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Novel Cuticular Hydrocarbons from the Cane Beetle *Antitrogus parvulus*—4,6,8,10,16-Penta- and 4,6,8,10,16,18-Hexamethyldocosanes—Unprecedented *anti-anti-anti*-Stereochemistry in the 4,6,8,10-Methyltetrad

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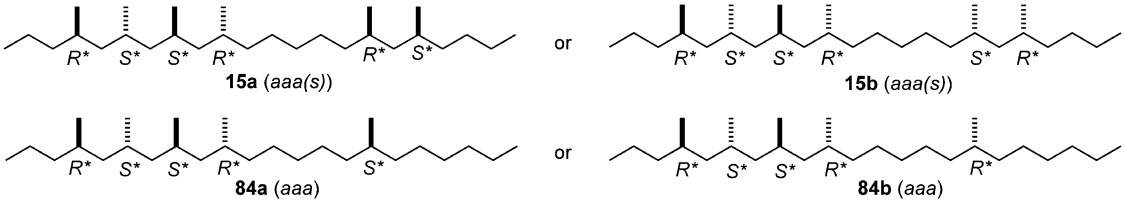

The major cuticular hydrocarbons from the cane beetle species *Antitrogus parvulus* are 4,6,8,10,-16-penta- and 4,6,8,10,16,18-hexamethyldocosanes, **1** and **2**, respectively. Stereoisomers of 2,4,6,8-tetramethylundecanal of established relative stereochemistry were derived from 2,4,6-trimethylphenol and were then coupled with appropriate methyl-substituted phosphoranes **62** and **25** to furnish alkenes, which on reduction provided diastereomers of **1** and **2**, respectively. Capillary gas chromatography, mass spectrometry, and high resolution ^{13}C NMR spectroscopy confirmed **1** as either **84a** or **84b** and **2** as either **15a** or **15b**. The novelty of these structures and their relative stereochemistry is briefly related to polyketide assembly.

Introduction

Larvae of certain melolonthine scarab beetles (known as canegrubs) are the chief pests of sugar cane crops in Australia.[1] Canegrubs feed on the roots of these plants, and the destruction of the regenerative portion of the underground stem greatly affects the ratoon crops in succeeding years. Currently, pest control is accomplished by the application of organophosphorus insecticides,[2] but problems such as insecticidal breakdown and resistance emphasize the importance of the development of environmentally benign management strategies.

Significant results have been achieved utilizing sex pheromones for monitoring and control of herbivorous scarab beetles,[3] and in principle this strategy could be applied to population control of the Australian canegrub complex. Although none of the scarab (canegrub) pheromones has been identified, the presence of such components is indicated by field studies and electron microscopy.[4] Several species of Melolonthine scarabs have been investigated initially with a focus on volatile pheromonal

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(1) Allsopp, P. G.; Chandler, K. J. *Proc. Int. Soc. Sugar-Cane Technol.* **1989**, *20*, 810.

(2) Bureau of Sugar Experiment Stations. *Australian Sugarcane Pests*; Angnew, J. R., Ed.; BSES: Indooroopilly, Australia, 1997.

(3) (a) Leal, W. S. *Annu. Rev. Entomol*. **1998**, *43*, 39. (b) Leal, W. S. *Korean J. Entomol*. **1995**, *34*, 9.

(4) (a) Allsopp, P. G. *Coleops. Bull*. **1993**, *47*, 51. (b) Allsopp, P. G.; Stickley, B. D. A. *Assessment of the Potential of Sex Pheromones as Strategic Lures for the Control of Canegrubs*; Final Report SRDC Project BS17S; 1991. (c) Allsopp, P. G. *J. Aust. Entomol. Soc*. **1990**, *29*, 261.

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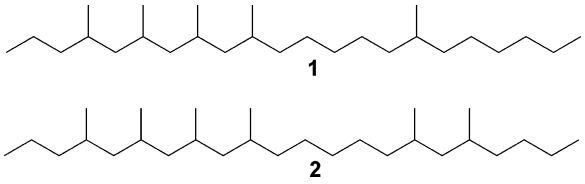
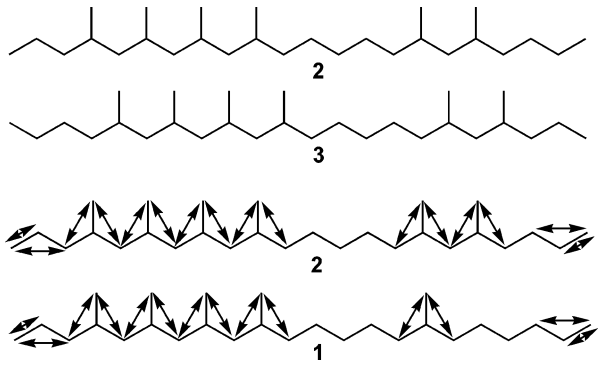
components, and this investigation has led to the report of novel long-chain allenic hydrocarbons.[5] In contrast, these components were at trace levels only, in the cuticular extract of one species, *Antitrogus parvulus*, but two new abundant hydrocarbons were detected and their constitutions and relative stereochemistry were determined.[6] In the present report, we describe in full the identification and then the syntheses of several diastereomers of these unprecedented hydrocarbons, 4,6,8,10,-16-pentamethyl- and 4,6,8,10,16,18-hexamethyldocosanes, **1** and **2**, respectively. Gas chromatographic comparisons of the natural compounds and the synthesized isomers then defined the unusual relative stereochemistry of these hydrocarbons, **1** and **2**.



Results and Discussion

Cuticular hydrocarbons were extracted from intact adult female *Antitrogus parvulus* beetles with hexane. Initial studies by gas chromatography−mass spectrometry (GCMS) revealed two unusual compounds, as indicated by fragmentation patterns, in the ratio of 45:38. The same compounds, along with a comparable amount of 9-methylpentadocosane, were also observed in adult male beetles, but none of these was present in the larval extract. Separation of the components in the female extract was carried out by preparative gas chromatography. Molecular ions of *m/z* 380.4373 and 394.4536 (high-resolution accurate mass analyses) corresponded to the formulas $C_{27}H_{56}$ and $C_{28}H_{58}$, respectively, which excluded the presence of any common functionality or unsaturation. A number of consecutive losses of 42 amu (C_3H_6 unit) in both mass spectra indicated an alternating methyl-branching pattern. The degree of methyl substitution was originally estimated by Kováts indices (KI), which are useful in the identification of mono-, di-, tri-, and tetramethylalkanes.[7] The effect of single or multiple methyl substitution on the KI value of a linear structure varies with the positions of the substituents, but is less than that for simple homologation. For example, alkanes of *N* carbon chain length have KI values as follows: for trimethyl substitution, $100N + 70 \leq \mathrm{KI} \leq 100N + 140$, and for tetramethyl substitution, $100N + 100 \leq \mathrm{KI} \leq 100N + 160$. With the lack of literature values, it seems reasonable to assume that the KI values for pentamethyl- and hexamethylalkanes will increase in proportion. The measured KI value of $C_{27}H_{56}$ (2396) was indicative of either a pentamethyl C22 alkane or less likely a tetramethyl C23 alkane, whereas $C_{28}H_{58}$ (2424) was indicative of a hexamethyl C22 alkane or less likely a pentamethyl C23 alkane.

High resolution ^{13}C NMR spectroscopy (187 MHz) confirmed the presence of five and six methyl branches in the C27 and C28 hydrocarbons, respectively, with the requisite number of methine and methylene signals. The location of methyl branches along the C22 carbon chain was determined by a combination of mass spectral and NMR interpretation and calculation. Mass spectral data indicated that in both molecules at least three methyls were located on alternate carbons in a C5 unit. ^{13}C NMR shifts were estimated for a number of alternative structures using an equation derived from the Lindeman−Adams rule.[8] The calculations enabled the elimination of a number of possibilities, and in the case of the C28 hydrocarbon, it was further deduced that the first methyl branch from each terminus was located on the fourth carbon from one end and the fifth carbon from the other. The calculated ^{13}C NMR shifts of the two structures, **2** and **3**, which differ only in the number of methylenes at each end of the molecule, were in best agreement with the experimental data for the C28 hydrocarbon. With the full assignment of the ^1H and ^{13}C NMR spectra, assisted by some two-dimensional NMR experiments [COSY and heteronuclear single quantum coherence (HSQC)], the heteronuclear multiple bond connectivity (HMBC) spectrum indicated that methylenes located between alternate methyl branches had connections to two methyl groups. This connectivity confirmed the presence of a subunit incorporating four alternate methyl groups and a further subunit with two alternate methyl branches, with the subunits separated by methylene groups. Additionally, one of the penultimate methylene groups exhibited connectivity to the first of the four alternate methyl substituents, but the other penultimate methylene lacked connectivity to the dimethyl group, allowing differentiation between structures **2** and **3** in favor of **2**. Overall, the ^{13}C NMR shift calculations and the mass spectral fragmentation pattern indicate the C28 hydrocarbon is an isomer of 4,6,8,10,16,18-hexamethyldocosane, **2**, and the C27 hydrocarbon is an isomer of 4,6,8,10,16-pentamethyldocosane, **1**, on the basis of similar strategies. The extreme similarity in the ^1H and ^{13}C NMR shifts of the tetramethyl unit of both hydrocarbons is to be noted and could reflect the same relative stereochemistry within that fragment of the molecules.



1,3-Dimethylated alkyl fragments are found in propionate-derived natural products, and two such structurally relevant compounds, **4** and **5**, are shown below. Both have an *all-syn* relationship of the pendant methyl groups and

(5) McGrath, M. J.; Fletcher, M. T.; König, W. A.; Moore, C. J.; Cribb, B. W.; Allsopp, P. G.; Kitching, W. *J. Org. Chem*. **2003**, *68*, 3739.

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(7) (a) Katritzky, A. R.; Chen, K.; Maran, U.; Carlson, D. A. *Anal. Chem*. **2000**, *72*, 101. (b) Carlson, D. A.; Bernier, U. R.; Sutton, B. D. *J. Chem. Ecol*. **1998**, *24*, 1845. (c) Khorasheh, F.; Gray, M. R.; Selucky, M. L. *J. Chromatogr*. **1989**, *481*, 1.

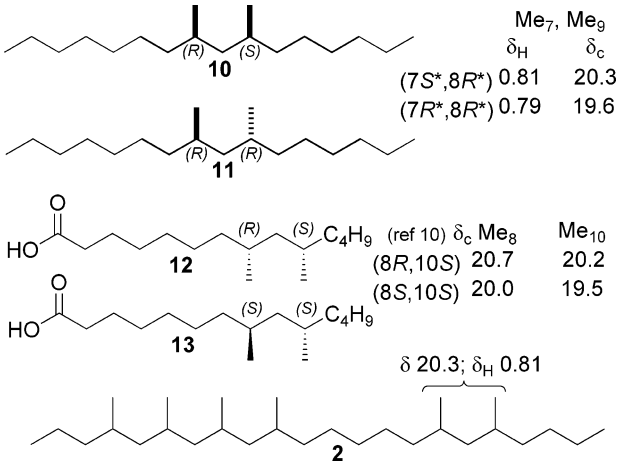
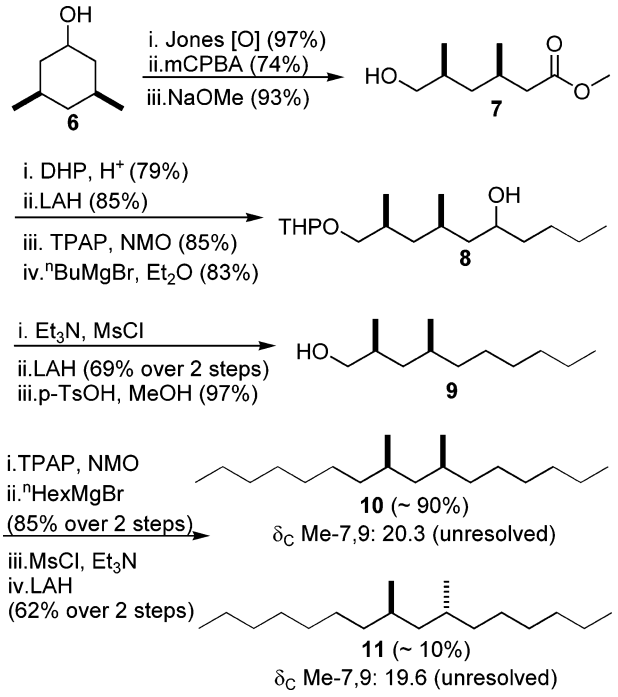


FIGURE 1. Selected ^{1}H and ^{13}C NMR data of synthetic and literature compounds bearing *syn*- and *anti*-1,3-dimethyl units.

SCHEME 1. Synthesis of *syn*- and *anti*-7,9-Dimethylhexadecane, 10 and 11



(*R*)-stereochemistry and are therefore worthy of consideration for the methyl tetrad unit in the new hydrocarbons, **1** and **2**. This possibility was heightened by our demonstration that the 16,18-dimethyl fragment in **2** was *syn*, in turn established by comparisons of methyl ^{13}C chemical shifts for *syn*- and *anti*-7,9-dimethylhexadecanes, **10** and **11** (Figure 1), respectively, acquired from predominantly *cis*- and *trans*-3,5-dimethylcyclohexanol, **6**, (~90:10) as shown in Scheme 1. The pendant methyl groups in **10** and **11** were identified by the DEPT sequence; in *syn* isomer **10**, these were unresolved at δ 20.3, and these were similarly unresolved at δ 19.6 in the *anti* isomer **11**. These trends in chemical shifts are consistent

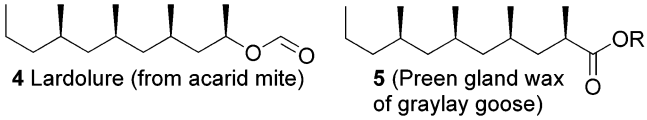
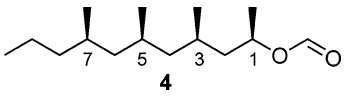


TABLE 1. High Field ^{1}H (750 MHz) and ^{13}C (187 MHz) NMR Data of Lardolure, 4



carbon number	δ_C	δ_H (*J* in Hz)
1	69.09	5.14 (m, 1H)
2	42.91	1.70 (m, 1H); 1.11 (m, 1H)
3	26.42	1.58 (m, 1H)
4	45.43	1.16 (m, 1H); 0.92 (m, 1H)
5	27.18	1.56 (m, 1H)
6	45.26	1.16 (m, 1H); 0.88 (m, 1H)
7	29.64	1.48 (m, 1H)
8	38.89	1.27 (m, 1H); 0.99 (m, 1H)
9	19.96	1.33 (m, 1H); 1.22 (m, 1H)
10	14.40	0.87 (t, *J* 7.0, 3H)
OCHO	160.98	8.04 (s, 1H)
Me-1	20.91	1.25 (d, *J* 6.2, 3H)
Me-3	20.21	0.86 (d, *J* 6.9, 3H)
Me-5	20.56	0.82 (d, *J* 6.0, 3H)
Me-7	20.36	0.83 (d, *J* 6.4, 3H)

with the calculated and experimental shifts, which were applied in the determination of the stereochemistry of two side chains in sambutoxin and the brodykinin inhibitor, L-755,897.[9] More recently, the relative (and absolute) configuration of the dimethylmyristoyl side chain of pneumocaudin B_0 was determined,[10] and the *syn* dimethyl ^{13}C NMR shifts are to a lower field (refer to **12** and **13** in Figure 1). On this basis, the 16,18-dimethyl fragment in **2** is *syn*, and this inclined us to the view that the methyl tetrad moiety may also be *all-syn*, as present in lardolure, **4**. Detailed NMR analyses and assignments of all carbon and proton signals of lardolure provided the data shown in Table 1. The data for hydrocarbons **1** and **2** are assembled in Table 2.

Comparisons of the data for **10** and **11** with those for lardolure indicated the *all-syn* arrangement was not present in the new hydrocarbons **1** and **2**. Of particular diagnostic value were the higher field chemical shifts of Me-4, 6, 8, 10 (δ 19.5−19.7) in **1** and **2** compared with Me-1, 3, 5, 7 (δ 20.2−20.9) in lardolure and also the chemical shift of C3 (δ 40.2) in **1** and **2** compared with C8 (δ 38.9) in lardolure. Studies of polymer systems with "methyl triads" in a 1,3,5-arrangement indicate that the ^{13}C shifts of pendant methyl groups are typically 0.8−1.2 ppm to a lower field when *all-syn*[11] compared with other arrangements, consistent with trends outlined above. Additionally, the methylene carbon shift (C8 in lardolure compared with C3 in **1** and **2**) is typically 1.0−1.2 ppm to a higher field in a *syn* ensemble. All of these comparisons indicate the methyl tetrad in **1** and **2** is not *all-syn*.

The foregoing analyses were applied to the methyl tetrad unit and indicated that the most favored arrange-

(8) (a) Lindeman, L. P.; Adams, J. Q. *Anal. Chem.* **1971**, *43*, 1245. (b) Wehrli, F. W.; Wirthlin, T. *Interpretation of Carbon-13 NMR Spectra*; Heydon: London, 1976; p 41.

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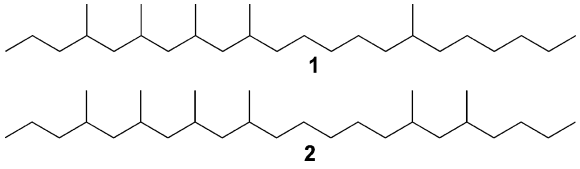
(10) Leonard, W. R.; Belyk, K. M.; Bender, D. R.; Conlon, D. A.; Hughes, D. L.; Reider, P. J. *Org. Lett.* **2002**, *4*, 4201.

