with the 1,28-dibenzyloxyoctacosane. The latter (1.6 g, 10%) was obtained by crystallization from acetone, mp 56–57°C. The mother liquor was evaporated to dryness and crystallized from EtOH. After two recrystallizations from EtOH 9.3 g (44%) of pure benzyl ether **6** was obtained; mp 28–29°C.

19-(17-Benzyloxyheptadecyl)-24-octadecyl-X-dotetraconten-19-ol (Mixture of X = 23 and 24) (7):

In a 500 mL 2-necked round-bottom flask equipped with a reflux condenser, ketone **4** (1.7 g, 2.0 mmol) and 1-benzyloxy-17-bromoheptadecane (1.2 g, 4.0 mmol) were dissolved in anhydr. THF (250 mL) and under Ar atmosphere a suspension of Li (2% Na) sand 15% in hexane (0.23 g, 5.0 mmol) was added. The flask was immersed in an ultrasonic bath and sonicated for 1.5 h at 50°C. The reaction was monitored by TLC until the disappearance of the starting ketone. The mixture was cooled to r.t., the excess Li was filtered off and the filtrate was poured onto ice and it was treated with sat. aq NH_4Cl (20 mL). The aqueous phase was extracted with Et_2O (3 × 100 mL) and the combined organic layer was washed with H_2O and dried (Na_2SO_4). After removal of the solvent the pale yellow solid residue (3.4 g) was chromatographed on silica gel (55 g). Elution with pentane (150 mL) afforded 0.1 g of a white solid (mixture of alkanes). With a mixture of pentane/Et_2O (3:1) three fractions were collected. Fraction 1 (0.9 g) was a mixture of 1-benzyloxy-18-phenyloctadecane and 19-benzyl-24-octadecyl-X-dotetraconten-19-ol. The hot MeOH soluble part of this mixture gave 0.2 g of 1-benzyloxy-18-phenyloctadecane (mp 47–48°C) after three recrystallizations from MeOH. The MeOH insoluble part was crystallized from *i*-PrOH and gave, after three recrystallizations, 0.4 g (21%) of 19-benzyl-24-octadecyl-X-dotetraconten-19-ol; mp 35–36°C. Fraction 2 (0.5 g) afforded the ether **7i**, 0.3 g (12%) after three recrystallizations from acetone; mp 39–41°C. Fraction 3 (1.4 g) gave after two recrystallizations from EtOH 0.8 g (36%) of pure alcohol **7d**; mp 51–52°C.

24-Octadecyl-19-dotetracontanol (8):

In a 2 L round-bottom flask equipped with a mechanical stirrer, thermometer and a Dean-Stark trap, a solution of *p*-TsOH · H_2O (4.46 g, 23.0 mmol) in benzene (700 mL) was heated to reflux where in the trap ca. 0.5 mL of H_2O was collected. After 30 min a solution of 19-octadecyl-19,24-dotetracontanediol (**3**; 147.1 g, 0.170 mol) in benzene (500 mL) was added and the mixture was refluxed for 2 h. It was then cooled to r.t., diluted with Et_2O (500 mL) and the resulting solution was washed with sat. aq $NaHCO_3$ (2 × 150 mL) and dried (Na_2SO_4). After evaporation of the solvent (rotary evaporator) the 145.2 g of a pale yellow residue was recrystallized twice from acetone to give 115.3 g (80%) of a white powder; mp 57–59°C (mixture of stereoisomers of unsaturated compound **3**). An aliquot of the powder (68.0 g, 79.0 mmol) was dissolved in cyclohexane (850 mL) and was placed in a 1 L stainless steel autoclave together with 10% Pd–C (5.6 g). The well-stirred mixture was hydrogenated at 40°C at 15 bar H_2 pressure for 18 h and then it was allowed to cool to r.t. The catalyst was removed by filtration on a silica gel column (50 g) with a mixture of Et_2O/cyclohexane as mobile phase (1:1) (300 mL). After evaporation of the solvent (rotary evaporator) the residue (68.9 g) was recrystallized twice from EtOH/THF (1:1, 140 mL) to afford 59.3 g (87%) of pure 24-octadecyl-19-dotetracontanol (**8**) as a white solid; mp 63–64°C.

24-Octadecyl-19-dotetracontanone (9):

In a 2 L round-bottom flask equipped with a mechanical stirrer, thermometer, reflux condenser and a dropping funnel PCC (37.0 g, 180 mmol) was covered with CH_2Cl_2 (300 mL). A solution of 24-octadecyl-19-dotetracontanol (**8**; 60.7 g, 70.6 mmol) in CH_2Cl_2 (1200 mL) was added at r.t. to the well-stirred suspension over 60 min. The black mixture was stirred for an additional period of 15 h, diluted with Et_2O (700 mL) and cyclohexane (300 mL) and the black

tar was eliminated by filtration. The filtrate was concentrated on a rotary evaporator, the dark residue was dissolved in hexane (1 L) and filtered on a Florisil (30–60 mesh; 30 g) column. After elimination of the solvent (rotary evaporator) the residue was recrystallized twice from EtOAc to give 45.8 g (74%) of pure ketone **9**; mp 64.5–65°C.