(11) (a) Asakuram, T.; Ômaki, K.; Zhu, S.-N.; Chûjô, R. *Polym. J.* **1984**, *16*, 717. (b) Tonelli, A. E.; Schilling, F. C. *Acc. Chem. Res.* **1981**, *14*, 233. (c) Tonelli, A. E. *Macromolecules* **1979**, *12*, 83. (d) Provasoli, A.; Ferro, D. R. *Macromolecules* **1977**, *10*, 874.

TABLE 2. High Field ^{1}H (750 MHz) and ^{13}C (187 MHz) NMR Data of 1 and 2

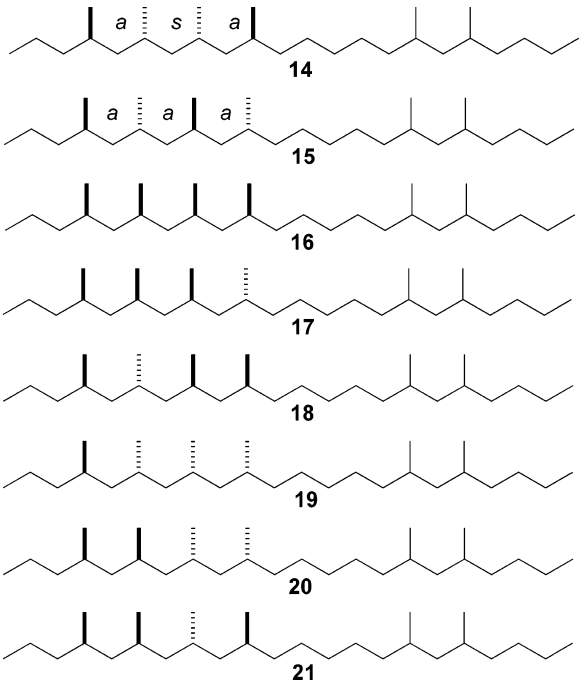


1			2		
atom number	δ_C	δ_H	atom number	δ_C	δ_H
C1	14.38	0.85	C1	14.39	0.85
C2	20.07	1.3	C2	20.08	1.3, 1.2
C3	40.22	1.2, 1.1	C3	40.22	1.2, 1.1
C4 (CH)	29.71	1.5	C4 (CH)	29.71	1.45
C5	45.55[b]	1.0	C5	45.56[c]	1.0
C6 (CH)	27.30	1.55	C6 (CH)	27.29	1.55
C7	46.54	1.0	C7	46.53	1.0
C8 (CH)	27.29	1.55	C8 (CH)	27.29	1.55
C9	45.56[b]	1.0	C9	45.54[c]	1.0
C10 (CH)	30.00	1.45	C10 (CH)	30.00	1.45
C11	37.88	1.2, 1.1	C11	37.88	1.2, 1.1
C12	27.06[d]	1.3, 1.2	C12	26.94[e]	1.3, 1.2
C13	30.34	1.2	C13	30.36	1.2
C14	27.11[d]	1.3, 1.2	C14	27.07[e]	1.3, 1.2
C15	37.09	1.25, 1.1	C15	36.88	1.25, 1.0
C16 (CH)	32.75	1.35	C16 (CH)	29.98	1.45
C17	37.09	1.25, 1.1	C17	45.22	1.2, 0.9
C18	27.04[d]	1.3, 1.2	C18 (CH)	29.98	1.45
C19	29.71	1.3, 1.2	C19	36.57	1.25, 1.0
C20	31.96	1.2	C20	29.17	1.25
C21	22.69	1.25	C21	23.07	1.25
C22	14.12	0.87	C22	14.18	0.87
Me-4, 10	19.65,[f] 19.59[f]	0.80 (d)	Me-4, 10	19.65,[g] 19.59[g]	0.79 (d)
Me-6, 8	19.56,[f] 19.55[f]	0.77 (d)	Me-6, 8	19.55,[g] 19.56[g]	0.77 (d)
Me-16	19.72	0.82 (d)	Me-16, 18	20.3, 20.3	0.81 (d)

[a–g] These chemical shift values are interchangeable.

ments were *anti-syn-anti* (*asa*) **14** or *anti-anti-anti* (*aaa*) **15**, with other arrangements **16**−**21** being improbable (all structures indicate relative stereochemistry only).

Confirmation of the constitutions and relative stereochemistry of these unusual hydrocarbons, **1** and **2**, required stereocontrolled syntheses so that spectroscopic



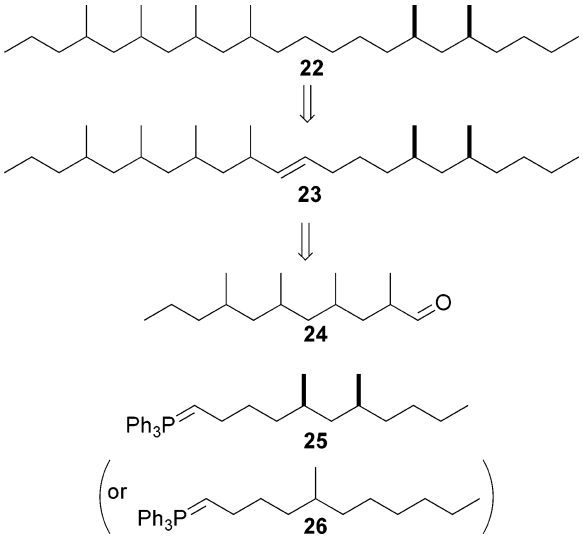


FIGURE 2. Retrosynthesis of 4,6,8,10,16-penta- and 4,6,8,-10,16,18-hexamethyldocosanes.

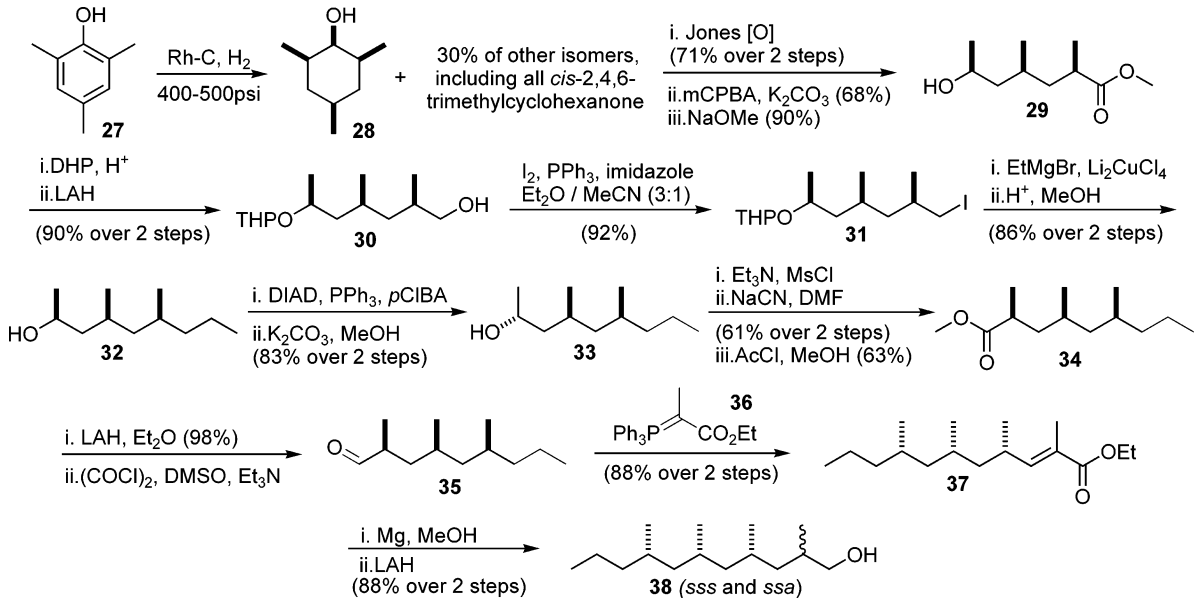
and chromatographic comparisons could be conducted. A Wittig coupling approach was adopted for the assembly of these systems, based on the disconnection shown in Figure 2. This allowed deployment of a common "tetramethyl fragment" for coupling with the mono- and dimethyl units, to furnish stereoisomers of systems **1** and **2**.

1. Synthesis of *sss*(*s*)- and *ssa*(*s*)-4,6,8,10,16,18-Hexamethyldocosanes, 16 and 17. The synthetic pathway is illustrated first for the *syn-syn-syn* (*sss*) "tetrad unit" (Scheme 2), which, although contraindicated by our analyses of ^{13}C NMR shifts, was nevertheless a precedented natural substructure and would provide valuable spectroscopic data. Reduction of 2,4,6-trimethylphenol, **27**, under forcing conditions (400−500 psi H_2) with Rh−C catalyst for 3 days afforded mainly the *all-cis* cyclohexanol **28**, together with some minor isomers (formed by stereoleakage from the desired *all-cis* hydrogenation of the phenol system), as well as the *all-cis* trimethylcyclohexanone.[12] Jones oxidation effected total conversion of the product to the cyclohexanone, with the *all-cis* isomer predominating. Baeyer−Villiger oxidation and methanolysis provided hydroxyester **29**, and after flash chromatography, the level of minor isomers did not exceed 10%, based on GCMS analyses. Protected iodo alcohol **31** experienced smooth two-carbon chain extension, followed by deprotection, secondary alcohol (Mitsunobu) inversion, and then one-carbon elongation, again with inversion, to the *all-syn* nitrile and thence to aldehyde **35**. Stabilized phosphorane coupling afforded α-methyl α,*β*-unsaturated enoate **37**, which on reduction with Mg-MeOH and LAH afforded the diastereomers *sss*- and *ssa*-2,4,6,8-tetramethylundecan-1-ol, **38**, which after oxidation (to aldehyde) were set for the crucial alkenylation-coupling reaction with *syn*-dimethyl phosphorane **25**, acquired as shown in Scheme 3 from initial processing of *cis*-3,5-dimethylcyclohexanol, **6**.

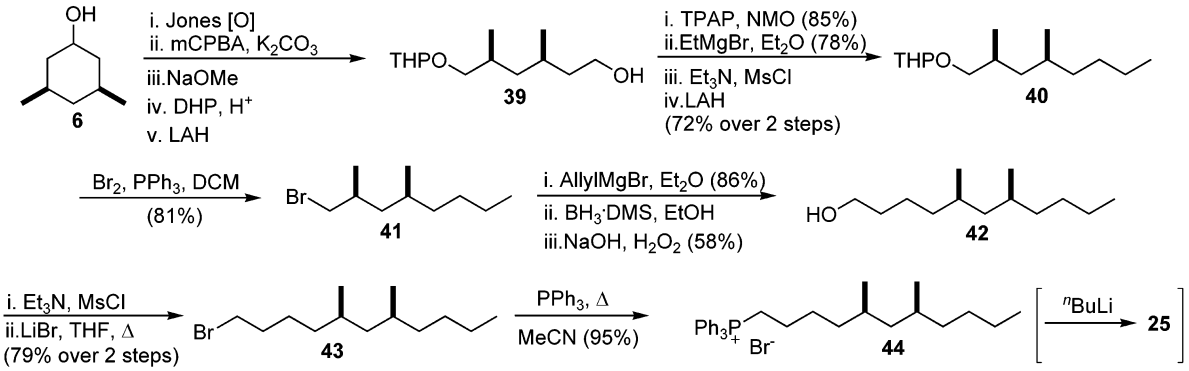
Swern oxidation of *sss*- and *ssa*-undecanol **38** afforded aldehyde **45**, which was then coupled with phos-

(12) (a) Mori, K.; Kuwahara, S. *Tetrahedron* **1986**, *42*, 5539. (b) Mori, K.; Kuwahara, S. *Tetrahedron* **1986**, *42*, 5545.

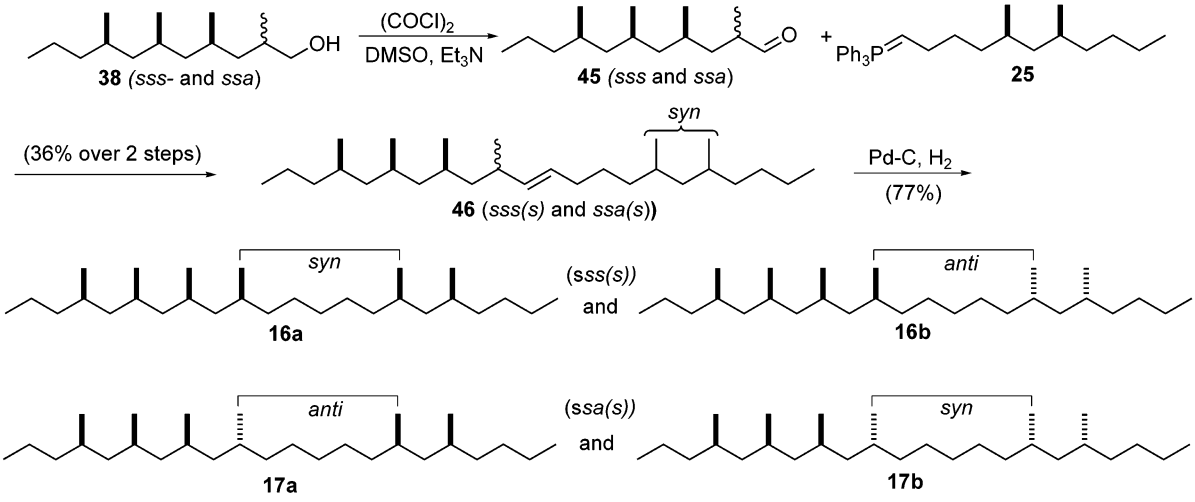
SCHEME 2. Synthesis of Tetramethylalkanol 38



SCHEME 3. Preparation of Dimethylalkyl Ylide 25



SCHEME 4. Coupling of Aldehyde 45 and the Wittig Ylide 25 in the Formation of the Hexamethyldocosanes 16 and 17



phorane **25** derived from Wittig salt **44** by deprotonation with ^{n}BuLi. Efficient coupling occurred to provide alkene **46**, which was hydrogenated under mild conditions (Pd−C, H_2, 1 atm) to provide isomers of 4,6,8,10,-16,18-hexamethyldocosane, **16** and **17**, as shown in Scheme 4.

The resulting diastereomers are grouped, in Scheme 4, into two pairs according to the stereochemistry of the "methyl tetrad". GCMS examination of the product mixture provided two peaks, one ascribed to the *sss*(*s*) pair, **16a** and **16b**, and the other to the *ssa*(*s*) pair, **17a** and **17b**, largely on the basis that the methyl tetrad is

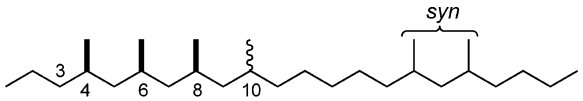
insulated by five methylene groups from the *syn* "methyl diad". The mass spectra of the two peaks were very similar, with low-abundance molecular ions (M^+ 394) and consecutive losses of 42 amu (C_3H_6), consistent with alternating methyl groups. These mass spectra closely resembled that of the natural C28 lipid, whose constitution was therefore very likely to be 4,6,8,10,16,18-hexamethyldocosane. Capillary GCMS comparisons of the synthetic mixture, which appeared as two peaks, and the natural sample revealed no coincidence, and therefore, despite the mass spectral agreement, the stereochemistry of the natural methyl tetrad was neither *syn-syn-syn* nor *syn-syn-anti.* Preparative gas chromatography, using 10% OV3 chrom P as the stationary phase, effected removal of the "Wittig dimer" (see Experimental Section for **16** and **17**) and partial separation of the synthetic mixture, with three fractions (or "slices") being collected from the broad eluant peak. The "first slice" consisted of mainly one isomer pair, and the "third slice" consisted of mainly the other isomer pair. The "central slice" contained all four isomers. Spectral data were obtained for the mixture and also for the partially separated samples.

2. NMR Analyses. The high resolution ^{13}C NMR (187 MHz) spectra of fractions 1 and 3 from preparative GC processing displayed the required number and types of signals for the hexamethyldocosane, but some signals were duplicated (and are therefore reported to three decimal places) because of the two possible arrangements of the distant *syn* methyl diad with respect to the methyl tetrad. However, it was clear that none of the synthetic diastereomers exhibited chemical shift correspondence with the natural component, as already strongly foreshadowed by the capillary GC comparisons. Nevertheless, very good ^{13}C chemical shift agreement was observed for the eastern half of *sss*(*s*)-**16** and *ssa*(*s*)-**17**, and the natural C28 component, confirming the methyl diad in the latter, is *syn*-configured, with a terminal *n*-butyl group. Some of the chemical shifts of *sss*(*s*)-**16** and *ssa*(*s*)-**17**, along with those for the natural lipid, **2,** and lardolure, **4**, are shown in Table 3.

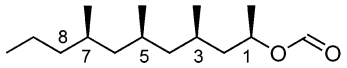
There are significant shift differences between **16** (*sss*(*s*)), **17** (*ssa*(*s*)), and the natural component, **2**, in the methyl tetrad region, indicating stereochemical variations. The tetramethyl groups resonated at δ 19.5−19.7 in the natural compound, but at δ 20.5−21.1 in **16**; whereas in **17**, Me-10 resonated at δ 19.4 but other methyls resonated at δ 20.4−20.7. Clearly, the *anti*-1,3-dimethyl arrangement led to a high field shift for Me-10 in the *ssa*(*s*) isomer. Thus, the orientations of the pendant methyl groups affect the ^{13}C shifts of such groups, including C3.