1,1,1-Trifluoro-17-octadecyne (10b):
BrMgNPr-i_2 was prepared in a 100 mL 2-necked round-bottom flask equipped with a dropping funnel and a reflux condenser. First Mg (1.46 g, 60.0 mmol) was covered with anhydr. THF (10 mL) and activated with 1,2-dibromoethane (0.47 g, 2.5 mmol), then a solution of BuBr (5.48 g, 40.0 mmol) in anhydr. THF (25 mL) was added dropwise over 15 min. The mixture was refluxed for 2.5 h, then cooled to r.t., diluted with anhydr. THF (20 mL) and transferred to another 250 mL 2-necked round-bottom flask. In this vessel i-Pr_2NH (4.55 g, 45.0 mmol) was added, the mixture was refluxed for 1 h and cooled to r.t.: solution of BrMgNPr-i_2. In another 250 mL 2-necked round-bottom flask 1,1,1-trifluoro-17-octadecene (**17**; 6.13 g, 20.0 mmol) was dissolved in CCl_4 (50 mL) and cooled to 0°C (ice bath). A solution of Br_2 (3.20 g, 20.0 mmol) in CCl_4 (10 mL) was added dropwise over a 1 h period. The mixture was stirred for 3 h at the same temperature and 5% aq $Na_2S_2O_3$ (50 mL) was added. The aqueous phase was extracted with Et_2O (50 mL) and the combined organic phase was dried (Na_2SO_4). After removal of the solvent (rotary evaporator) the residue, the crude dibromo compound (9.7 g), was dissolved in a solution of KOH (18.0 g, 0.320 mol) in abs. EtOH (65 mL). The resulting bright yellow mixture was heated to reflux for 4 h, then cooled to r.t., diluted with hexane (250 mL). The organic phase was washed with H_2O (3 × 250 mL), the aqueous phase was extracted with hexane (100 mL), the combined organic layer was dried (Na_2SO_4) and the solvent was eliminated (rotary evaporator). The residue (6.37 g) was added to the prepared solution of BrMgNPr-i_2, the mixture was refluxed for 5 h and allowed to cool to r.t. where it was carefully hydrolyzed with sat. aq NH_4Cl (50 mL), then H_2O (25 mL) and Et_2O (50 mL) were added. The organic phase was washed with brine (50 mL). The aqueous phase was extracted with Et_2O (100 mL), the combined organic layer was dried (Na_2SO_4) and the solvent was removed on a rotary evaporator to give 6.26 g of dark-brown crude alkyne **10b**. Filtration on silica gel (30 g) with hexane as mobile phase afforded 5.63 g of a slightly yellow liquid which gave after recrystallization from 94% weight EtOH at 5°C 4.86 g (80%) of the pure acetylene derivative, **10b**, as a colorless liquid (mp 15°C), (GC: 99.2% pure, I_{200} = 1768).

IR (film): ν = 3315, 2930, 2850, 2120, 1470, 1440, 1390, 1255, 1140, 1050, 840, 725, 630 cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 1.27 (m, 22 H), 1.56 (m, 4 H), 1.94 (t, 1 H, J = 2.7), 2.07 (m, 2 H), 2.19 (dt, 2 H, J = 2.6, 6.9).

^{13}C NMR ($CDCl_3$/TMS): δ = 18.40, 21.86 (q, J = 2.8), 28.55, 28.72, 28.78, 29.12, 29.18, 29.36, 29.51, 29.55, 29.61, 29.63, 33.77 (q, J = 28), 67.97, 84.71, 127.32 (q, J = 276).

MS (EI): m/z (%) = 304 (M^+, 0.2), 109 (14), 96 (57), 95 (40), 82 (79), 81 (100), 69 (23), 67 (62), 57 (22), 55 (51), 45 (51), 41 (46).

1-Methoxy-15-hexadecyne (10c):
In a 100 mL 2-necked round-bottom flask 1-methoxy-15-hexadecene (**20**; 5.09 g, 20.0 mmol) was dissolved in CCl_4 (25 mL) and cooled to 0°C (ice bath). A solution of Br_2 (3.36 g, 21.0 mmol) in CCl_4 (5 mL) was added dropwise in 90 min. The red-orange mixture was stirred 2 h at the same temperature, allowed to warm to r.t. then 5% aq $Na_2S_2O_3$ (25 mL) was added. The aqueous phase was extracted with Et_2O (2 × 25 mL) and the combined organic phase was dried (Na_2SO_4). The solvent was removed on a rotary evaporator. The residue (8.13 g) was transferred in one portion into another 250 mL 2-necked round-bottom flask containing a solution of KOH (18.0 g, 0.320 mol) in abs. EtOH (65 mL). The mixture was refluxed for 4 h then at r.t. Et_2O (50 mL) and H_2O (100 mL) were added. The organic phase was washed with H_2O (3 × 100 mL). The aqueous layer was extracted with Et_2O (4 × 50 mL) and the combined organic phase was dried (Na_2SO_4). The solvent was eliminated on a rotary evaporator and the residue (5.41 g) was filtered on silica gel (40 g) with hexane/Et_2O (90:10) (240 mL) as mobile phase. The evaporation residue, 5.21 g of yellow liquid, was transferred to a 250 mL 2-necked round-bottom flask containing BrMgNPr-i_2 prepared from BuBr (5.48 g, 40.0 mmol), Mg (1.46 g, 60.0 mmol) and i-Pr_2NH (4.55 g, 45.0 mmol) in anhydr. THF (35 mL) (*vide supra*: alkyne **10b**). The mixture was refluxed for 7 h, cooled to r.t., the excess reagent was hydrolyzed with sat. aq NH_4Cl (50 mL; exothermic reaction) then Et_2O (50 mL) was added. The separated organic phase was washed with brine (50 mL), the aqueous layer was extracted with Et_2O (2 × 50 mL) and the combined organic phase was dried (Na_2SO_4). The solvent was removed on a rotary evaporator and the residue (4.95 g) was chromatographed on silica gel (100 g) with hexane/Et_2O (90:10) (250 mL) as mobile phase. After evaporation of the solvent the residue, 4.35 g of a yellow liquid, was distilled in a Kugelrohr at 108–110°C/1.4 × 10^{-2} mbar to give 4.09 g (81%) of alkyne **10c** as colorless liquid (GC: 98.4% pure, I_{200} = 1832).

IR (film): ν = 3310, 2920, 2850, 2120, 1465, 1385, 1120, 960, 725, 630 cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 1.27 (m, 20 H), 1.57 (m, 4 H), 1.94 (t, 1 H, J = 2.6), 2.19 (dt, 2 H, J = 2.6, 7.0), 3.34 (s, 3 H), 3.37 (t, 2 H, J = 6.5).

^{13}C NMR ($CDCl_3$/TMS): δ = 18.40, 26.15, 28.52, 28.76, 29.09, 29.49, 29.58, 58.46, 67.98, 72.98, 84.76.

MS (EI): m/z (%) = 252 (M^+, 1), 135 (8), 121 (11), 107 (14), 97 (20), 96 (25), 95 (40), 85 (21), 83 (25), 82 (48), 81 (67), 69 (36), 68 (36), 67 (62), 55 (69), 45 (100).

1-Benzyloxy-16-heptadecyne (10i):
In a 1 L 3-necked round-bottom flask, equipped with a magnetic stirrer, thermometer and a reflux condenser, 1,3-diaminopropane (300 mL) was placed and a suspension of KH (20% in mineral oil, 22.4 g, 112 mmol) was slowly introduced within a 1 h period at r.t. After 2.0 h a solution of 1-benzyloxy-15-heptadecyne (**24**; 22.0 g, 64.2 mmol) in 1,3-diaminopropane (60 mL) was added in 5 min then after a further 5 min period, H_2O (100 mL) was added. The aqueous layer was extracted with hexane (4 × 200 mL), the combined organic phase was washed with 15% aq H_2SO_4 (100 mL), sat. aq $NaHCO_3$ (2 × 100 mL) and dried (Na_2SO_4). The solvent was removed on a rotary evaporator and the colorless residue (46.0 g) was chromatographed on silica gel (250 g). Hexane (750 mL) eluted the mineral oil coming from the KH suspension. Elution with benzene/cyclohexane (15:85) (1.5 L) resulted in 21.5 g of a white solid. Recrystallization from hexane (200 mL) at −30°C afforded finally 19.1 g (87%) of pure 1-benzyloxy-16-heptadecyne **(10i)** as white crystals (GC: 99.4% pure, I_{220} = 2594); mp 34.0–34.5°C.

IR (CCl_4/CS_2): ν = 3310, 3090, 3070, 3030, 2930, 2850, 2120, 1495, 1455, 1360, 1100, 1030, 735, 695, 630 cm^{-1}.

^1H NMR($CDCl_3$/TMS): δ = 1.26 (m, 22 H), 1.54 (m, 4 H), 1.95 (t, 1 H, J = 2.6), 2.19 (dt, 2 H, J = 2.6, 7.0), 3.47 (t, 2 H, J = 6.6), 4.51 (s, 2 H), 7.34 (m, 5 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 18.39, 26.21, 28.51, 28.76, 29.09, 29.48, 29.59, 29.63, 29.78, 68.00, 70.55, 72.84, 84.74, 127.40, 127.56, 128.29, 138.82.

MS (EI): m/z (%) = 342 (M^+, 6), 341 (5), 145 (5), 133 (11), 120 (12), 107 (20), 95 (14), 92 (35), 91 (100), 81 (19), 69 (14), 67 (15), 55 (24).

19,24-Dioctadecyl-17-dotetracontyn-19-ol (11a):
In a 1 L 3-necked round-bottom flask equipped with a magnetic stirrer, reflux condenser and a thermometer 1-octadecyne (**10a**; 3.07 g, 12.3 mmol) was dissolved in anhydr. THF (500 mL) under Ar. The solution was cooled to −20°C (ice/salt bath) and BuLi 1.6 M in hexane (7.6 mL, 12.2 mmol) was added within 5 min then the mixture was allowed to warm to r.t. in about 1 h. Solid ketone **9** (8.50 g, 9.91 mmol) was then added portionwise in 10 min at the same temperature whereby a white suspension resulted which turned to a clear solution within 30 min. The mixture was then hydrolyzed with sat. aq NH_4Cl (200 mL) and Et_2O (200 mL) was added. The aqueous phase was extracted with cyclohexane (2 × 50 mL) and the combined organic phase was dried (Na_2SO_4). The solvent was

distilled on a rotary evaporator and the residue (12.18 g) was chromatographed on silica gel (240 g) with benzene/cyclohexane (15:85) (1.2 L) as mobile phase. The white residue (8.82 g) was recrystallized from EtOAc (450 mL) to give the ynol **11a** (7.36 g, 67%); mp 54–56 °C.

Propargylic Alcohols 11b, c, i; General Procedure

The alkyne **10b, c, i** (1.10 equiv) dissolved in anhydr. THF (16 mL/mmol alkyne **10**) was cooled to – 20 °C (ice/salt bath), BuLi 1.6 M in hexane (1.2 equiv) was added within 10 min and the mixture was allowed to warm to r.t. (in the case of alkyne **10b** BuMgBr, 1.10 equiv, was added at r.t. and the mixture was refluxed for 2 h and allowed to cool to r.t.). Solid ketone **9** (1.00 equiv) was added at the same temperature in 15 min. The initial white suspension turned to a clear solution after 30 min. The solution was left at r.t. for 5 h, then hydrolyzed with sat. aq NH_4Cl (6 mL/mmol alkyne **10**) and diluted with Et_2O (10 mL/mmol **10**). The aqueous phase was dried (Na_2SO_4). Distillation of the solvent on a rotary evaporator afforded the crude ynols **11b, c, i** that were purified by specific methods described below.