3. Minor Synthetic Isomers. Accompanying the two major peaks (assigned to **16** (*sss*(*s*)) and **17** (*ssa*(*s*))) in the capillary gas chromatogram were a number of minor ones, and their mass spectra confirmed them as stereoisomers of the major components. GCMS comparisons were made by consecutive injections of synthetic and natural samples, and neither of the major synthetic isomers matched the natural one, which did, however, coincide with the minor peak of longest retention time. The minor isomers arise because of stereoleakage during the predominating *syn*-reduction of 2,4,6-trimethylphenol, **27**, and the resulting mixture of minor 2,4,6-trimethylcyclohexanols was carried on to eventually provide isomers of the hexamethyldocosane system. However, due to low levels of those isomers and separation difficulties, their stereochemistries were not determinable under these conditions. This situation is outlined in Scheme 5. On this basis, there should be twelve minor isomers of the final C28 hydrocarbon, which would result in six GC peaks, for the reason outlined above.

TABLE 3. ^{13}C Chemical Shifts (187 MHz, $CDCl_3$) for Pendant Methyl Groups and C3 in 2, Synthetic Isomers 16 (*sss*(*s*)) and 17 (*ssa*(*s*)), and 4



16 and **17** *sss(s)* and *ssa(s)*

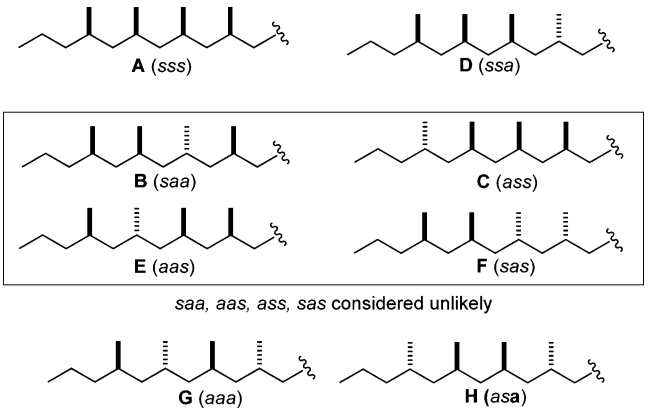


4 lardolure

2 δ_C	**16** (*sss*(*s*)) δ_C	**17** (*ssa*(*s*)) δ_C	**4** δ_C
40.218 (C3)	38.86 (C3)	39.03 (C3)	38.89 (C8)
19.646	21.049, 21.044[a] (Me-8)[b]	20.719 (Me-6)	20.91 (Me-1)
19.586	21.033 (Me-6)[b]	20.438 (Me-4)[c]	20.56 (Me-5)
19.564	20.559, 20.556[a] (Me-10)	20.385 (Me-8)[c]	20.36 (Me-7)
19.550	20.501 (Me-4)	19.437, 19.429[a] (Me-10)	20.21 (Me-3)

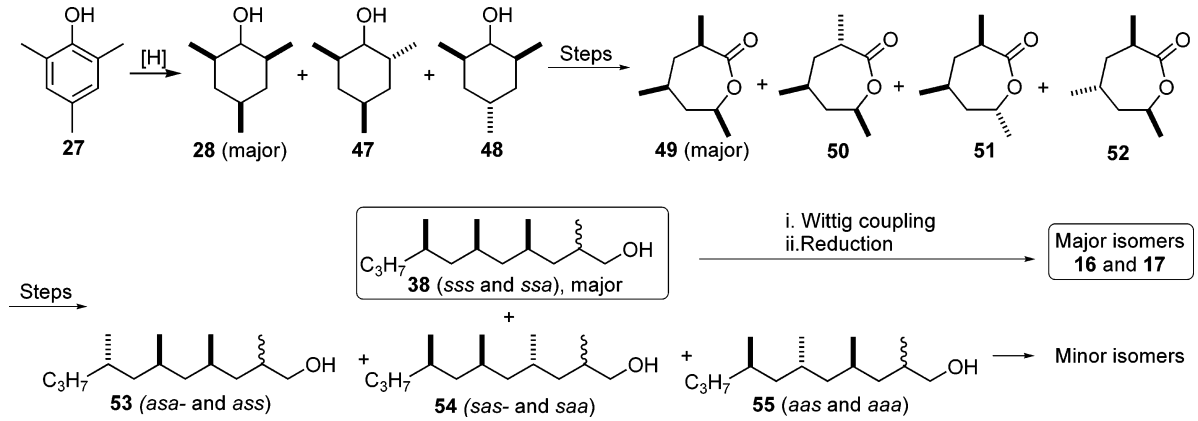
[a] Duplications of the ^{13}C chemical shifts were observed in these cases, presumably because of proximity to two *syn* arrangements of the methyl diad unit. [b,c] These chemical shift assignments are interchangeable.

The lack of stereochemical correspondence between the synthesized (major) isomers and the natural component implied that the relative stereochemistry was novel among polyketide-based natural products of this relatively simple type. However, the spectral data of **16** (*sss*(*s*)) and **17** (*ssa*(*s*)) did provide assistance in the selection of the next target diastereomer for synthesis. Analysis of the stereochemical possibilities in terms of likely NMR shifts of methyl groups experiencing *syn* or *anti* 1,3-interactions with other methyl groups led to the following assessments of likely relative stereochemistry in the methyl tetrad moiety.

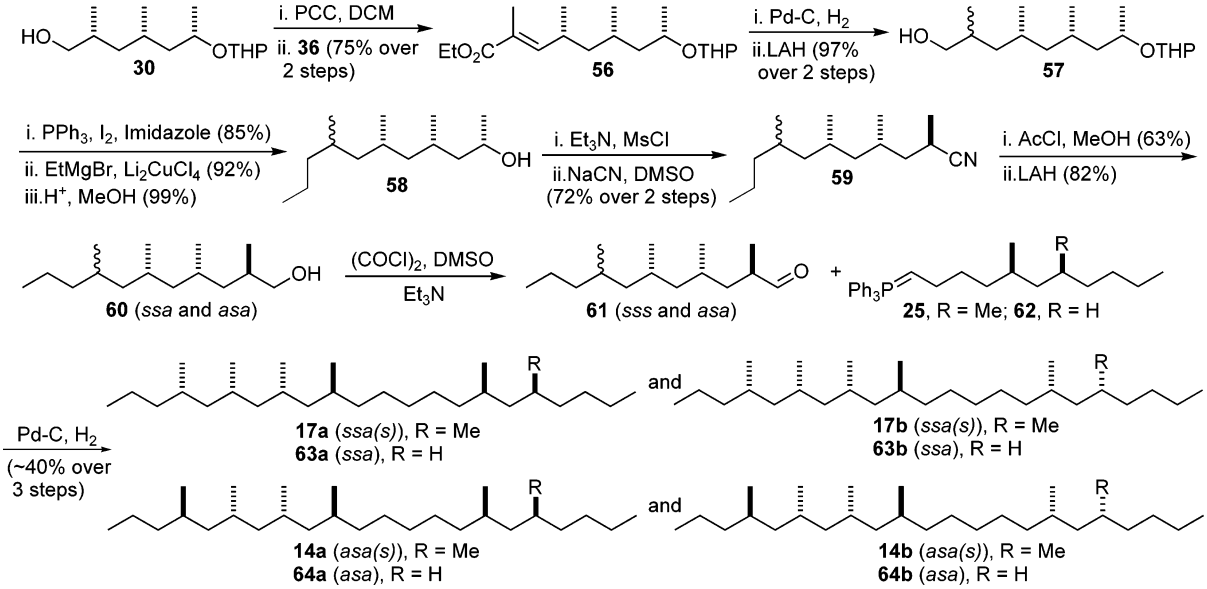


It was anticipated that the *aaa* arrangement would provide methyl shifts at ~δ 19, whereas the shifts for Me-6 and Me-8 of the *asa* isomer are difficult to predict, as these two methyl groups experience a *syn* and *anti*

SCHEME 5. Origin of the Minor Isomers in the Synthetic Sample of 16 and 17



SCHEME 6. Preparation of Hexamethyldocosanes 14 and 17 and Pentamethyldocosanes 63 and 64



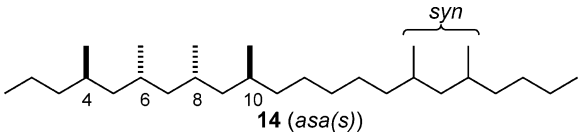
interaction and there is limited data for *syn*/*anti* trimethyl structures but no relevant data for tetramethyl structures other than the *all-syn* arrangement. Thus, predictions of shifts for C4 and C6 methyl groups in **G** (*aaa*) and **H** (*asa*) were difficult, and both were considered as likely candidates. The *asa* isomer was chosen as the next target, and this appeared accessible by a modification of the route that provided **16** and **17** (*sss*(*s*) and *ssa*(*s*), respectively), described above. In addition, the adapted route would again provide **17**, assisting in chromatographic and spectral comparisons.

4. Syntheses of *ssa*(*s*)- and *asa*(*s*)-4,6,8,10,16,18-Hexamethyldocosanes, 17 and 14, and *ssa*- and *asa*-4,6,8,10,16-Pentamethyldocosanes, 63 and 64. The previously described monoprotected diol **30** was oxidized (PCC) and the resulting aldehyde was coupled with the stabilized phosphorane **36** to install the fourth methyl group as part of an α,β-enoate. Reduction, iodination, ethylation, and deprotection provided tetramethyldecanol **58**. Mesylation, inverting cyanide displacement, hydrolysis, and reduction furnished a mixture of *ssa*- and *asa*-alcohols **60**, ready for oxidation and Wittig coupling. 5-Methylundecyl iodide was acquired by orthodox procedures from 2-octanone and converted to the Wittig salt. The aldehyde and phosphorane(s) were then coupled and reduced to provide the hexamethyldocosanes, **14** and **17**, and pentamethyldocosanes, **63** and **64**, as shown in Scheme 6.

Again, four diastereomers of the C28 system were formed, two of *ssa*(*s*), **17a** and **17b** already acquired, and two of the *asa*(*s*) system, **14a** and **14b**, along with minor isomers. The capillary GC trace consisted of two major peaks, the first for the two *ssa*(*s*) isomers, **17a** and **17b**, and the second for the two new *asa*(*s*) isomers, **14a** and **14b**, the mass spectra of which were very similar to that for the natural C28 component. High resolution ^{1}H and ^{13}C NMR spectra were obtained for the mixture, and extraction of shifts for the previously obtained *ssa*(*s*) isomers, **17**, provided some shifts for the *asa*(*s*) isomers, **14**. This failed to match those of the natural component, and the comparison for the methyl tetrad is shown in Table 4. It is clear that the two *anti* arrangements in **14a** and **14b** did not move all the methyl shifts (Me-4,6,8,10) below δ 20. The ^{13}C shifts of adjacent methylenes, especially C3, also differed, although there was excellent correspondence for the C13 to C22 shifts, reinforcing the conclusion that the 16,18-dimethyl arrangement was *syn*.

GCMS examinations and comparisons of the *ssa*(*s*) and *asa*(*s*) mixture, **17** and **14**, with the natural C28 extract

TABLE 4. Selected Pendant Methyl ^{13}C NMR Data (187 MHz, $CDCl_3$) of 14 (*asa*(*s*)) and the Natural C28 Component, 2



14 (*asa(s)*)

2 δ_C	**14** (*asa*(*s*)) δ_C
19.646	20.079 (Me-6)[a]
19.586	20.065 (Me-8)[a]
19.564	19.435 (Me-4)[b]
19.550	19.429 (Me-10)[b]

[a,b] These assignments are interchangeable.

confirmed again that the natural C28 isomer had a slightly longer retention time. Similar GCMS and NMR data for the synthesized 4,6,8,10,16-pentamethyldocosane systems confirmed the constitution of the C27 natural compound, but capillary GC confirmed that this possessed neither of the *asa* or *ssa* arrangements.

After careful comparisons of the ^{13}C shift data for the *sss*, *ssa,* and *asa* arrangements, re-evaluation of the stereochemical possibilities for the methyl tetrad now inclined us to the *anti-anti-anti* ensemble. A direct way to access the *aaa* tetrad would involve utilization of an intermediate **65**, in the sequence that proceeded from a minor isomer formed in the Rh-catalyzed hydrogenation. However, this monoprotected diol **65** would derive from **48** (Figure 3), which is one of the minor isomers (<10%) from the reduction of 2,4,6-trimethylphenol, and is not an attractive option.

Fortunately, a plausible route was to utilize the *all-cis*-2,4,6-trimethylcyclohexanol, **28**, but with extra steps to effect chain shortening of a primary to a secondary alcohol, followed by inverting cyanide displacement of oxy-groups, as summarized in Figure 4.

5. Syntheses of *aaa*(*s*)- and *aas*(*s*)-4,6,8,10,16,18-Hexamethyldocosanes, 15 and 18, and *aaa*- and *aas*-4,6,8,10,16-Pentamethyldocosanes, 84 and 85. After considerable experimentation, the adopted procedure commenced with silyl-protected hydroxyacid **71**,[13] which via the Weinweb amide was converted to the methyl ketone **73** and underwent a slow but efficient Baeyer−Villiger reaction to monoprotected diol **74** (Scheme 7). Once again, mesylate displacement by cyanide effected the necessary stereochemical inversion, and application of the steps outlined previously led to desired alcohols **66** and **67**. Nitrile hydrolysis was conducted under acidic conditions in both cases, as basic hydrolysis (to avoid desilylation) induced some epimerization.

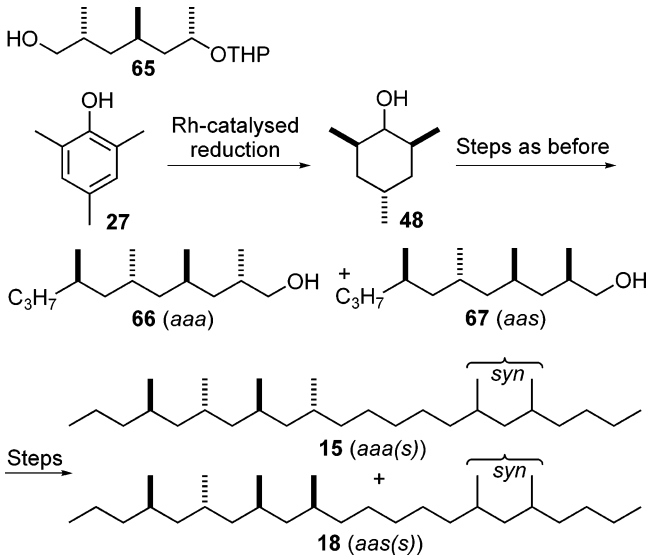


FIGURE 3. Proposed synthetic route for **15** and **18**.

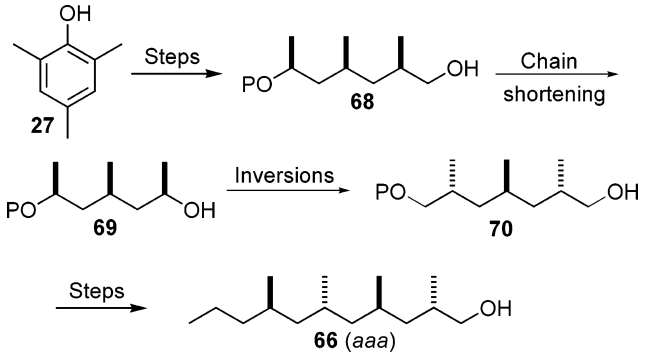
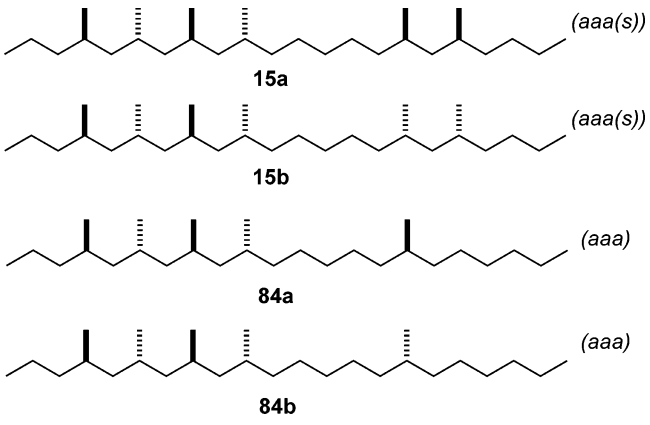


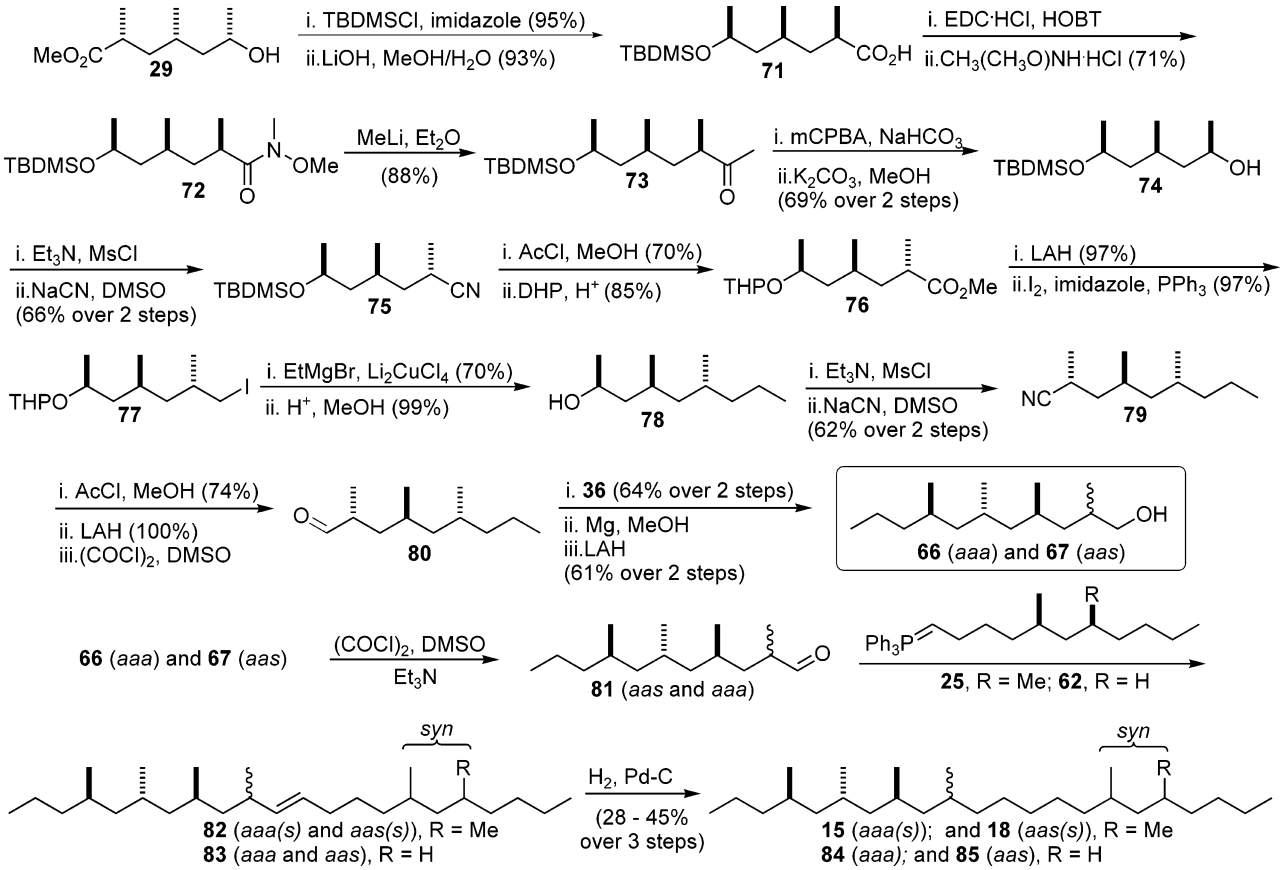
FIGURE 4. Proposed synthetic scheme for tetramethylalkanol **66**.