1,1,1-Trifluoro-19,24-dioctadecyl-17-dotetracontyn-19-ol **(11b)**

From 1,1,1-trifluoro-17-octadecyne (**10b**; 2.37 g, 7.80 mmol) in anhydr. THF (100 mL), BuMgBr prepared from BuBr (2.74 g, 20.0 mmol) and Mg (0.97 g, 40 mmol) in anhydr. THF (20 mL), and ketone **9** (6.00 g, 7.00 mmol). The mixture was left overnight at r.t. then hydrolyzed. The crude ynol **11b** (8.55 g) was chromatographed on silica gel (100 g). Cyclohexane/benzene (95:5) (300 mL) eluted 1.1 g (mixture of alkyne **10b** and ketone **9**). Elution with cyclohexane/Et_2O (90:10) (600 mL) afforded ynol **11b** (7.65 g) that was recrystallized from EtOH/hexane (75:25) (200 mL) at 0 °C to give 6.91 g (85%) of pure ynol **11b**; mp 43–44.5 °C.

1-Methoxy-17,22-dioctadecyl-15-tetracontyn-17-ol **(11c)**:

From 1-methoxy-15-hexadecyne (**10c**; 3.61 g, 14.3 mmol) in anhydr. THF (250 mL), BuLi (15.1 mL, 15.6 mmol) and ketone **9** (11.15 g, 13.00 mmol). The ynol was chromatographed on silica gel (100 g). Elution with cyclohexane/benzene (85:15) (500 mL) afforded 4.31 g of a mixture of unreacted ketone **9** and ynol **11c**. Elution with cyclohexane/Et_2O (90:10) afforded 9.98 g of ynol **11c** containing the excess 1-methoxy-15-hexadecyne. The first fraction was again chromatographed on silica gel (50 g). A mixture of cyclohexane/benzene (95:5) (450 mL) eluted 0.53 g (0.62 mmol) of ketone **9**. Finally elution with cyclohexane/Et_2O (90:10) (400 mL) gave 3.89 g of ynol **11c**. The total amount of ynol **11c** (13.87 g) obtained in the two chromatographic separations was recrystallized from EtOH/hexane (2:1) (260 mL) at 5 °C to give 13.20 g (91%) of pure propargylic alcohol **11c**; mp 43–47 °C.

1-Benzyloxy-18,23-dioctadecyl-16-hentetracontyn-18-ol **(11i)**:

From 1-benzyloxy-16-heptadecyne (**10i**; 10.98 g, 32.06 mmol) in anhydr. THF (500 mL), BuLi (22.5 mL, 36.0 mmol) and ketone **9** (25.0 g, 29.2 mmol). The crude ynol **11i** was recrystallized twice from Et_2O/MeOH (3:2, 750 mL each time) to give 32.9 g (94%) of pure white alcohol **11i**; mp 44–49 °C.

19,24-Dioctadecyl-19-dotetracontanol (12a):

In a 250 mL autoclave a solution of ynol **11a** (4.00 g, 3.61 mmol) in cyclohexane (75 mL) was placed together with 10% Pd–C (0.47 g) and the agitated mixture was hydrogenated at 40 °C under 12 bar H_2 pressure for 20 h. The mixture was then allowed to cool to r.t. and the catalyst was removed by filtration on a silica gel column (70 g). After elution with further cyclohexane/Et_2O (1:1) (250 mL) the solvent was evaporated (rotary evaporator) and the white solid residue (3.9 g) was recrystallized from cyclohexane/EtOAc (2:8) (56 mL) to give the alcohol **12a** as a white powder (2.82 g, 70%); mp 67–71 °C.

Tertiary Alcohols 12b–d; General Procedure:

In a stainless steel autoclave a solution of ynol **11b, c, i** in cyclohexane (50 mL/mmol ynol) was placed together with 10% Pd C (0.12 g/mmol ynol). The well-stirred mixture was hydrogenated at 40 °C under 10–15 bar H_2 pressure for 20 h. The mixture was allowed to cool to r.t. and the catalyst was filtered on a silica gel column (5 g/g alcohol **11**) with Et_2O/cyclohexane (1:1) as mobile phase. Distillation of the solvent on a rotary evaporator afforded the crude tertiary alcohols **12b–d** that were purified by methods indicated in the following descriptions.

1,1,1-Trifluoro-19,24-dioctadecyl-19-dotetracontanol **(12b)**:

From ynol **11b** (6.91 g, 5.95 mmol) in cyclohexane (400 mL) and 10% Pd–C (0.50 g). The crude alcohol **12b** (7.13 g) was recrystallized from EtOH/hexane (5:2) (210 mL) to give 6.79 g (98%) of pure tertiary alcohol **12b**; mp 63–65 °C.

1-Methoxy-17,22-dioctadecyl-17-tetracontanol **(12c)**:

From ynol **11c** (12.21 g, 11.00 mmol) in cyclohexane (400 mL) and 10% Pd–C (0.56 g). The crude tertiary alcohol **12c** was recrystallized from EtOH/hexane (2:1) (300 mL) at 5 °C to give 12.1 g (99%) of pure methoxyalcohol **12c**; mp 69.0–72.5 °C.

18,23-Dioctadecyl-1,18-hentetracontanediol **(12d)**:

From ynol **11i** (22.0 g, 18.3 mmol) in cyclohexane (900 mL) and 10% Pd–C (2.17 g). The crude tertiary alcohol **12d** was recrystallized twice from EtOAc to give 19.0 g (93%) of pure diol **12d**; mp 66–69 °C.