Separations of mixtures of **15** and **18** (C28 system) and **84** and **85** (C27 system) were performed by preparative GC, as outlined previously. Both synthetic mixtures exhibited almost identical peak separations, but these separations were more pronounced than in the previous *sss*(*s*)- and *ssa*(*s*)-C28 and *ssa*(*s*)- and *asa*(*s*)-C28 systems. The products were collected in three portions for each system, with the first fraction containing principally one major diastereomeric pair (*aas*), the middle fraction containing a mixture, and the third fraction containing mainly the *aaa*, with ~28% of the *aas* diastereomers. Some low level minor isomers were also present, for the reasons outlined earlier. The mass spectra of all of the synthesized C28 diastereomers were very similar and closely resembled that of the natural hexamethyldocosane. This was also the case for the pentamethyl C27 system.

Co-injections and capillary gas chromatographic comparisons of the synthetic hexamethyldocosane isomers with the natural component established that the natural compound was a diastereomer of the *aaa*(*s*) system, **15a** or **15b**, as shown below. Similarly the pentamethyldocosane was either **84a** or **84b**.



SCHEME 7. Formation of Tetramethylalkanols 66 and 67, and the Wittig Coupling Leading to the Formation of Hydrocarbons 15, 18, 84, and 85



6. *aaa*(*s*)- and *aas*(*s*)-4,6,8,10,16,18-Hexamethyldocosanes, 15 and 18, Respectively. High resolution ^{1}H and ^{13}C NMR spectra were obtained for the mixture and for the first and third fractions from preparative GC purification. Although the ^{1}H NMR spectra were relatively uninformative, the ^{13}C NMR spectra provided the basis for the crucial distinction between these isomeric sets, that is, between *aas*(*s*)-**18** (two isomers) and *aaa*(*s*)-**15** (two isomers). The assigned ^{13}C NMR data of the natural C28 compound and of the *aas*(*s*) and *aaa*(*s*) isomers are shown in Table 5.

Similarities in the chemical shifts of C1 to C6 and C14 to C22 of **18** (*aas*(*s*)) and **15** (*aaa*(*s*)) are observed, which is not surprising as the major difference concerns the relative stereochemistry of the C10 methyl group. Some signal duplication for the synthetic samples, especially in the C10 to C16 region, was noticed, and this reflects the two possible arrangements of the *syn*-16,18-dimethyl unit relative to the methyl tetrad. This lack of signal duplication for the natural sample strongly, but not surprisingly, implies the presence of a single stereoisomer. The agreement between the chemical shifts of fraction 3 (preparative GC) and those of the natural sample was in harmony with the results from the capillary GC co-injection experiment. The relative stereochemistry of the methyl tetrad in the preparative GC fractions was deduced by chemical shift comparisons. For any *syn*-1,3-dimethyl unit present, the methyl shifts were $>\delta$ 20, whereas in the *anti* arrangement the shifts were $<\delta$ 20, as demonstrated in Figure 5.

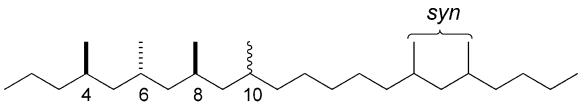
For fraction 1, from the preparative GC separation, the methyl tetrad shifts were δ 20.359, 20.354, 20.195, 19.614, and 19.325, with the duplicated signals (δ 20.359 and 20.354) associated with Me-10, which experiences a measurable interaction with the remote *syn*-dimethyl unit. The signals with chemical shifts $>\delta$ 20 were assigned to Me-8 and Me-10 in **18** (*aas*(*s*)), because of their *syn* nature, whereas the methyl shifts in fraction 3 were all within δ 19.5−19.7, as expected for an *all-anti* array. Consequently, the relative stereochemistry of the methyl tetrad in the natural hexamethyldocosane was *anti-anti-anti*. However, the stereochemical nexus between the "tetrad" and *syn* "diad" methyl units was indeterminate because of the "pentamethylene" insulation between them.

7. 4,6,8,10,16-Pentamethyldocosanes, 84 (*aaa*) and 85 (*aas*). Similarly, high resolution NMR data were acquired for preparative GC fractions 1 and 3 of the *aas*- and *aaa*-pentamethyldocosane system. The ^{13}C chemical shift data are listed in Table 6.

Again, the two diastereomeric pairs *aas* and *aaa* exhibited comparable shifts for C1 to C6 and C14 to C22. Within each system, signal duplication was again detected, especially between C10 and C16, ascribable as before to differing interactions between Me-16 and the methyl tetrad moiety. The system matching the natural component had shifts of δ 19.650, 19.645, 19.589, 19.569,

(13) Hoffmann, R. W.; Stenkamp, D. *Tetrahedron* **1999**, *55*, 7169.

TABLE 5. ^{13}C NMR (187 MHz, $CDCl_3$) Data of the Synthetic Isomers, 15 and 18, and the Natural C28 Hydrocarbon, 2[l]



15 (*aaa(s)*) and **18** (*aas(s)*)

carbon numbering	δ_C **2**	**15** (*aaa*(*s*))	**18** (*aas*(*s*))
C1	14.386	14.386	14.392
C2	20.077	20.079	20.067
C3	40.218	40.221	40.150
C4 (CH)	29.711	29.717	29.687
C5	45.559[a]	45.551[b]	[45.548, 45.540][c]
C6 (CH)	27.293[d]	27.299[e]	27.339[f]
C7	46.534	[46.541, 46.538]	45.946[g]
C8 (CH)	27.288[d]	27.292[e]	27.299[f]
C9	45.544[a]	[45.580, 45.565][b]	45.840[g]
C10 (CH)	29.999[h]	30.005	[29.901, 29.888]
C11	37.882	[37.885, 37.875]	[36.988, 36.964][i]
C12	26.937	[26.939, 26.925]	[26.940, 26.928][j]
C13	30.362	[30.364, 30.343]	[30.424, 30.392]
C14	27.065	[27.068, 27.062]	[26.964, 26.952][j]
C15	36.877	[36.882, 36.869]	[36.893, 36.867][i]
C16 (CH)	29.979[h]	29.995[f]	[30.0129, 29.995][k]
C17	45.217	45.227	45.227
C18 (CH)	29.979[h]	29.985[f]	29.985[k]
C19	36.566	36.573	36.576
C20	29.174	29.176	29.181
C21	23.068	23.070	23.076
C22	14.179	14.178	14.184
Me- 4, 6, 8, 10	19.646, 19.586, 19.564, 19.550	[19.651, 19.648], 19.590, 19.570, 19.555	[20.359, 20.354], 20.195, 19.614, 19.325
Me-16, 18	20.301	20.300	20.303

[a−k] These assignments are interchangeable. [l] Square brackets indicate these ^{13}C shifts are duplicated.

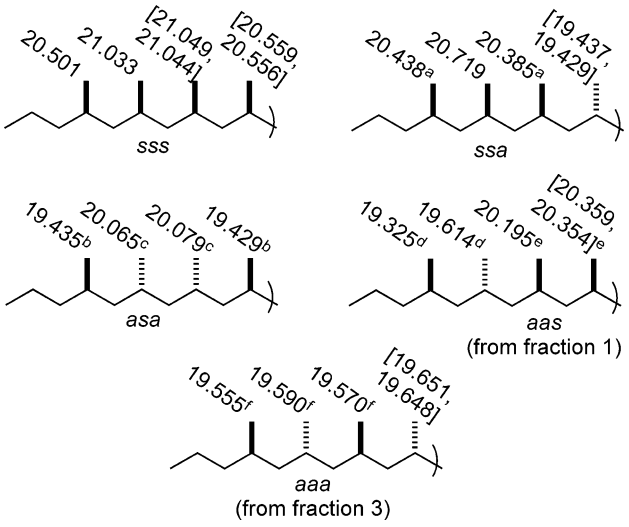
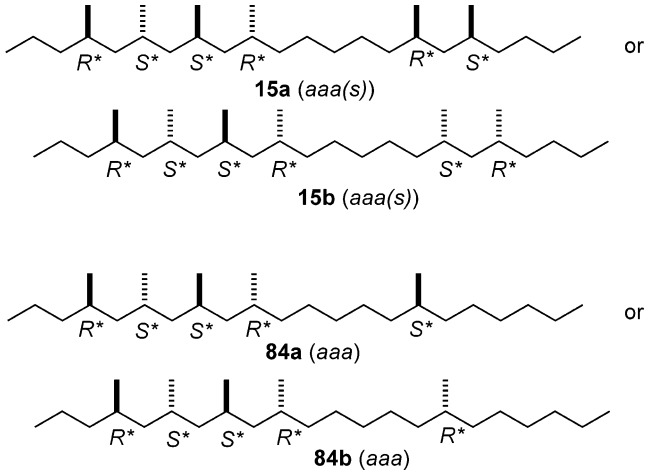


FIGURE 5. Comparisons of the high field ^{13}C NMR (187 MHz) shifts of the pendant methyl groups in the methyl tetrad region of all the synthetic hexamethyldocosane isomers. Square brackets indicate these chemical shift assignments are duplicated. Superscript a−f indicate these chemical shift values are interchangeable.

and 19.553, representing an *all-anti* array, a conclusion drawn above for the hexamethyldocosane component.

Summary

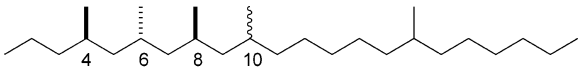
The 4,6,8,10,16,18-hexa- and 4,6,8,10,16-pentamethyldocosanes therefore have the relative stereochemistries shown below.



These novel structures and stereochemistries raise a number of biosynthetic issues. With **2**, four acetate and seven propionate units appear to be employed, but the direction of assembly is masked by the absence of a terminal carboxylate group as shown below in Scheme 8.

The stereochemical alternation within the methyl tetrad contrasts with the established situation for polyketides from the graylag goose, some molluscs, and other insects. For this reason, lipids **1** and **2** are of interest with respect to the details of the fatty acid synthase-like elongation steps in the polyketide chain construction. Further work will be directed to the determination of the absolute stereochemistry of these novel components. The single set of signals in the high resolu-

TABLE 6. ^{13}C NMR Data (187 MHz, $CDCl_3$) of the Synthetic Isomers, 84 and 85, and the Natural C27 Hydrocarbon, 1[m]

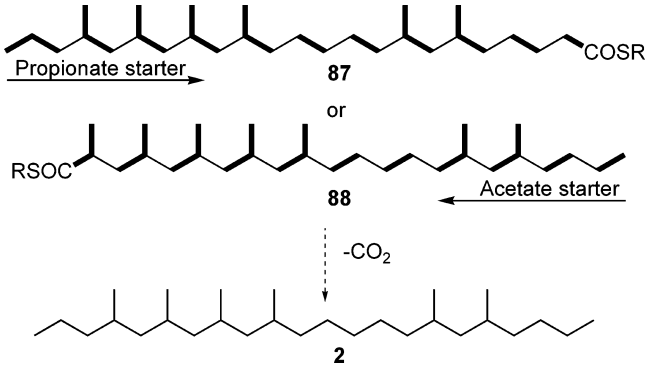


84 (*aaa*) and **85** (*aas*)

carbon numbering	δ_C		
	1	**84** (*aaa*)	**85** (*aas*)
C1	14.380	14.386	14.392
C2	20.074	20.079	20.070
C3	40.218	40.222	40.154
C4 (CH)	29.712	29.716	29.692
C5	45.545[a]	45.549[b]	45.549[c]
C6 (CH)	27.295[d]	27.301[e]	27.344[f]
C7	46.538	46.548	45.844[c]
C8 (CH)	27.291[d]	27.295[e]	27.304[f]
C9	45.561[a]	[45.577, 45.566][b]	[45.951, 45.947]
C10 (CH)	29.996	[30.000, 29.997]	[29.900, 29.894]
C11	37.879	[37.884, 37.879]	[36.984, 36.976]
C12	27.060[h]	27.064[g]	27.061[i]
C13	30.339	[30.344, 30.336]	[30.406, 30.387]
C14	27.106[h]	[27.110, 27.106][g]	[27.131, 27.122]
C15	37.093[j]	37.103[k]	37.114[l]
C16 (CH)	32.751	32.754	32.764
C17	37.089[j]	37.095[k]	37.106[l]
C18	27.044[h]	27.050[g]	[26.944, 26.934][i]
C19	29.712	29.697	29.709
C20	31.957	31.962	31.974
C21	22.694	22.710	22.710
C22	14.116	14.122	14.128
Me-4, 6, 8, 10	19.646, 19.585, 19.564, 19.549	[19.650, 19.645], 19.589, 19.569, 19.553	20.362, [20.201, 20.198], 19.615, 19.328
Me-16	19.724	[19.728, 19.722]	[19.730, 19.726]

[a–l] These chemical shifts are interchangeable. [m] Square brackets indicate these chemical shifts are duplicated.

SCHEME 8. Proposed Biosynthesis of Hexamethyldocosane 2, Involving Propionate and Acetate Units



tion ^{13}C NMR spectra of both natural lipids confirms diastereomeric homogeneity or perhaps one single enantiomer. Distinction between **15a** and **15b** would require enantiocontrolled syntheses utilizing coupling of enantiopure tetramethyl- and dimethyl-substituted fragments, followed by comparisons of high resolution ^{13}C NMR spectra. We know the configuration of the *syn*-dimethyl unit has detectable effects on the most proximal regions of the tetramethyl unit. Determination of the absolute stereochemistry would follow from comparisons of the optical rotations of the natural sample and synthesized enantiomers of the established diastereomer.

Conclusion

We have determined the constitutions of two novel cuticular lipids from the cane beetle, *Antitrogus parvulus*, as 4,6,8,10,16-penta- and 4,6,8,10,16,18-hexamethyldocosanes. The relative stereochemistry was demonstrated to be *anti-anti-anti* in the methyl tetrad moiety and *syn* in the 16,18-methyl diad, by stereocontrolled syntheses commencing with *all-syn* reduction of 2,4,6-trimethylphenol to furnish stereoisomers of 2,4,6,8-tetramethylundecanal. These were coupled with appropriate phosphoranes to provide alkenes and then the target penta- and hexamethyldocosanes. Combined gas chromatography–mass spectrometry, capillary gas chromatographic comparisons, and high resolution NMR spectroscopy then confirmed the constitutions and relative stereochemistries of the natural lipids. Possible biosynthetic assembly of these lipids is briefly commented on.

Experimental Section

1. Synthesis of *syn*- and *anti*-7,9-Dimethylhexadecane, 10 and 11 (Refer to Scheme 1). a. 3,5-Dimethylcyclohexanone. At 0 °C, Jones reagent (8 M in H_2O/H_2SO_4, 8.0 mL) was added slowly to an acetone solution (80 mL) of *cis*-3,5-dimethylcyclohexanol (**6**; 6.0 g, 46.9 mmol, commercial supplier, containing mainly the *cis* isomer with ~10–15% of the *trans* isomer). After being stirred at room temperature for 2 h, the mixture was quenched by the addition of ^iPrOH and filtered through a plug of silica gel and Celite layers. The filtrate was concentrated and poured into water (40 mL) and then extracted with diethyl ether (3 × 20 mL). The combined ethereal extracts were washed with saturated $NaHCO_3$ (15 mL) and brine (15 mL). Removal of the solvent under reduced pressure provided 3,5-dimethylcyclohexanone (5.7 g, 97%), which was used in the next reaction without further purification. ^1H NMR (400 MHz, *J* in Hz): δ 2.28 (br d, 2H), 1.88 (t, *J* 12.7, 2H), 1.80 (m, 2H), 0.98 (d, *J* 6.2, 6H). ^{13}C NMR (100 MHz): δ 211.2, 49.3, 33.1, 22.3. GCMS: *m/z* 126 (M^+, 13), 111

(21), 82 (12), 69 (98), 56 (53), 55 (38), 41 (100). These spectral data matched those reported.[14]

b. 4,6-Dimethyloxepan-2-one. 3,5-Dimethylcyclohexanone (5.7 g, 45.2 mmol) in dichloromethane (10 mL) was added slowly to a mixture of *m*CPBA (70%, 11.7 g, 47.5 mmol) and $NaHCO_3$ (4.9 g, 57.9 mmol) in dichloromethane (80 mL). The suspension was stirred for 6 h before being filtered through a sintered glass funnel. The solid was washed with cold hexane (20 mL), and the combined organic filtrates were washed with aqueous Na_2SO_3 (2% solution, 10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (30% diethyl ether in hexane) to give the title lactone (4.8 g, 74%) as a clear liquid. ^{1}H NMR (400 MHz, *J* in Hz): δ 3.49 (d, *J* 5.6, 2H), 2.48 (m, 2H), 2.35−1.40 (m, 4H), 1.01 (d, *J* 6.6, 3H), 0.92 (d, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 174.7, 74.0, 46.5, 41.8, 33.8, 29.6, 23.9, 18.6. GCMS: *m/z* 142 (M^+, 1), 112 (42), 97 (27), 83 (14), 69 (100), 55 (46), 41 (87). These spectral data matched those reported.[15]

c. Methyl 6-Hydroxy-3,5-dimethylhexanoate, 7. Under an inert atmosphere, Na pieces (0.61 g, 26.5 mmol) were carefully added to anhydrous MeOH (25 mL) at 0 °C. The resulting solution of NaOMe was added dropwise to 4,6-dimethyloxepan-2-one (3.8 g, 26.8 mmol) in MeOH (25 mL) at 0 °C, and the reaction mixture was stirred for 3.5 h. The reaction was quenched with saturated NH_4Cl (20 mL), followed by extraction of the aqueous layer with dichloromethane (3 × 20 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated. Methyl ester **7** (4.3 g, 93%) was obtained as a clear liquid after flash chromatography (15% EtOAc in hexane). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.59 (s, 3H), 3.40 (m, 2H), 2.23 (ddd, *J* 14.6, 7.7, 5.6, 2H), 1.96 (m, 1H), 1.62 (m, 1H), 1.32 (m, 1H), 0.94 (m, 1H), 0.89 (d, *J* 7.0, 3H), 0.86 (d, *J* 7.9, 3H). ^{13}C NMR (100 MHz): δ 173.9, 67.5, 51.3, 41.1, 40.4, 33.0, 27.6, 20.4, 16.1. GCMS: *m/z* 144 (M^+ − 28, 8), 125 (5), 111 (4), 101 (100), 83 (50), 69 (35), 55 (61), 41 (74). Anal. Calcd for $C_9H_{18}O_3$: C, 62.0; H, 10.4. Found: C, 62.2; H, 10.7.

d. Methyl 3,5-Dimethyl-6-(tetrahydro-2*H*-pyran-2-yloxy)hexanoate. A catalytic amount of TsOH, hydroxyester **7** (3.1 g, 24.7 mmol), and 2,2-dihydropyran (2.4 mL, 26.3 mmol) in dichloromethane (40 mL) were stirred for 4 h. The solution was washed with saturated $NaHCO_3$ (3 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated to give the required THP ether (4.0 g, 79%) as two diastereomers after flash chromatography (10% diethyl ether in hexane). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.52 (t, *J* 4.2, 2H), 3.62 (s, 6H), 3.98−3.05 (m, 8H), 2.20 (m, 4H), 1.95−1.40 (m, 20H), 0.92 (d, *J* 6.6, 12H). ^{13}C NMR (100 MHz): δ 173.7, 99.1, 98.7, 72.8, 72.7, 62.9, 62.0, 51.3, 41.4, 41.2, 41.1, 30.9, 30.8, 30.7, 27.9, 25.5, 25.4, 20.4, 19.7, 17.8, 17.7. GCMS: Only one GC peak was observed. *m/z* 184 (M^+ − 74, <1), 173 (3), 157 (6), 125 (19), 101 (20), 85 (100), 67 (14), 55 (38), 41 (50). Anal. Calcd for $C_{14}H_{26}O_3$: C, 65.1; H, 10.1. Found: C, 65.4; H, 10.4.

e. 3,5-Dimethyl-(6-tetrahydropyran-2-yloxy)-hexan-1-ol, 39. The above THP-protected ester (4.2 g, 16.2 mmol) was dissolved in anhydrous diethyl ether (15 mL) and added slowly to LAH (0.91 g, 23.9 mmol) in diethyl ether (20 mL) at 0 °C under an inert atmosphere. The grayish mixture was stirred for 2 h, followed by the addition of $Na_2SO_4 \cdot 10H_2O$ (9.1 g). The suspension was stirred for 5 h, and the hydrated sulfate was filtered off. After the white solid was washed thoroughly with more diethyl ether (15 mL), the combined filtrates were dried ($MgSO_4$) and concentrated. The crude oil was purified by flash chromatography (25% diethyl ether in hexane, and then 50%) to furnish alcohol **39** (3.2 g, 85%, two diastereomers) as a clear liquid. ^{1}H NMR (400 MHz, *J* in Hz): δ 4.52 (dd, *J* 4.3, 2.6, 2H), 3.84 (m, 2H), 3.68 (m, 2H), 3.63 (m, 2H), 3.59 (dd, *J* 9.4, 5.7, 1H), 3.53 (dd, *J* 9.3, 6.8, 1H), 3.48 (m, 2H), 3.22 (dd, *J* 9.3, 5.0, 1H), 3.13 (dd, *J* 9.4, 6.5, 1H), 1.83 (m, 4H), 1.69 (m, 4H), 1.61−1.48 (m, 14H), 1.38 (m, 4H), 0.93 (d, *J* 6.7, 3H), 0.91 (d, *J* 6.7, 3H), 0.89 (d, *J* 6.6, 6H). ^{13}C NMR (100 MHz): δ 99.2, 99.1, 73.1, 72.5, 62.5, 62.4, 61.0, 60.8, 41.5, 41.1, 39.8, 39.7, 30.9, 30.8, 30.74, 30.72, 27.0, 26.7, 25.5, 20.47, 20.44, 19.8, 19.7, 18.2, 18.1. GCMS: Only one GC peak was observed. *m/z* 200 (M^+ − 32, <1), 172 (<1), 145 (1), 129 (3), 111 (7), 101 (9), 85 (100), 69 (46), 55 (78), 41 (45). Anal. Calcd for $C_{13}H_{26}O_3$: C, 67.8; H, 11.4. Found: C, 67.6; H, 11.7.

f. 3,5-Dimethyl-6-(tetrahydro-2*H*-pyran-2-yloxy)hexanal. 4-Methylmorpholine *N*-oxide (2.5 g, 21.3 mmol) and tetrapropylammonium perruthenate (0.18 g, 0.52 mmol) were added to a solution of primary alcohol **39** (3.2 g, 13.9 mmol) in dichloromethane (20 mL) under an inert atmosphere. The dark brown reaction was stirred for 6 h and then filtered through a layer of silica gel. The silica gel was washed with extra dichloromethane, and then the solvent was removed under reduced pressure and the residue was purified by column chromatography (10% diethyl ether in hexane) to give the corresponding aldehyde (2.7 g, 85%, two diastereomers) as a clear liquid. ^{1}H NMR (400 MHz, *J* in Hz): δ 9.74 (t, *J* 2.2, 2H), 4.54 (dd, *J* 4.4, 2.7, 1H), 4.52 (dd, *J* 4.9, 2.8, 1H), 3.82 (m, 2H), 3.59 (dd, *J* 9.4, 5.8, 1H), 3.50 (dd, *J* 9.4, 6.9, 1H), 3.48 (m, 2H), 3.21 (dd, *J* 9.4, 5.6, 1H), 3.13 (dd, *J* 9.5, 6.5, 1H), 2.38 (dq, *J* 8.4, 2.2, 2H), 2.20−2.13 (m, 4H), 1.84−1.76 (m, 4H), 1.68 (m, 2H), 1.59−1.47 (m, 8H), 1.37 (m, 2H), 0.96 (d, *J* 6.4, 6H), 0.93 (d, *J* 6.7, 3H), 0.92 (d, *J* 6.7, 3H). ^{13}C NMR (100 MHz): δ 203.0, 99.2, 98.9, 72.8, 72.7, 62.3, 62.2, 50.8, 71.4, 71.3, 31.0, 30.9, 30.69, 30.68, 25.76, 25.75, 25.49, 25.48, 20.68, 20.67, 19.6, 19.5, 17.79, 17.76. GCMS: Only one GC peak was observed. *m/z* 184 (M^+ − 28, <1), 143 (<1), 127 (2), 109 (19), 101 (13), 85 (100), 69 (16), 55 (29), 41 (40). Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.4; H, 10.6. Found: C, 68.2; H, 10.8.

g. 7,9-Dimethyl-10-(tetrahydro-2*H*-pyran-2-yloxy)decan-5-ol, 8. Under an inert atmosphere, a solution of *n*-butyl bromide (1.7 mL, 16.2 mmol) in diethyl ether (15 mL) was added dropwise to a suspension of Mg turnings (1.9 g, 78.2 mmol) in diethyl ether (2 mL) with a crystal of iodine, so that a gentle reflux was maintained. The mixture was allowed to stir for another 30 min before being transferred to a solution of 3,5-dimethyl-6-(tetrahydro-2*H*-pyran-2-yloxy)hexanal (1.8 g, 7.9 mmol) in diethyl ether (10 mL) via cannula. The reaction was stirred for a further 15 min and quenched with saturated NH_4Cl (15 mL). Extractions with diethyl ether (3 × 15 mL) were followed by the combination of the organic extracts, another washing with brine (15 mL), and drying ($MgSO_4$); then the solvent was evaporated. The desired alcohol **8** (1.9 g, 83%, four diastereomers) was obtained after flash chromatography (10% EtOAc in hexane). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.51 (m, 1H), 3.85 (m, 1H), 3.49 (m, 2H), 3.15 (m, 2H), 1.96−1.25 (m, 18H), 0.97−0.89 (m, 9H). ^{13}C NMR (100 MHz): δ 99.3, 99.2, 74.0, 73.2, 69.6, 69.2, 62.3, 62.2, 44.8, 44.7, 42.4, 42.3, 38.1, 37.3, 31.3, 30.9, 30.8, 30.7, 27.9, 27.8, 26.7, 26.6, 25.5, 25.4, 22.7, 20.1, 20.0, 18.0, 17.9, 14.1. GCMS: Only one GC peak was observed. *m/z* 201 (M^+ − 85, <1), 183 (1), 165 (1), 145 (1), 127 (5), 111 (6), 101 (11), 85 (100), 69 (20), 55 (19), 41 (31). Anal. Calcd for $C_{17}H_{34}O_3$: C, 71.3; H, 12.0. Found: C, 71.6; H, 12.2.

h. 2-(2,4-Dimethyldecyloxy)-tetrahydro-2*H*-pyran. To secondary alcohol **8** (1.6 g, 5.6 mmol) in dichloromethane (30 mL) was added triethylamine (4.7 mL, 33.5 mmol) and mesyl chloride (0.85 mL, 10.4 mmol) at 0 °C. The mixture was stirred for 1 h, and then diethyl ether (20 mL) was added. After filtration and solvent removal, the crude mesylate was redissolved in diethyl ether (30 mL) and then added slowly to a suspension of LAH (0.23 g, 6.1 mmol) in diethyl ether (5 mL) at 0 °C. The suspension was refluxed for 2 h and subsequently cooled to 0 °C before being quenched with $Na_2SO_4 \cdot 10H_2O$ (2.3 g) and stirred for another 2 h. After filtration and concentration, the crude oil was subjected to flash chromatography (5% EtOAc in hexane) to furnish the required THP ether (1.0 g, 69%, two diastereomers). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.55 (m, 1H), 3.81 (m, 2H), 3.47 (m, 2H), 3.62−3.20 (ddd, *J* 9.3, 5.4, 5.1, 2H), 3.44−3.04 (ddd, *J* 9.4, 7.7, 7.0, 2H), 1.81−1.23

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(m, 20H), 0.86 (t, *J* 6.9, 3H), 0.84 (d, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 99.1, 98.7, 73.7, 73.3, 62.2, 61.9, 41.7, 41.6, 36.8, 36.7, 31.9, 31.0, 30.9, 30.8, 30.7, 30.1, 30.0, 29.7, 26.8, 26.7, 25.6, 22.7, 20.4, 20.3, 19.6, 19.4, 18.1, 18.0, 14.1. GCMS: Only one GC peak was observed. *m/z* 197 ($M^+ - 73$, <1), 169 (1), 126 (1), 85 (100), 57 (25), 41 (26). Anal. Calcd for $C_{17}H_{34}O_2$: C, 75.5; H, 12.7. Found: C, 75.6; H, 12.6.

i. *syn*-2,4-Dimethyldecan-1-ol, 9. To a solution of 2-(2,4-dimethyldecyloxy)tetrahydro-2*H*-pyran (90 mg, 0.33 mmol) in methanol (20 mL) was added *p*-toluenesulfonic acid (10 mg). The solution was stirred for 2 h and quenched with saturated $NaHCO_3$ (10 mL). Upon concentration, the solution was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (10% EtOAc in hexane) to yield alcohol **9** (60 mg, 97%). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.42 (ddd, *J* 10.5, 6.9, 5.2, 2H), 1.82−1.21 (m, 14H), 0.89 (d, *J* 6.7, 6H), 0.86 (t, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 68.4, 41.0, 36.7, 33.1, 31.9, 30.0, 29.6, 26.8, 22.7, 20.3, 17.3, 14.1. GCMS: *m/z* 153 ($M^+ -$ 33, 1), 126 (11), 111 (29), 83 (73), 71 (35), 70 (35), 69 (35), 57 (92), 55 (86), 43 (93), 41 (100). Anal. Calcd for $C_{12}H_{26}O$: C, 77.3; H, 14.1. Found: C, 77.0; H, 14.2.

j. *syn*-7,9-Dimethylhexadecan-10-ol. According to the procedure mentioned above, alcohol **9** was oxidized to its corresponding aldehyde by 4-methylmorpholine *N*-oxide and tetrapropylammonium perruthenate (refer to Scheme 1). [GCMS: *m/z* 153 ($M^+ - 31$, <1), 141 (1), 126 (17), 111 (94), 85 (21), 71 (54), 58 (64), 57 (76), 43 (100), 41 (83).] This aldehyde was treated with *n*-hexylmagnesium bromide (prepared from *n*-hexyl bromide (85 μL, 0.60 mmol) and Mg turnings (75 mg, 3.1 mmol) in diethyl ether (10 mL)) in the Grignard procedure described earlier to provide the required alcohol as two diastereomers in 85% yield. ^{1}H NMR (400 MHz, *J* in Hz): δ 3.45 (m, 1H), 1.75−1.20 (m, 24H), 0.87−0.81 (m, 12H). ^{13}C NMR (100 MHz): δ 74.8, 41.2, 36.6, 35.2, 34.7, 31.9, 30.2, 30.0, 29.7, 29.4, 26.8, 26.7, 26.2, 22.7, 22.6, 14.1, 14.0. GCMS: Only one peak was observed. *m/z* 252 ($M^+ - 18$, <1), 185 (5), 154 (3), 115 (23), 97 (91), 69 (34), 57 (37), 55 (100), 43 (65), 41 (51). Anal. Calcd for $C_{18}H_{38}O$: C, 79.9; H, 14.2. Found: C, 80.2; H, 14.4.

k. *syn*-7,9-Dimethylhexadecane, 10. *syn*-7,9-Dimethylhexadecan-10-ol was reduced to alkane **10** (with the major and minor isomers being the *syn* and the *anti* ones, respectively) in 62% yield over two steps via mesylation and hydride displacement (refer to Scheme 1). Anal. Calcd for $C_{18}H_{38}$: C, 84.9; H, 15.1. Found: C, 85.1; H, 15.4. **10** (*syn*): ^{1}H NMR (400 MHz, *J* in Hz): δ 1.48−1.19 (m, 26H), 0.87 (t, *J* 6.6, 6H), 0.81 (d, *J* 6.6, 6H). ^{13}C NMR (100 MHz): δ 45.2, 36.9, 32.0, 31.9, 30.0, 29.7, 29.4, 26.9, 26.8, 22.7, 20.3, 14.1. GCMS: *m/z* 239 ($M^+ - 15$, 1), 169 (4), 155 (4), 126 (6), 99 (9), 85 (41), 71 (68), 57 (100), 43 (91). **11** (*anti*): ^{1}H NMR (400 MHz): δ 1.48−1.19 (m, 26H), 0.87 (t, *J* 6.6, 6H), 0.79 (d, *J* 6.6, 6H). ^{13}C NMR (100 MHz): δ 44.9, 38.0, 30.1, 29.9, 29.8, 29.6, 29.3, 27.1, 19.6, 14.1.