19,24-Dioctadecyl-19-dotetracontene (13):

In a 100 mL 3-necked round-bottom flask equipped with a magnetic stirrer, thermometer and a Dean-Stark trap a solution of *p*-TsOH · H_2O (0.24 g, 1.25 mmol) in benzene (70 mL) was introduced and refluxed for 30 min. The mixture was allowed to cool, alcohol **12a** (1.53 g, 1.38 mmol) was added and the solution was refluxed for 2 h. The mixture was cooled to r.t. and diluted with Et_2O (50 mL). The organic phase was washed with sat. aq $NaHCO_3$ (2 × 50 mL) and dried (Na_2SO_4). The solvent was distilled on a rotary evaporator and the slightly yellow solid residue was filtered on silica gel (34 g) with hexane (500 mL) to give a white solid (1.42 g). Recrystallization from EtOAc (80 mL) gave 1.15 g (76%) of white solid composed of all possible isomers of unsaturated compound **13** (19,24-dioctadecyl-19-dotetracontene, *cis* and *trans*-19,24-dioctadecyl-18-dotetracontene); mp 55–57.5 °C.

18,18,18-Trifluoro-1-octadecanol (15):

In a 500 mL conical flask, 18,18,18-trifluorooctadecyl acetate (**14**; 19.06 g, 52.0 mmol) was dissolved in 94% EtOH (300 mL) and a solution of NaOH (4.16 g, 104 mmol) in H_2O (20 mL) was added. After about 1.5 h at r.t., when the alcohol **15** started to crystallize, H_2O (30 mL) was added and the mixture was cooled to + 5 °C to complete crystallization. The solid was filtered, washed with cold 80% EtOH (50 mL) and finally recrystallized from hexane to give 16.5 g (98%) of pure alcohol **15** as white crystals; mp 65–65.5 °C. (GC: 99.6% pure, $I_{220} = 2026$).

IR (CCl_4/CS_2): ν = 3630, 2930, 2850, 1465, 1385, 1255, 1145, 1050, 840, 725, 655 cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 1.27 (m, 24 H), 1.31 (m, 2 H), 1.46 (m, 4 H), 2.08 (m, 2 H), 3.65 (t, 2 H, J = 6.5).

^{13}C NMR ($CDCl_3$/TMS): δ = 21.84 (q, J = 2.9), 25.76, 28.70, 29.16, 29.34, 29.44, 29.53, 29.64, 32.83, 33.75 (q, J = 28), 63.04, 127.32 (q, J = 276).

MS (EI): m/z (%) = 323 ($M^+ - 1$, 1), 306 (20), 278 (13), 264 (2), 153 (10), 139 (13), 125 (19), 111 (35), 98 (21), 97 (69), 84 (38), 83 (100), 70 (56), 69 (90), 55 (97), 43 (74).

18-Bromo-1,1,1-trifluorooctadecane (16):

In a 250 mL round-bottom flask alcohol **15** (13.84 g, 42.7 mmol) and Ph_3P (13.43 g, 51.2 mmol) were dissolved in CH_2Cl_2 (130 mL). The mixture was cooled to 0 °C (ice bath) and solid NBS (9.11 g, 51.2 mmol) was added in small portions within 5 min. After 15 min at the same temperature, absolute EtOH (20 mL) was added to destroy excess NBS and the solvent was removed on a rotary evaporator. The dark red solid residue (37.5 g) was dissolved in 94% weight EtOH (130 mL) and cooled to + 5 °C. The crystals (15.53 g) were collected and washed with cold 94% EtOH (50 mL). The mother liquor was cooled to – 30 °C to give a further 0.64 g of pink crystals. The crude bromide, **16** (16.17 g), was recrystallized from 94% EtOH (140 mL) at – 30 °C to give 15.63 g (94%) of pure

colorless bromide **16**; mp 29.5–30.0 °C. (GC: 99.4% pure, $I_{220} = 2134$).

IR (CCl_4/CS_2): ν = 2930, 2850, 1465, 1385, 1255, 1145, 840, 725, 655 cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 1.27 (m, 26 H), 1.55 (m, 2 H), 1.87 (quint., 2 H, J = 7.0), 2.07 (m, 2 H), 3.42 (t, 2 H, J = 6.9).

^{13}C NMR ($CDCl_3$/TMS): δ = 21.85 (q, J = 2.9), 28.20, 28.71, 28.78, 29.18, 29.36, 29.44, 29.54, 29.61, 32.89, 33.77 (q, J = 28), 33.83, 127.32 (q, J = 276).

MS (EI): m/z (%) = 388 (M^+ + 2, 2), 386 (2), 307 (5), 151 (12), 149 (15), 137 (68), 135 (72), 97 (12), 85 (28), 83 (22), 71 (51), 69 (44), 57 (100), 55 (61), 43 (93), 41 (45).

1,1,1-Trifluoro-17-octadecene (17):

In a 100 mL round-bottom flask 1,1,1-trifluoro-18-octadecyl bromide (**16**; 11.62 g, 30.0 mmol) and 18-crown-6 (0.19 g, 0.72 mmol) were dissolved in cyclohexane (50 mL) and KOBu-*t* (8.08 g, 72.0 mmol) was added. The mixture was refluxed for 30 min, allowed to cool to r.t. and H_2O (50 mL) was added followed by Et_2O (50 mL). The organic layer was washed with H_2O (100 mL) and the combined aqueous phase was extracted with Et_2O (50 mL). The combined organic phase was dried (Na_2SO_4) and the solvent was removed on a rotary evaporator to give 9.62 g of a pale yellow liquid. Filtration on a silica gel column (50 g) with hexane as mobile phase (200 mL) gave 7.45 g (81%) of pure trifluoroalkene **17** as a colorless liquid (GC: 98.7% pure, $I_{200} = 1744$). Elution with hexane/Et_2O (90:10) (300 mL) gave 2.07 g (18%) of a second fraction: 1-*tert*-butoxy-18,18,18-trifluorooctadecane (GC: 97% pure, $I_{220} = 2131$); mp 62.5–64.5 °C.