2. Synthesis of (5,7-Dimethylundecyl)triphenylphosphonium Iodide, 44 (Refer to Scheme 3). a. 5,7-Dimethyl-8-(tetrahydropyran-2-yloxy)octan-3-ol. 3,5-Dimethyl-6-(tetrahydro-2*H*-pyran-2-yloxy)hexanal (refer to the synthetic route of **10** and **11** for the preparation) was reacted with EtMgBr (prepared from EtBr and magnesium turnings in diethyl ether) in the manner described above (refer to Scheme 1) to provide the required secondary alcohol (78%, four diastereomers). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.55−4.48 (m, 4H), 3.88−3.80 (m, 4H), 3.62−3.56 (m, 6H), 3.50−3.43 (m, 6H), 3.24 (dd, *J* 9.4, 4.6, 1H), 3.23 (dd, *J* 9.4, 5.3, 1H), 3.18 (dd, *J* 9.5, 6.2, 1H), 3.10 (dd, *J* 9.4, 6.8, 1H), 1.83−1.23 (m, 60H), 0.95−0.86 (m, 36H). ^{13}C NMR (100 MHz): δ 99.43, 99.35, 99.2, 98.8, 63.0, 62.6, 62.3, 62.2, 44.9, 44.8, 44.3, 44.2, 42.32, 42.29, 41.3, 40.7, 40.5, 31.09, 31.08, 30.9, 30.83, 30.81, 30.7, 30.3, 30.2, 27.2, 26.8, 26.6, 25.51, 25.50, 25.46, 25.44, 21.2, 21.1, 20.12, 20.10, 20.08, 19.8, 19.6, 19.5, 18.7, 18.5, 18.0, 17.9, 9.9, 9.8. GCMS: Only one GC peak was observed. *m/z* 200 ($M^+ - 58$, <1), 172 (<1), 145 (1), 129 (3), 111 (8), 101 (11), 85 (100), 69 (46), 55 (37), 41 (37). Anal. Calcd for $C_{15}H_{30}O_3$: C, 69.7; H, 11.7. Found: C, 69.8; H, 12.0.

b. 2-(2,4-Dimethyloctyloxy)tetrahydropyran, 40. 5,7-Dimethyl-8-(tetrahydropyran-2-yloxy)octan-3-ol was reduced to THP ether **40** (72%, two diastereomers) by the mesylation and hydride displacement protocol described earlier (refer to Scheme 1). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.56 (t, *J* 3.2, 1H), 4.53 (dd, *J* 4.2, 2.7, 1H), 3.84 (m, 2H), 3.60 (dd, *J* 9.4, 5.4, 1H), 3.48 (m, 2H), 3.43 (dd, *J* 9.4, 7.8, 1H), 3.23 (dd, *J* 9.3, 5.1, 1H), 3.07 (dd, *J* 9.4, 7.1, 1H), 1.81 (m, 2H), 1.69−0.85 (m, 28H), 0.92 (d, *J* 6.7, 3H), 0.90 (d, *J* 6.7, 3H), 0.86 (t, *J* 6.9, 6H), 0.85 (d, *J* 6.6, 6H). ^{13}C NMR (100 MHz): δ 99.2, 98.6, 73.3, 73.0, 62.3, 61.9, 41.7, 41.6, 36.5, 36.4, 30.9, 30.8, 30.74, 30.72, 30.02, 29.99, 29.1, 25.6, 25.5, 23.0, 20.4, 20.3, 19.6, 19.4, 18.1, 18.0, 14.1. GCMS: Only one GC peak was observed. *m/z* 157 ($M^+ -$ 85, <1), 141 (<1), 101 (2), 85 (100), 71 (14), 57 (36), 43 (94). Anal. Calcd for $C_{15}H_{30}O_2$: C, 74.3; H, 12.5. Found: C, 74.1; H, 12.7.

c. 1-Bromo-2,4-dimethyloctane, 41. Under an inert atmosphere, bromine (0.65 mL, 12.7 mmol) was added to triphenylphosphine (3.47 g, 13.2 mmol) in dichloromethane (10 mL) at 0 °C and stirred for 30 min. To this was added THP ether **40** (1.5 g, 6.2 mmol) in dichloromethane (1 mL), and the mixture was stirred at room temperature for 3.5 h. After the addition of MeOH (2 mL) and dichloromethane (10 mL), the solution was stirred for another 10 min and then washed with saturated $NaHCO_3$ (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$) and concentrated. Flash chromatography (hexane) furnished bromide **41** (1.2 g, 81%). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.39 (dd, *J* 9.8, 4.3, 1H), 3.28 (dd, *J* 9.7, 6.3, 1H), 1.87 (m, 1H), 1.45 (m, 1H), 1.38 (dd, *J* 13.2, 6.7, 1H), 1.30−0.85 (m, 7H), 0.99 (d, *J* 6.6, 3H), 0.87 (t, *J* 6.8, 3H), 0.85 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 42.5, 41.7, 36.5, 32.5, 30.0, 29.0, 23.0, 20.0, 19.4, 14.1. GCMS: *m/z* 165 ($M^+ - 57$, 17), 163 (18), 122 (2), 120 (3), 83 (18), 69 (6), 55 (34), 43 (100). Anal. Calcd for $C_{13}H_{27}Br$: C, 59.3; H, 10.3. Found: C, 59.8; H, 10.7.

d. 5,7-Dimethylundecan-1-ol, 42. Allylmagnesium bromide (1.0 M in diethyl ether, 20 mL, commercial supplier) was slowly added to a solution of bromide **41** (0.92 g, 4.2 mmol) in THF (10 mL) under an inert atmosphere. The reaction was refluxed for 3 days, followed by quenching with saturated NH_4Cl (10 mL) at 0 °C. The aqueous phase was separated and extracted with diethyl ether (3 × 10 mL). The combined organic portions were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. 5,7-Dimethylundec-1-ene (0.66 g, 86%) was obtained after (two) flash chromatographic purifications (hexane). [^{1}H NMR (400 MHz, *J* in Hz): δ 5.78 (qt, *J* 10.1, 6.6, 1H), 4.98 (dq, *J* 17.3, 1.8, 1H), 4.91 (ddt, *J* 10.0, 2.3, 1.2, 1H), 2.00 (m, 2H), 1.62−0.80 (m, 12H), 0.85 (t, *J* 6.8, 3H), 0.84 (d, *J* 6.7, 3H), 0.82 (d, *J* 6.7, 3H). ^{13}C NMR (100 MHz): δ 139.5, 113.9, 45.1, 36.6, 36.1, 31.2, 30.0, 29.6, 29.2, 23.1, 20.3, 20.1, 14.2. GCMS: *m/z* 140 ($M^+ - 42$, 1), 125 (9), 111 (1), 97 (2), 83 (17), 69 (29), 55 (43), 43 (100).] The alkene (0.60 g, 3.3 mmol) was redissolved in dichloromethane (3 mL), and to this was added BH_3·DMS (5.0 M in diethyl ether, 0.17 mL) dropwise at 0 °C under an inert atmosphere. After 3 h of stirring at room temperature, ethanol (15 mL) was added dropwise, followed by cautious addition of 2 M NaOH (20 mL). After recooling to 0 °C, H_2O_2 (30 wt %, 3 mL) was added dropwise and the heterogeneous solution was stirred at ~50 °C for 1 h. The reaction was poured into H_2O (30 mL) and extracted with dichloromethane (3 × 15 mL). The combined extracts were washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was purified (flash chromatography) to afford the pure alcohol **42** (0.38 g, 58%). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.63 (dt, *J* 6.6, 5.7, 2H), 1.59−0.80 (m, 17H), 0.86 (t, *J* 6.7, 3H), 0.83 (d, *J* 6.6, 3H), 0.82 (d, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 63.1, 45.2, 36.7, 36.5, 33.2, 30.02, 29.99, 29.2, 23.1, 20.3, 20.2, 14.2. Anal. Calcd for $C_{13}H_{28}O$: C, 77.9; H, 14.1. Found: C, 77.8; H, 14.4.

e. 1-Bromo-5,7-dimethylundecane, 43. Alcohol **42** (0.34 g, 1.7 mmol) was mesylated in the manner described earlier (refer to Scheme 1). [GCMS: *m/z* 140 ($M^+ - 138$, <1), 125 (30), 109 (7), 97 (21), 83 (70), 79 (32), 69 (75), 55 (100).] The crude mesylate was taken up in THF (10 mL) and refluxed for 1.5 h with LiBr (0.45 g, 5.2 mmol). After the reaction was quenched with H_2O (5 mL), the aqueous layer was separated and extracted with diethyl ether (3 × 10 mL). The combined ethereal extracts were dried ($MgSO_4$) and concentrated. Bromide **43** (0.35 g, 79% over two steps) was obtained as a colorless liquid after column chromatography (hexane). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.39 (t, *J* 6.8, 2H), 1.83 (m, 2H), 1.51−0.80 (m, 14H), 0.87 (t, *J* 7.1, 3H), 0.84 (d, *J* 6.8, 3H), 0.82 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 45.1, 36.5, 35.9, 34.0, 33.2, 30.0, 29.9, 29.2, 25.5, 23.1, 20.3, 20.2, 14.2. GCMS: *m/z* 249 ($M^+ - 15$, 1), 247 (1), 207 (1), 205 (1), 165 (4), 163 (5), 137 (25), 135 (27), 127 (9), 97 (11), 85 (44), 71 (51), 55 (100). Anal. Calcd for $C_{13}H_{27}Br$: C, 59.3; H, 10.3. Found: C, 59.6; H, 10.8.

f. (5,7-Dimethylundecyl)triphenylphosphonium Bromide, 44. Alkyl bromide **43** (0.29 g, 1.1 mmol) and triphenylphosphine (0.46 g, 1.8 mmol) were refluxed in MeCN (8 mL) for 4 days. The solvent was evaporated, and the residue was washed thoroughly with hexane several times to remove the excess triphenylphosphine. After being dried under vacuum, Wittig salt **44** (0.48 g, 95%) was acquired as a viscous oil and used in the coupling reaction without further purification. ^{1}H NMR (400 MHz, *J* in Hz): δ 7.84−7.66 (m, 15H), 3.76 (m, 2H), 1.60 (m, 3H), 1.36 (m, 2H), 1.25−0.80 (m, 11H), 0.81 (t, *J* 6.8, 3H), 0.75 (d, *J* 6.5, 3H), 0.74 (d, *J* 6.8, 3H). ^{13}C NMR (100 MHz): δ 135.0 (d, *J* 3.3), 133.7 (d, *J* 10.0), 130.5 (d, *J* 12.6), 128.5 (d, *J* 7.3), 118.4 (d, *J* 85.6), 45.1, 36.6, 36.3, 29.9, 29.8, 29.1, 28.1 (d, *J* 15.3), 23.1 (d, *J* 4.6), 23.0, 22.9, 20.3, 20.0, 14.1.

3. Synthesis of *sss*(*s*)- and *ssa*(*s*)-4,6,8,10,16,18-Hexamethyldocosanes, 16 and 17 (Refer to Schemes 2 and 4). a. 2,4,6-Trimethylcyclohexanone. 2,4,6-Trimethylphenol, **27** (6.0 g, 44.1 mmol) and rhodium (10% on activated carbon, 0.29 g) in hexane (80 mL) were stirred under a hydrogen atmosphere (500 psi) for 3 days in a high pressure autoclave. The reaction was filtered through Celite, followed by the removal of the solvent to yield a crude mixture consisting mainly of the *all-cis* alcohol. GCMS analysis indicated four components in the ratio of ~70:15:10:5, in which a minor one was later identified as the cyclic ketone. [GCMS of the major *all-cis* trimethylcyclohexanol: *m/z* 141 ($M^+ - 1$, 7), 123 (1), 109 (13), 95 (8), 84 (26), 71 (95), 55 (46), 43 (100).] The mixture was treated with Jones reagent (8 M in H_2O/H_2SO_4, ~6.5 mL) in acetone (100 mL) to furnish the title ketone (4.4 g, 71%, ~85% *all-cis* isomer) after flash chromatography (15% diethyl ether in hexane). ^{1}H NMR (400 MHz, *J* in Hz): δ 2.43 (dm, *J* 6.6, 1.3, 2H), 2.00 (m, 3H), 1.09 (dq, *J* 12.9, 1.4, 2H), 0.97 (d, *J* 6.5, 6H), 0.93 (d, *J* 6.2, 3H). ^{13}C NMR (100 MHz): δ 214.8, 45.3, 44.2, 32.0, 21.2, 14.5. GCMS: *m/z* 140 (M^+, 20), 125 (4), 112 (8), 97 (26), 82 (42), 69 (100), 52 (69), 41 (92). These spectral data matched those reported.[12]

b. 3,5,7-Trimethyloxepan-2-one. 2,4,6-Trimethylcyclohexanone (3.4 g, 24.3 mmol) was converted to the desired lactone in 68% yield via Baeyer−Villiger oxidation with *m*CPBA and $NaHCO_3$ as mentioned earlier (refer to Scheme 1). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.50 (dt, *J* 9.5, 6.4, 1H), 2.70 (dm, *J* 6.5, 1.5, 1H), 1.86−1.75 (m, 2H), 1.63 (ddt, *J* 14.1, 3.6, 1.7, 1H), 1.38−1.23 (m, 2H), 1.32 (d, *J* 6.4, 3H), 1.16 (d, *J* 6.7, 3H), 0.92 (d, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 177.6, 74.9, 44.3, 40.3, 36.8, 34.8, 22.6, 18.5. GCMS: *m/z* 156 (M^+, <1), 141 (<1), 112 (11), 97 (12), 83 (11), 70 (96), 55 (100), 41 (88). These spectral data matched those reported.[12]

c. Methyl 6-Hydroxy-2,4-dimethylheptanoate, 29. 3,5,7-Trimethyloxepan-2-one was converted to hydroxyester **29** in 90% yield via methanolysis, using the procedure described earlier (refer to Scheme 1). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.87 (ddq, *J* 9.0, 6.2, 4.2, 1H), 3.64 (s, 3H), 2.55 (ddq, *J* 9.2, 7.0, 5.6, 1H), 1.70 (ddd, *J* 14.4, 9.2, 5.2, 1H), 1.58 (m, 1H), 1.53 (br s, 1H), 1.40 (ddd, *J* 13.9, 9.0, 5.1, 1H), 1.60 (d, *J* 6.2, 3H), 1.13 (d, *J* 7.0, 3H), 0.90 (d, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 177.4, 65.7, 51.4, 41.6, 27.7, 24.1, 19.5, 17.9. GCMS: *m/z* 173 ($M^+ - 15$, <1), 157 (1), 144 (6), 129 (2), 113 (3), 101 (100), 88 (48), 69 (57), 55 (35), 45 (58). These spectral data matched those reported.[12]

d. 2,4-Dimethyl-6-(tetrahydropyran-2-yloxy)heptan-1-ol, 30. Hydroxyester **29** (3.3 g, 17.6 mmol) was protected as the corresponding THP ether (two diastereomers) in the same manner described earlier (refer to Scheme 1). [^{1}H NMR (400 MHz): δ 4.69 (t, *J* 3.6, 1H), 4.59 (t, *J* 3.8, 1H), 3.92−3.74 (m, 4H), 3.47 (m, 2H), 2.54 (m, 2H), 1.82−1.47 (m, 22H), 1.20 (d, *J* 6.2, 3H), 1.13 (d, *J* 6.9, 3H), 1.12 (d, *J* 7.0, 3H), 1.07 (d, *J* 6.1, 3H), 0.91 (d, *J* 6.5, 3H), 0.89 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 177.5, 99.5, 95.1, 72.8, 68.4, 62.8, 62.2, 51.42, 51.38, 44.9, 44.6, 41.6, 41.5, 37.19, 37.16, 31.3, 31.2, 27.4, 27.2, 25.6, 25.5, 22.3, 20.1, 20.0, 19.8, 19.7, 19.6, 19.5, 17.76, 17.73. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 171 ($M^+ - 101$, 35), 139 (28), 111 (27), 85 (100), 69 (38), 55 (28), 41 (36). Second diastereomer: 171 ($M^+ - 101$, 26), 139 (20), 111 (19), 85 (100), 69 (31), 55 (24), 41 (29).] The above ester was then reduced to alcohol **30** (3.9 g, 90% over two steps as two diastereomers) using the LAH protocol described previously (refer to Scheme 1). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.65 (dd, *J* 4.8, 3.4, 1H), 4.59 (dd, *J* 4.8, 2.8, 1H), 3.88 (m, 3H), 3.75 (m, 1H), 3.46 (m, 5H), 3.37 (ddd, *J* 11.6, 11.0, 6.1, 1H), 1.79−1.40 (m, 21H), 1.26 (m, 1H), 1.17 (d, *J* 6.2, 3H), 1.08 (d, *J* 6.1, 3H), 0.91 (d, *J* 6.8, 3H), 0.89 (d, *J* 7.0, 3H). ^{13}C NMR (100 MHz): δ 99.8, 95.7, 73.0, 69.4, 68.3, 67.9, 62.9, 44.9, 44.7, 41.4, 41.3, 33.0, 31.4, 31.3, 27.1, 26.7, 25.54, 25.50, 22.6, 20.8, 20.1, 20.0, 19.9, 17.5, 17.2. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 159 ($M^+ - 85$, 2), 143 (29), 125 (7), 101 (17), 85 (100), 69 (88), 55 (68), 41 (74). Second diastereomer: 159 ($M^+ - 85$, 1), 143 (19), 125 (6), 101 (13), 85 (100), 69 (81), 55 (62), 41 (70). Anal. Calcd for $C_{14}H_{28}O_3$: C, 68.8; H, 11.6. Found: C, 68.6; H, 11.8.