IR (film): ν = 3070, 2920, 2850, 1640, 1470, 1440, 1390, 1255, 1145, 1050, 910, 840, 725, 655 cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 1.27 (m, 24 H), 1.56 (m, 2 H), 2.04 (m, 4 H), 4.93 (ddt, 1 H, J = 10.3, 2.1, 1.2), 5.00 (ddt, 1 H, J = 17.1, 2.1, 1.5), 5.83 (ddt, 1 H, J = 17.1, 10.3, 6.6).

^{13}C NMR ($CDCl_3$/TMS): δ = 21.87 (q, J = 2.9), 28.73, 29.00, 29.18, 29.37, 29.52, 29.56, 29.63, 29.66, 33.78 (q, J = 28), 33.82, 114.05, 127.33 (q, J = 276), 139.22.

MS (EI): m/z (%) = 306 (M^+, 12), 278 (3), 193 (5), 179 (6), 165 (6), 111 (23), 98 (16), 97 (55), 84 (31), 83 (76), 70 (53), 69 (72), 57 (72), 56 (67), 55 (100), 43 (91), 41 (71).

1-tert-Butoxy-18,18,18-trifluorooctadecane:

IR (film): ν = 2920, 2850, 1465, 1440, 1390, 1360, 1335, 1315, 1255, 1140, 1115, 720, 655 cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 1.26 (m, 35 H), 1.57 (m, 4 H), 2.06 (m, 2 H), 3.40 (t, 2 H, J = 6.7).

^{13}C NMR ($CDCl_3$/TMS): δ = 21.86 (q, J = 3.0), 26.25, 27.60, 28.73, 29.19, 29.37, 29.56, 29.63, 29.67, 29.84, 30.80, 33.78 (q, J = 28), 61.69, 70.99, 127.33 (q, J = 276).

MS (EI): m/z (%) = 307 (M^+ − *t*-BuO, 30), 306 (7), 237 (5), 167 (8), 113 (9), 111 (14), 99 (14), 97 (28), 85 (36), 83 (42), 71 (59), 69 (38), 57 (100), 55 (38), 43 (65).

15-Hexadecen-1-ol (19):

In a 500 mL conical flask 15-hexadecenyl acetate (**18**; 8.47 g, 30.0 mmol) was dissolved in 94% weight EtOH (170 mL) and a solution of NaOH (2.40 g, 60.0 mmol) in H_2O (10 mL) was added at r.t. The mixture was left for 20 h at this same temperature, then it was diluted with H_2O (200 mL) and extracted with Et_2O (100 mL). The organic phase was washed with H_2O (2 × 100 mL) and brine (100 mL). The aqueous phase was extracted with Et_2O (2 × 100 mL) and the combined organic phase was dried (Na_2SO_4). The solvent was eliminated on a rotary evaporator and the residue was recrystallized from hexane at 0 °C to give 6.52 g (90%) of the pure alcohol, **19** (GC: 98.7% pure, $I_{200} = 1866$); mp 37–38 °C.

IR (CCl_4/CS_2): ν = 3615, 3300, 3075, 2915, 2850, 1640, 1465, 1050, 990, 910, 720, 635 cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 1.27 (m, 22 H), 1.58 (m, 2 H), 2.05 (q, 2 H, J = 6.2), 3.65 (t, 2 H, J = 6.5), 4.94 (ddt, 1 H, J = 10.2, 2.1, 1.2), 5.00 (ddt, 1 H, J = 17.0, 2.1, 1.5), 5.83 (ddt, 1 H, J = 17.0, 10.2, 6.6).

^{13}C NMR ($CDCl_3$/TMS): δ = 25.75, 28.94, 29.13, 29.42, 29.48, 29.59, 29.63, 32.81, 33.78, 63.00, 114.03, 139.20.

MS (EI): m/z (%) = 240 (M^+, 0.1), 222 (3), 124 (11), 123 (10), 110 (18), 109 (17), 97 (22), 96 (53), 95 (34), 83 (37), 82 (79), 81 (46), 69 (51), 68 (52), 67 (42), 55 (100), 43 (33), 41 (62).

1-Methoxy-15-hexadecene (20):

In a 100 mL 3-necked round-bottom flask, equipped with a reflux condenser and a dropping funnel, Mg (0.97 g, 40 mmol) was covered with anhydr. THF (30 mL) and activated with 1,2-dibromoethane (0.47 g, 2.5 mmol). A solution of BuBr (4.11 g, 30.0 mmol) in anhydr. THF (10 mL) was then introduced dropwise over a 15 min period and the mixture was heated to reflux for 2 h. In another 250 mL 3-necked round-bottom flask, equipped with a reflux condenser and a dropping funnel, 15-hexadecenol (**19**; 6.01 g, 25.0 mmol) was dissolved in anhydr. THF (25 mL) and $(MeO)_2SO_2$ (7.57 g, 60.0 mmol) was added in one portion. The Grignard reagent was transferred to the dropping funnel and added to this solution within 10 min. The mixture was refluxed for 24 h, allowed to cool to r.t. and hydrolyzed with sat. aq $NaHCO_3$ (100 mL). The aqueous phase was extracted with Et_2O (2 × 100 mL) and the combined organic phase was dried (Na_2SO_4). The solvent was removed on a rotary evaporator. Chromatography of the residue on silica gel (80 g) with benzene/hexane (50:50, 300 mL) as mobile phase gave after evaporation of the solvent 5.90 g (93%) of methoxyalkene **20** as a colorless liquid (GC: 98.5% pure, $I_{200} = 1810$).