e. 2-(6-Iodo-1,3,5-trimethylhexyloxy)tetrahydropyran, 31. At 0 °C, iodine (3.5 g, 13.8 mmol) was added portionwise to a solution of triphenylphosphine (5.4 g, 20.6 mmol), imidazole (1.4 g, 20.6 mmol), and alcohol **30** (1.7 g, 6.9 mmol) in diethyl ether/MeCN (3:1, 40 mL). The milky yellow solution was stirred in the dark at room temperature overnight, and then it was diluted with diethyl ether (20 mL) and washed with aqueous NaS_2O_3 (5%, 20 mL). The aqueous layer was extracted with diethyl ether (3 × 15 mL), and the combined organic fractions were dried ($MgSO_4$). After the removal of solvent, the residual paste was triturated with hexane (3 × 15 mL). The combined hexane fractions were concentrated and purified (flash chromatography, 10% diethyl ether in hexane) to furnish iodide **31** (2.2 g, 92%, two diastereomers). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.69 (t, *J* 3.8, 1H), 4.59 (dd, *J* 4.9, 2.8, 1H), 3.91−3.82 (m, H), 3.76 (m, 1H), 3.23 (dd, *J* 7.5, 4.2, 1H), 3.20 (dd, *J* 7.6, 3.3, 1H), 3.12 (dd, *J* 6.2, 1.7, 1H), 3.09 (dd, *J* 6.1, 1.6, 1H), 1.83−1.48 (m, 20H), 1.28 (m, 2H), 1.22 (d, *J* 6.2, 3H), 1.16−0.98 (m, H), 1.08 (d, *J* 6.2, 3H), 0.96 (d, *J* 6.5, 3H), 0.94 (d, *J* 6.5, 3H), 0.90 (d, *J* 6.6, 3H), 0.88 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 99.8, 95.2, 72.9, 68.4, 62.4, 45.0, 44.8, 44.4, 44.3, 31.9, 31.7, 31.3, 31.2, 26.7, 25.6, 25.5, 21.2, 20.3, 20.1, 20.0, 19.72, 19.66, 18.2, 18.0. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 354 (M^+, 1), 253 (11), 183 (12), 169 (20), 125 (4), 101 (9), 85 (100), 69 (31), 55 (44), 41 (78). Second diastereomer: 354 (M^+, 1), 253 (10), 211 (6), 197 (10), 183 (12), 169 (19), 101 (10), 85 (100), 69 (30), 55 (44), 41 (79). Anal. Calcd for $C_{14}H_{28}IO_2$: C, 47.5; H 7.7. Found: C, 47.6; H, 7.6.

f. *syn*-4,6-Dimethylnonan-2-ol, 32. A solution of iodide **31** (4.8 g, 13.4 mmol) and Li_2CuCl_4 (1.0 M in THF, 6.7 mL) in anhydrous THF was slowly added to EtMgBr (2.8 M in diethyl ether, 13.5 mL) at 0 °C under an inert atmosphere. The resulting deep purple solution was stirred for 4 h, followed by careful addition of saturated NH_4Cl (15 mL) and extraction with diethyl ether (3 × 25 mL). The combined organic layers

were washed with brine (10 mL), dried ($MgSO_4$), and concentrated to afford the crude THP ether as two diastereomers. [^{1}H NMR (400 MHz, *J* in Hz): δ 4.75 (t, *J* 3.2, 1H), 4.63 (dd, *J* 5.0, 2.9, 1H), 3.92 (m, 3H), 3.80 (m, 1H), 3.51 (m, 2H), 1.85−1.03 (m, 32H), 1.25 (d, *J* 6.3, 3H), 1.11 (d, *J* 6.0, 3H), 0.88 (d, *J* 6.5, 3H), 0.86 (t, *J* 7.0, 6H), 0.85 (d, *J* 6.6, 3H), 0.84 (d, *J* 6.7, 3H), 0.82 (d, *J* 6.7, 3H).] The above THP ether underwent deprotection in the manner described earlier (refer to Scheme 1) to furnish the secondary alcohol **32** (2.0 g, 86% over two steps). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.89 (m, 1H), 1.69 (m, 1H), 1.45 (m, 2H), 1.37−0.96 (m, 8H), 1.18 (d, *J* 6.2, 3H), 0.88 (d, *J* 6.6, 3H), 0.86 (t, *J* 7.0, 3H), 0.83 (d, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 65.8, 46.8, 45.8, 39.1, 29.6, 26.7, 24.4, 20.2, 20.00, 19.99, 14.4. GCMS: *m/z* 157 ($M^+ - 15$, <1), 111 (6), 97 (1), 85 (10), 69 (22), 55 (21), 45 (100), 43 (70). Anal. Calcd for $C_{11}H_{24}O$: C, 76.7; H, 14.0. Found: C, 77.2; H, 14.0.

g. 4,6-Dimethylnonan-2-yl 4-Chlorobenzoate. Diisopropyl azodicarboxylate (1.4 mL, 7.1 mmol) in THF (10 mL) was added dropwise to a solution of alcohol **32** (1.0 g, 5.8 mmol), *p*-chlorobenzoic acid (1.1 g, 7.0 mmol), and triphenylphosphine (2.7 g, 10.2 mmol) in THF (20 mL) at 0 °C. The pale yellow solution was stirred for 1.25 h and diluted with diethyl ether (20 mL). After the solution was washed with H_2O (15 mL) and brine (15 mL), the organic phase was dried ($MgSO_4$), concentrated, and purified by flash chromatography (2% diethyl ether in hexane, then 5%) to furnish the corresponding benzoate ester. ^{1}H NMR (400 MHz, *J* in Hz): δ 7.95 (dt, *J* 8.7, 2.0, 2H), 7.38 (dt, *J* 8.72, 2.0, 2H), 5.23 (m, *J* 6.64, 1H), 1.62 (m, 1H), 1.54 (dd, *J* 14.4, 6.7, 1H), 1.31 (d, *J* 6.2, 3H), 1.30−0.85 (m, 9H), 0.91 (d, *J* 6.3, 3H), 0.82 (d, *J* 6.6, 3H), 0.78 (d, *J* 7.2, 3H). ^{13}C NMR (100 MHz): δ 165.2, 139.1, 130.9, 129.4, 128.6, 70.7, 45.0, 43.3, 38.9, 29.7, 29.6, 27.2, 20.5, 20.22, 20.16, 19.8, 14.3. GCMS: *m/z* 225 ($M^+ - 85$, <1), 197 (<1), 181 (<1), 157 (8), 139 (75), 111 (53), 85 (36), 69 (60), 55 (44), 43 (100). Anal. Calcd for $C_{18}H_{27}ClO_2$: C, 69.5; H, 8.7. Found: C, 69.0; H, 8.9.

h. *anti*-4,6-Dimethylnonan-2-ol, 33. The above benzoate was redissolved in MeOH (8 mL), and K_2CO_3 (2.4 g, 17.4 mmol) was added with a few drops of H_2O. The suspension was stirred for 2.5 h, followed by the addition of H_2O (15 mL) and extraction with dichloromethane (3 × 15 mL). The combined organic phases were washed with brine (15 mL), dried ($MgSO_4$), and concentrated. The alcohol was purified by flash chromatography (10% diethyl ether in hexane, and then 40%) to afford the pure alcohol **33** (0.83 g, 83% over two steps). ^{1}H NMR (400 MHz): δ 3.88 (m, 1H), 1.57 (m, 1H), 1.49 (m, 1H), 1.38−1.19 (m, 5H), 1.16 (d, *J* 6.2, 3H), 1.04−0.85 (m, 4H), 0.87 (d, *J* 6.6, 3H), 0.86 (t, *J* 7.0, 3H), 0.82 (t, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 66.4, 47.1, 45.3, 39.0, 29.7, 27.4, 23.6, 20.7, 20.3, 20.0, 14.4. This alcohol is a diastereomer of the fully characterized secondary alcohol **32**.

i. 2,4,6-Trimethylnonan-1-ol. Alcohol **33** (0.64 g, 3.7 mmol) was mesylated using the same procedure mentioned earlier (refer to Scheme 1). [GCMS of the mesylate: *m/z* 156 ($M^+ - 80$, <1), 111 (32), 97 (12), 85 (33), 79 (21), 69 (90), 55 (68), 43 (100).] With extreme care, NaCN (0.90 g, 18.4 mmol) was added to the above mesylate in anhydrous DMF (10 mL). The orange mixture was heated to ~85 °C for 24 h and then diluted with H_2O (20 mL) and extracted with diethyl ether (3 × 15 mL). The aqueous layer was drained into diluted NaOCl, whereas the combined organic layers were washed with more H_2O (3 × 5 mL), dried ($MgSO_4$), and concentrated. The desired nitrile (0.41 g, 61% over two steps) was obtained as a clear liquid after purification by flash chromatography (10% diethyl ether in hexane). [^{1}H NMR (400 MHz, *J* in Hz): δ 2.66 (m, 1H), 1.77 (m, 1H), 1.65 (m, 1H), 1.48 (m, 1H), 1.34−0.95 (m, 7H), 1.29 (d, *J* 7.0, 3H), 0.88 (d, *J* 6.8, 3H), 0.85 (t, *J* 7.5, 3H), 0.84 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 122.9, 45.1, 41.3, 39.1, 29.5, 28.3, 23.5, 19.94, 19.90, 19.6, 18.7, 14.3. GCMS: *m/z* 181 (M^+, <1), 166 (4), 152 (9), 139 (13), 124 (6), 110 (19), 97 (22), 83 (5), 68 (36), 55 (56), 43 (100).] Anhydrous MeOH (20 mL) was placed in a two-necked flask equipped with a $NaHCO_3$ trap. Acetyl chloride (10 mL) was added very slowly at 0 °C, and the resulting solution was stirred for 10 min. 2,4,6-Trimethylnonanenitrile (0.28 g, 1.5 mmol) in dry MeOH (2 mL) was added in one portion to the cold solution and stirred for 2 days. The solution was then diluted with H_2O (80 mL), followed by dichloromethane extractions (4 × 15 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (2 × 10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated to give methyl ester **34** (0.22 g, 63%). [GCMS: *m/z* 171 ($M^+ - 43$, 3), 129 (6), 111 (3), 101 (70), 88 (100), 69 (27), 55 (24).] Ester **34** was then reduced immediately with LAH to give the desired alcohol (0.19 g, 98%) as a clear oil. ^{1}H NMR (400 MHz, *J* in Hz): δ 3.52 (dt, *J* 10.6, 5.0, 1H), 3.55 (ddt, *J* 10.6, 5.3, 1.2, 1H), 1.71 (dm, *J* 6.8, 1.7, 1H), 1.57 (m, *J* 7.2, 1H), 1.49 (m, 1H), 1.36−1.16 (m, 5H), 1.13−0.85 (m, 4H), 0.91 (d, *J* 6.8, 3H), 0.86 (t, *J* 6.8, 3H), 0.85 (d, *J* 6.8, 3H), 0.82 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 68.3, 45.2, 41.3, 38.8, 33.1, 29.7, 27.5, 20.9, 20.4, 19.9, 17.5, 14.4. GCMS: *m/z* 153 ($M^+ - 17$, <1), 139 (<1), 125 (20), 111 (24), 97 (12), 83 (71), 69 (70), 57 (100). Anal. Calcd for $C_{12}H_{26}O$: C, 77.4; H, 14.1. Found: C, 77.2; H, 14.5.

j. Methyl 2,4,6,8-Tetramethylundec-2-enoate, 37. DMSO (0.11 mL, 0.95 mmol) was added dropwise to a solution of oxalyl chloride (0.10 mL, 1.15 mmol) in dichloromethane (2 mL) at −78 °C. After 5 min of stirring, 2,4,6-trimethylnonan-1-ol (71 mg, 0.38 mmol) in dichloromethane (1.5 mL) was added and the reaction mixture was stirred for 1 h. Following the addition of triethylamine (0.55 mL, 3.81 mmol), the solution was stirred for 15 min at −78 °C and another 20 min at 0 °C. Diethyl ether (20 mL) was added, and the organic solution was washed with brine (2 × 5 mL), dried ($MgSO_4$), and concentrated. The crude aldehyde **35** was redissolved in dichloromethane (2 mL) and dried over 4 Å sieves for several hours. [GCMS: *m/z* 184 (M^+, <1), 166 (<1), 141 (<1), 126 (6), 111 (2), 95 (3), 85 (7), 71 (31), 57 (43), 43 (100).] This aldehyde solution was refluxed overnight with ylide **36** (prepared from ethyl 2-bromopropionate and triphenylphosphine,[16] 0.18 g, 0.50 mmol). After the removal of solvent, the residue was triturated with hexane (3 × 5 mL). The combined organic fractions were concentrated and purified by column chromatography (5% diethyl ether in hexane) to give ester **37** (90 mg, 88%) as a clear oil. ^{1}H NMR (400 MHz, *J* in Hz): δ 6.48 (dq, *J* 10.3, 1.5, 1H), 4.16 (qq, *J* 10.8, 7.1, 2H), 2.60 (m, 1H), 1.83 (d, *J* 1.5, 3H), 1.50−0.85 (m, 10H), 1.27 (t, *J* 7.0, 3H), 0.95 (d, *J* 6.5, 3H), 0.85 (t, *J* 7.2, 3H), 0.80 (d, *J* 6.5, 3H), 0.79 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 168.4, 148.2, 126.2, 60.3, 45.6, 44.3, 39.3, 30.9, 29.6, 28.1, 20.6, 20.4, 19.98, 19.96, 14.4, 14.3, 12.5. GCMS: *m/z* 268 (M^+, 1), 223 (3), 179 (2), 155 (4), 142 (5), 115 (40), 102 (16), 83 (22), 69 (33), 55 (24), 43 (100).

k. 2,4,6,8-Tetramethylundecan-1-ol, 38 (*sss* and *ssa*). Mg turnings (25 mg, 1.0 mmol) were added to the unsaturated ester **37** (28 mg, 0.10 mmol) in anhydrous MeOH (4 mL). Gas evolution was observed after 20 min of stirring, and after 4 h, all Mg pieces had dissolved and a white precipitate had formed. After cooling to 0 °C, 2.5 M HCl (5 mL) was added to dissolve the solid, followed by extraction with diethyl ether (3 × 8 mL). The combined ethereal extracts were washed with saturated $NaHCO_3$ (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The crude product, identified as a mixture of the methyl and ethyl esters, was dissolved in diethyl ether (1 mL) and dried over 4 Å sieves for several hours. [GCMS: Four GC peaks were observed. Methyl ester, first diastereomer: *m/z* 256 (M^+, 1), 225 (<1), 213 (1), 185 (1), 166 (1), 139 (2), 129 (6), 101 (100), 88 (92), 69 (34), 57 (45), 43 (94). Second diastereomer: 256 (M^+, 1), 225 (<1), 185 (1), 166 (1), 139 (2), 129 (5), 111 (6), 101 (100), 88 (93), 69 (29), 57 (40), 43 (83). Ethyl ester, first diastereomer: 270 (M^+, 1), 227 (1), 185 (1), 143 (2), 125 (1), 115 (88), 102 (100), 87 (16), 74 (20), 69 (28), 55 (38), 43 (91). Second diastereomer: 270 (M^+, 1), 255 (<1), 227 (1), 185

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(1), 143 (5), 125 (2), 115 (86), 102 (100), 87 (15), 69 (29), 55 (40), 43 (98).] The ester solution was reduced further with LAH to provide alcohol **38** (21 mg, 88%) after column chromatography (10% diethyl ether in hexane). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.53 (dd, *J* 10.44, 4.92, 1H), 3.45 (dd, *J* 10.50, 5.92, 1H), 3.39 (dd, *J* 10.52, 6.56, 1H), 3.35 (dd, *J* 10.44, 6.88, 1H), 1.71−0.97 (m, 32H), 0.92 (d, *J* 6.68, 3H), 0.91−0.78 (5 × d, 21H). ^{13}C NMR (100 MHz): δ 69.3, 68.2, 46.1, 45.52, 45.46, 45.1, 41.1, 40.1, 39.0, 38.8, 33.3, 33.1, 29.74, 29.68, 27.55, 27.43, 27.22, 27.1, 21.04, 21.00, 20.6, 20.5, 20.4, 20.2, 19.98, 19.94, 17.6, 16.1, 14.4. Anal. Calcd for $C_{15}H_{32}O$: C, 78.4; H, 14.1. Found: C, 78.2; H, 14.3.