IR (film): ν = 3080, 2920, 2850, 1640, 1465, 1390, 1120, 995, 910, 725, 635 cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 1.26 (m, 22 H), 1.58 (m, 2 H), 2.05 (q, 2 H, J = 6.6), 3.34 (s, 3 H), 3.37 (t, 2 H, J = 6.5), 4.93 (ddt, 1 H, J = 10.3, 2.2, 1.2), 5.00 (ddt, 1 H, J = 17.0, 2.2, 1.6), 5.83 (ddt, 1 H, J = 17.0, 10.3, 6.6).

^{13}C NMR ($CDCl_3$/TMS): δ = 26.15, 28.97, 29.15, 29.50, 29.60, 29.65, 33.80, 58.47, 72.99, 114.04, 139.23.

MS (EI): m/z (%) = 254 (M^+, 1), 222 (7), 138 (6), 137 (6), 124 (11), 123 (10), 110 (18), 109 (17), 97 (24), 96 (59), 95 (34), 83 (42), 82 (100), 81 (48), 71 (24), 69 (49), 68 (49), 55 (88), 45 (86), 43 (29), 41 (62).

16-Heptadecen-1-ol (22):

In a 250 mL 3-necked round-bottom flask Mg (4.5 g, 0.19 mol) was covered with anhydr. THF (150 mL) and in an Ar atmosphere activated with 1,2-dibromoethane (3.5 g, 20.0 mmol). A solution of 10-undecenyl bromide (**21**; 30.78 g, 0.132 mol) in anhydr. THF (50 mL) was then added at a rate as to maintain a gentle reflux (ca. 30 min). The mixture was refluxed for further 1 h, cooled to r.t. and transferred to a dropping funnel attached to a 500 mL 3-necked round-bottom flask containing 6-iodohexyl acetate (32.05 g, 0.120 mol) and CuBr (0.21 g, 1.5 mmol) dissolved in anhydr. THF (100 mL). The mixture was cooled to − 30 °C and the Grignard reagent was added dropwise over a 90 min period while maintaining the temperature between − 25 and − 30 °C. The dark blue mixture was warmed to − 10 °C, stirred for 90 min and warmed to + 10 °C where it was hydrolyzed with sat. aq NH_4Cl (100 mL). The aqueous phase was extracted with hexane (3 × 50 mL) the combined organic phase was dried (Na_2SO_4) and the solvent was removed in a rotary evaporator. The yellow liquid residue (38.7 g) was filtered on silica gel (50 g) with EtOAc as mobile phase, the solvent was removed and the colorless liquid (37.9 g) was dissolved in 94% weight EtOH (380 mL). To this solution 45% aq NaOH (30 mL) was added, the mixture was stirred for 3 h at r.t., then Et_2O (1.0 L) was added. The organic phase was separated, washed with H_2O (200 mL), brine (200 mL) and dried (Na_2SO_4). Distillation of the solvent on a rotary evaporator gave 33.0 g of a pale yellow liquid. Chromatography on silica gel (165 g) with hexane (800 mL) and with hexane/Et_2O (1:1, 500 mL) gave respectively 2.28 g of an unidentified first fraction and 29.3 g of 16-heptadecen-1-ol (**22**). Two recrystallizations from hexane afforded 23.9 g (79%) of pure alcohol **22** (GC: 98.5% pure, $I_{200} = 1969$); mp 44.5–45.5 °C.

IR (CCl_4/CS_2): ν = 3630, 3400, 3080, 2930, 2860, 1640, 1465, 1050, 995, 910, 785, 765, 745 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.26 (m, 24 H), 1.57 (m, 2 H), 2.05 (q, 2 H, J = 6.6), 3.65 (t, 2 H, J = 6.5), 4.93 (ddt, 1 H, J = 10.2, 2.2, 1.2), 5.00 (ddt, 1 H, J = 17.0, 2.2, 1.6), 5.83 (ddt, 1 H, J = 17.0, 10.2, 6.7).

^{13}C NMR ($CDCl_3$/TMS): δ = 25.76, 28.96, 29.15, 29.43, 29.50, 29.60, 29.65, 32.84, 33.79, 63.04, 114.04, 139.22.

MS (EI): m/z (%) = 254 (M^+, 0.1), 236 (4), 138 (7), 137 (6), 124 (12), 123 (11), 110 (20), 109 (18), 97 (25), 96 (59), 95 (35), 83 (41), 82 (83), 81 (46), 69 (54), 68 (50), 67 (41), 57 (26), 55 (100), 41 (60).

16-Heptadecyn-1-ol (23):[17,23]

In a 500 mL 3-necked round-bottom flask equipped with a mechanical stirrer, thermometer and a reflux condenser a solution of 16-heptadecen-1-ol (**22**; 16.45 g, 64.6 mmol) in CCl_4 (300 mL) was cooled to 0 °C (ice bath). A solution of Br_2 (10.9 g, 68.2 mmol) in CCl_4 (40 mL) was then added dropwise within 2 h. After 15 min at 0 °C the excess Br_2 was reduced with 5% aq $Na_2S_2O_3$ (50 mL). The organic phase was washed with sat. aq $NaHCO_3$ (2 × 50 mL) and dried (Na_2SO_4). The solvent was removed on a rotary evaporator and the white solid residue (30.2 g) was recrystallized twice from hexane (300 mL each time) to give 24.3 g (91%) of 16,17-dibromo-1-heptadecanol; mp 44–46 °C.

In a 1 L 3-necked round-bottom flask equipped with a mechanical stirrer, a thermometer and a reflux condenser a solution of 16,17-dibromo-1-heptadecanol (24.3 g, 58.7 mmol) and KOH (47.0 g, 0.84 mol) in abs. EtOH (500 mL) was refluxed for 16 h, then H_2O (100 mL) was added and EtOH was partly distilled off (350 mL). The concentrated mixture was cooled to r. t. and extracted with cyclohexane (3 × 125 mL) and Et_2O (2 × 80 mL). The combined organic phase was dried (Na_2SO_4) and the solvent was removed on a rotary evaporator to give 18.4 g of a mixture of 16-heptadecyn-1-ol (**23**; 76%) and (*E*)-17-bromo-16-heptadecen-1-ol (24%). This mixture was transferred to a 2.0 L 3-necked round-bottom flask containing BrMgNPr-i_2 prepared from BuBr (40.1 g, 251 mmol), Mg (7.12 g, 293 mmol) and i-Pr_2NH (4.19 g, 41.4 mmol) in anhydr. THF (800 mL) (*vide supra*, alkyne **10b**). The mixture was refluxed for 4 h, cooled to r. t. and hydrolyzed with brine (170 mL). The aqueous phase was extracted with Et_2O (2 × 80 mL), the combined organic phase was washed with sat. aq $NaHCO_3$ (2 × 80 mL) and dried (Na_2SO_4). The solvent was removed on a rotary evaporator and the residue (14.2 g) was distilled in a Kugelrohr at 175 °C/6.6 × 10^{-2} mbar to give 12.38 g of a white solid. Recrystallization from Et_2O (125 mL) at −30 °C gave 11.14 g (64%) of pure 16-heptadecynol (**23**, GC: 99.9% pure, I_{200} = 1990); mp 56–57 °C.

IR (CCl_4/CS_2): ν = 3630, 3310, 2930, 2860, 2120, 1465, 1250, 1050, 725, 630 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.27 (m, 24 H), 1.54 (m, 2 H), 1.95 (t, 1 H, J = 2.7), 2.19 (dt, 2 H, J = 2.6, 7.0), 3.65 (t, 2 H, J = 6.5).

^{13}C NMR ($CDCl_3$/TMS): δ = 18.36, 25.72, 28.48, 28.72, 29.06, 29.40, 29.45, 29.56, 29.59, 32.79, 62.97, 67.97, 84.72.

MS (EI): m/z (%) = 252 (M^+, 0.004), 135 (5), 124 (4), 121 (7), 110 (8), 109 (15), 97 (15), 96 (36), 95 (43), 83 (24), 82 (60), 81 (89), 79 (22), 69 (44), 68 (37), 67 (76), 57 (19), 55 (100), 43 (40), 41 (78).

1-Benzyloxy-15-heptadecyne (24):

In a 1 L 3-necked round-bottom flask equipped with a magnetic stirrer, thermometer and a reflux condenser NaH (20% in mineral oil, 2.0 g, 83.3 mmol) was placed and the oil was removed by washing with hexane (3 × 25 mL). The hydride was covered with anhydr. DMF (250 mL), the mixture was cooled to −20 °C (ice/salt bath) and a solution of the ynol **23** (19.8 g, 78.4 mmol) in anhydr. DMF (100 mL) was added within 15 min. The mixture was stirred for further 5 min before introducing a solution of BnBr (14.2 g, 83.0 mmol) in anhydr. DMF (100 mL). The cold reaction mixture was now stirred for 15 min then it was allowed to warm to r. t. where it turned brown. After 5 h the mixture was hydrolyzed with sat. aq NH_4Cl (200 mL), 15% aq H_2SO_4 (150 mL) and diluted with hexane (200 mL). The aqueous phase was extracted with Et_2O (2 × 100 mL) then hexane (3 × 150 mL); the combined organic phase was washed with sat. aq $NaHCO_3$ (100 mL), dried (Na_2SO_4) and the solvent was removed in a rotary evaporator. The residue (25.5 g) was submitted to column chromatography on silica gel (200 g) with benzene/cyclohexane (15:85) (2.0 L) as mobile phase. After removal of the solvent the white solid residue (21 g) was recrystallized from hexane (250 mL) at −30 °C to give 20.8 g (77%) of pure benzyl ether, **24**, as white crystals (GC: 99.5% pure, I_{220} = 2640); mp 33.5–34.0 °C.

IR (CCl_4/CS_2): ν = 3090, 3060, 3030, 2930, 2850, 1495, 1455, 1360, 1205, 1105, 1030, 735, 695, 615 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.27 (m, 20 H), 1.60 (m, 4 H), 1.79 (t, 3 H, J = 2.5), 2.12 (m, 2 H), 3.47 (t, 2 H, J = 6.6), 4.51 (s, 2 H), 7.34 (m, 5 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 3.39, 18.74, 26.21, 28.91, 29.12, 29.17, 29.48, 29.54, 29.60, 29.63, 29.79, 70.56, 75.23, 79.40, 127.40, 127.57, 128.30, 138.83.

MS (EI): m/z (%) = 342 (M^+, 13), 341 (6), 327 (3), 159 (5), 147 (16), 143 (14), 131 (7), 109 (8), 107 (19), 95 (20), 92 (27), 91 (100), 81 (18), 69 (14), 67 (17), 55 (25), 53 (5), 43 (11).

This paper reports on part of a Project financed by the "Fonds National Suisse de la Recherche Scientifique". The authors gratefully acknowledge help of Dr. Philippe Mussche from Chrompack (Middelburg, Holland; high temperature gas chromatography), Dr. Raymond Houriet (Laboratoire de Technologie des Poudres de l'EPFL; X-ray fluorescence), Dr. Bruno Domon (Ciba-Geigy, Basel; mass spectra) and Dr. Armin Pfenninger (Chemie Uetikon, Uetikon am See; 1-bromooctadecane).

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