l. *sss*(*s*)- and *ssa*(*s*)-4,6,8,10,16,18-Hexamethyldocosanes, 16 and 17. The tetramethyl alcohols **38** (*sss* and *ssa*; 21 mg, 0.092 mmol) were oxidized under Swern conditions, described earlier, to provide the crude aldehyde **45**. The aldehyde was redissolved in THF (0.5 mL) for the coupling reaction. At −78 °C, ^{n}BuLi (0.7 M in hexane, 0.18 mL) was added slowly to a solution of Wittig salt **44** (69 mg, 0.13 mmol) in THF (1.5 mL). The bright orange solution was stirred for 45 min at 0 °C and recooled to −78 °C. The aldehyde solution was added dropwise to the above and allowed to stir overnight, while the temperature rose gradually. The excess ylide was quenched by saturated NH_4Cl (3 mL), followed by extraction with diethyl ether (3 × 10 mL). The combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. The corresponding alkenes (25 mg, 60%) were obtained as a clear liquid, which was mixed with 40% of the Wittig dimer, 5,7,-16,18-tetramethyldocosane, after flash chromatography (hexane). Subsequently, Wittig dimer formation in these coupling reactions could be completely suppressed by rigorous exclusion of oxygen by solvent degassing etc. (demonstrated in the formation of **15**, **18**, **84**, and **85**). [^{1}H NMR (400 MHz, *J* in Hz): δ 5.38−5.01 (m, 4H), 2.52 (m, 4H), 1.98 (m, 4H), 1.49−1.03 (m, 52H), 0.91−0.78 (m (should contain 12 × d and 4 × t), 48H). ^{13}C NMR (100 MHz): δ 137.0, 136.3, 129.9, 128.5, 127.8, 45.9, 45.7, 45.6, 45.2, 45.1, 44.7, 39.1, 38.8, 36.58, 36.55, 30.0, 29.9, 29.75, 29.70, 29.2, 27.8, 27.7, 27.6, 27.4, 27.3, 27.1, 23.1, 22.3, 20.95, 20.86, 20.75, 20.72, 20.68, 20.5, 20.35, 20.32, 20.29, 20.27, 20.00, 19.95, 14.4, 14.2. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 392 (M^+, <1), 308 (<1), 264 (<1), 225 (<1), 209 (<1), 195 (<1), 181 (1), 167 (1), 153 (1), 139 (1), 125 (7), 111 (10), 97 (8), 85 (19), 69 (41), 57 (58), 43 (100). Second diastereomer: 392 (M^+, <1), 308 (<1), 264 (<1), 225 (<1), 209 (<1), 195 (1), 181 (1), 167 (1), 153 (2), 139 (1), 125 (7), 111 (10), 97 (9), 85 (19), 69 (39), 57 (59), 43 (100).] The above alkene mixture (22 mg, 0.056 mmol) was redissolved in hexane (1.5 mL) and stirred under a balloon of H_2 for 6 h with a catalytic amount of Pd−C (10% active, ∼5 mg). After filtration through silica gel, the filtrate was concentrated to furnish the required alkanes (**16** and **17** together with the dimer from the Wittig coupling, 17 mg, 77%) as a clear liquid. The separation of the alkanes was carried out using preparative GC. **16** and **17**: ^{1}H NMR (750 MHz, *J* in Hz): δ 1.55 (m, 4H), 1.49−1.43 (m, 8H), 1.32−1.13 (m, 52H), 1.03 (m, 4H), 0.87 (d, *J* 7.1, 6H), 0.86 (d, *J* 7.2, 6H), 0.84−0.78 [m with 0.814 (d, *J* 6.6), 0.812 (d, *J* 6.7), 36H]. **16**: ^{13}C NMR (187 MHz): δ 45.74, 45.23, 45.19, 38.86, 36.89, 36.88, 36.58, 36.52, 36.50, 30.42, 30.38, 30.06, 30.007, 30.000, 29.994, 29.985, 29.75, 29.18, 27.45, 27.43, 26.97, 26.94, 26.91, 26.90, 26.88, 23.07, 21.05, 21.04, 21.03, 20.559, 20.556, 20.50, 20.30, 19.95, 14.44, 14.18. GCMS: *m/z* 394 (M^+, <1), 309 (<1), 281 (<1), 267 (<1), 253 (<1), 239 (<1), 225 (1), 211 (1), 197 (2), 183 (2), 169 (1), 155 (5), 141 (3), 127 (5), 113 (8), 99 (12), 85 (31), 71 (59), 57 (93), 43 (100). **17**: ^{13}C NMR (187 MHz): δ 46.19, 45.50, 45.23, 45.22, 44.46, 44.45, 39.03, 38.26, 38.25, 36.89, 36.88, 36.58, 30.36, 30.09, 30.08, 30.06, 30.00, 29.99, 29.70, 29.18, 27.35, 27.27, 27.19, 27.18, 26.95, 26.94, 23.07, 20.72, 20.44, 20.39, 20.30, 19.99, 19.43, 14.44, 14.18. GCMS: *m/z* 394 (M^+, <1), 309 (<1), 281 (<1), 267 (<1), 253 (<1), 239 (<1), 225 (1), 211 (1), 197 (2), 183 (2), 169 (2), 155 (5), 141 (2), 127 (4), 113 (7), 99 (10), 85 (29), 71 (54), 57 (91), 43 (100).

4. Syntheses of *ssa*- and *asa*-4,6,8,10,16-Pentamethyldocosanes, 63 and 64, and *ssa*(*s*)- and *asa*(*s*)-4,6,8,10,16,-18-Hexamethyldocosanes, 17 and 14 (Refer to Scheme 6). a. Ethyl 2,4,6-Trimethyl-8-(tetrahydropyran-2-yloxy)-non-2-enoate, 56. At 0 °C, PCC (3.6 g, 16.7 mmol) was added to the monoprotected alcohol **30** (2.5 g, 10.2 mmol) in dry dichloromethane (50 mL). The dark brown mixture was stirred at room temperature for 5 h and concentrated under reduced pressure. The resulting paste was washed thoroughly with diethyl ether (3 × 60 mL), and the ethereal solution was passed through layers of silica gel and Celite. After drying ($MgSO_4$), the solvent was evaporated to provide the crude aldehyde as two diastereomers. [^{1}H NMR (400 MHz, *J* in Hz): δ 9.58 (d, *J* 2.4, 1H), 9.56 (d, *J* 2.4, 1H), 4.68 (t, *J* 3.8, 1H), 4.58 (dd, *J* 4.7, 2.7, 1H), 3.93−3.72 (m, 4H), 3.47 (m, 2H), 2.44 (dq, *J* 7.0, 2.3, 2H), 1.83−1.47 (m, 16H), 1.23 (d, *J* 7.0, 3H), 1.21 (d, *J* 7.1, 3H), 1.09 (d, *J* 6.0, 6H), 1.08 (d, *J* 7.0, 3H), 0.93 (d, *J* 6.5, 3H). GCMS: Only one peak was observed. *m/z* 141 (M^+ − 101, 15), 123 (37), 101 (7), 85 (100), 67 (18), 55 (44).] The aldehyde was redissolved in dichloromethane (20 mL) and refluxed with ylide **36** to give the unsaturated ester **56** (2.5 g, 75%, two diastereomers) according to the procedure described earlier (refer to Scheme 2). ^{1}H NMR (400 MHz, *J* in Hz): δ 6.47 (dq, *J* 10.0, 1.4, 2H), 4.71 (t, *J* 3.3, 1H), 4.57 (dd, *J* 4.8, 3.1, 1H), 4.16 (q, *J* 7.1, 2H), 3.93−3.72 (m, 4H), 3.45 (m, 2H), 2.60 (m, 2H), 1.82 (d, *J* 1.4, 6H), 1.77−1.43 (m, 20H), 1.27 (t, *J* 7.2, 3H), 1.26 (t, *J* 7.2, 3H), 1.19 (d, *J* 6.2, 3H), 1.06 (d, *J* 6.1, 3H), 0.98 (d, 6.6, 3H), 0.96 (d, 6.4, 3H), 0.87 (d, *J* 6.5, 3H), 0.84 (d, *J* 6.4, 3H). ^{13}C NMR (100 MHz): δ 148.1, 126.2, 94.7, 68.3, 61.9, 60.3, 45.5, 44.8, 31.1, 30.8, 27.2, 25.6, 20.4, 19.6, 19.5, 19.3, 14.3, 12.5. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 242 (M^+ − 84, 2), 198 (4), 151 (21), 123 (16), 113 (24), 109 (8), 95 (13), 85 (100), 67 (29), 55 (30). Second diastereomer: 242 (M^+ − 84, 1), 198 (6), 179 (2), 151 (22), 123 (15), 113 (26), 85 (100), 67 (23), 55 (18). Anal. Calcd for $C_{19}H_{34}O_4$: C, 69.9; H, 10.5. Found: C, 69.6; H, 10.2.

b. 2,4,6-Trimethyl-8-(tetrahydropyran-2-yloxy)nonanol, 57. By following the procedure mentioned earlier (refer to Scheme 4), unsaturated ester **56** (0.70 g, 2.1 mmol) was hydrogenated with Pd−C (10%, ∼40 mg) under H_2 to afford the saturated ester (0.65 g, 93%, four diastereomers). [GCMS: Four GC peaks were observed. First diastereomer: *m/z* 243 (M^+ − 85, <1), 227 (11), 181 (14), 139 (1), 125 (4), 111 (11), 85 (100), 69 (35), 55 (43), 41 (58). Second diastereomer: 243 (M^+ − 85, <1), 227 (8), 181 (15), 139 (1), 125 (4), 111 (11), 101 (5), 85 (100), 69 (37), 55 (47), 41 (60). Third diastereomer: 243 (M^+ − 85, <1), 227 (8), 181 (11), 139 (1), 125 (3), 111 (9), 101 (4), 85 (100), 69 (29), 55 (36), 41 (46). Fourth diastereomer: 243 (M^+ − 85, <1), 227 (8), 181 (10), 139 (1), 125 (8), 111 (8), 101 (4), 85 (100), 69 (28), 55 (37), 41 (48).] The ester mixture was further reduced to alcohol **57** (0.55 g, 97%, four diastereomers) using the LAH reduction protocol mentioned in Scheme 1. ^{1}H NMR (400 MHz, *J* in Hz): δ 4.70 (t, *J* 3.5, 2H), 4.59 (dd, *J* 4.6, 2.3, 2H), 3.93−3.73 (m, 8H), 3.53−3.43 (m, 9H), 3.36 (m, 3H), 1.85−1.10 (m, 112H), 1.07−0.83 (m including δ 1.07 (d, 6.0), 48H). ^{13}C NMR (100 MHz): δ 99.8, 99.6, 95.04, 94.97, 69.1, 68.6, 68.5, 68.2, 62.9, 62.8, 62.22, 62.19, 46.3, 46.2, 45.6, 45.5, 45.1, 44.8, 44.7, 44.5, 41.3, 40.5, 33.2, 33.1, 31.3, 31.2, 27.46, 27.42, 27.14, 27.09, 26.9, 26.5, 26.4, 25.6, 25.5, 22.67, 22.63, 21.0, 20.9, 20.8, 20.64, 20.59, 20.3, 20.1, 20.0, 19.9, 19.8, 19.7, 19.6, 19.5, 17.5, 16.34, 16.26, 14.1. GCMS: Only one GC peak was observed. *m/z* 256 (M^+ − 30, <1), 224 (<1), 185 (10), 129 (1), 111 (13), 101 (14), 85 (100), 69 (31), 55 (34). Anal. Calcd for $C_{17}H_{34}O_3$: C, 71.3; H, 12.0. Found: C, 71.4; H, 12.1.

c. 4,6,8-Trimethylundecan-2-ol, 58. Iodination of alcohol **57** (0.36 g, 1.3 mmol), according to the procedure described in Scheme 2, furnished the desired iodide in 85% yield. [GCMS: Two GC peaks were observed. First diastereomer: *m/z* 395 (M^+ − 1, <1), 295 (5), 253 (2), 225 (5), 183 (5), 169 (10), 111 (5), 97 (7), 85 (100), 69 (28), 55 (51), 41 (74). Second diastereomer: 395 (M^+ − 1, <1), 295 (5), 253 (2), 225 (4), 183 (5), 169 (9),

111 (5), 97 (7), 85 (100), 69 (28), 55 (55), 41 (81). Anal. Calcd for $C_{17}H_{32}IO_2$: C, 51.5; H, 8.4. Found: C, 51.0; H, 8.5.] The above iodide underwent a Grignard displacement with EtMgBr and Li_2CuCl_4 (refer to Scheme 2 for procedure) to acquire the corresponding THP ether (0.28 g, 92%, four diastereomers). [GCMS: Four GC peaks were observed. First diastereomer: *m/z* 254 ($M^+ - 44$, <1), 225 (<1), 197 (2), 141 (2), 127 (3), 113 (5), 99 (6), 85 (100), 71 (28), 57 (53), 43 (67). Second diastereomer: 298 (M^+, <1), 254 (<1), 225 (<1), 197 (2), 141 (2), 127 (3), 113 (6), 99 (8), 85 (100), 71 (28), 57 (53), 43 (67). Third diastereomer: 254 ($M^+ - 44$, <1), 225 (<1), 197 (1), 141 (2), 127 (3), 113 (5), 99 (6), 85 (100), 71 (23), 57 (44), 43 (59). Fourth diastereomer: 254 ($M^+ - 44$, <1), 225 (<1), 197 (1), 141 (2), 127 (3), 113 (5), 99 (6), 85 (100), 71 (23), 57 (47), 43 (61).] The protecting group was removed by a standard protocol (refer to Scheme 1 for procedure) to furnish alcohol **58** (0.23 g, 99%). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.88 (ddq, *J* 9.7, 6.2, 3.8, 2H), 1.70 (m, 2H), 1.55 (m, 2H), 1.49−1.40 (m, 6H), 1.34−0.90 (m, 24H), 1.17 (d, *J* 6.2, 3H), 1.16 (d, *J* 6.2, 3H), 0.87 (d, *J* 6.6, 3H), 0.86 (d, *J* 6.2, 3H), 0.85 (t, *J* 7.0, 3H), 0.813 (d, *J* 6.8, 3H), 0.808 (d, *J* 6.8, 3H), 0.792 (d, *J* 6.5, 3H), 0.787 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 65.7, 29.70, 29.67, 27.2, 27.1, 26.6, 26.5, 24.42, 24.38, 20.7, 20.4, 20.2, 20.10, 20.08, 19.9, 19.8, 19.3, 14.4, 14.3. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 199 ($M^+ - 15$, 1), 153 (7), 127 (4), 111 (48), 97 (18), 85 (39), 69 (100), 57 (75). Second diastereomer: 199 ($M^+ - 15$, <1), 153 (6), 127 (4), 111 (44), 97 (17), 85 (38), 69 (100), 57 (74). Anal. Calcd for $C_{14}H_{30}IO$: C, 78.4; H, 14.1. Found: C, 78.4; H, 14.5.

d. 2,4,6,8-Tetramethylundecan-1-ol, 60 (*ssa* and *asa*). Alcohol **58** (0.20 g, 0.93 mmol) was mesylated by following the standard mesylation procedure (refer to Scheme 1 for detail). [GCMS: Two GC peaks were observed. First diastereomer: *m/z* 196 ($M^+ - 96$, 1), 153 (6), 127 (6), 111 (37), 97 (20), 83 (22), 79 (13), 69 (100), 57 (56). Second diastereomer: 196 ($M^+ - 96$, 1), 153 (8), 127 (6), 111 (41), 97 (21), 83 (25), 79 (13), 69 (100), 57 (51).] The crude mesylate was then reacted with sodium cyanide (0.26 g, 5.3 mmol) in anhydrous DMSO (2 mL) at ~80 °C overnight under an inert atmosphere. Nitrile **59** (0.15 g, 72%) was obtained by column chromatography (hexane, and then 5% diethyl ether in hexane). [^{1}H NMR (400 MHz, *J* in Hz): δ 2.63 (ddq, *J* 7.6, 7.0, 2.4, 2H), 1.72−0.98 (m, 36H), 1.28 (d, *J* 7.0, 6H), 0.96−0.79 (m, 12H), 0.82 (d, *J* 6.5, 6H). ^{13}C NMR (100 MHz): δ 123.49, 123.43, 45.3, 44.86, 44.87, 44.0, 41.8, 41.5, 40.5, 38.7, 29.74, 29.72, 28.03, 27.97, 27.4, 27.3, 23.1, 20.8, 20.5, 20.3, 20.12, 20.10, 19.9, 19.8, 19.3, 18.1, 18.0, 14.4, 14.3. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 222 ($M^+ - 1$, 1), 208 (11), 180 (35), 152 (42), 139 (41), 124 (13), 110 (51), 97 (38), 85 (23), 70 (27), 55 (100). Second diastereomer: 222 ($M^+ - 1$, 1), 208 (13), 180 (36), 152 (50), 139 (50), 124 (16), 110 (53), 97 (41), 85 (22), 71 (76), 55 (100).] The above nitrile was hydrolyzed under the same kind of acidic conditions described earlier (refer to Scheme 2) to the required methyl ester (70.0 mg, 63%). [^{1}H NMR (400 MHz, *J* in Hz): δ 3.64 (d, *J* 1.6, 6H), 2.50 (m, 2H), 1.56−1.09 (m, 36H), 1.10 (d, *J* 6.9, 6H), 0.86 (t, *J* 7.0, 3H), 0.85 (t, *J* 7.2, 3H), 0.82 (d, *J* 6.4, 3H), 0.81 (d, *J* 6.5, 6H), 0.80 (d, *J* 6.9, 6H), 0.79 (d, *J* 6.7, 3H). ^{13}C NMR (100 MHz): δ 51.46, 51.44, 46.0, 45.5, 45.2, 44.4, 41.1, 40.7, 40.5, 38.8, 37.1, 29.72, 29.69, 27.8, 27.7, 27.3, 27.2, 20.7, 20.5, 20.11, 20.08, 20.0, 19.8, 19.3, 16.9, 16.8, 14.4, 14.3.] The above ester (63 mg, 0.25 mmol) was reduced with LAH (refer to Scheme 1 for detail) to afford the required alcohol **60** (46 mg, 82%). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.45 (ddd, *J* 10.6, 5.9, 1.5, 2H), 3.37 (ddd, *J* 10.6, 6.5, 1.5, 2H), 1.69 (m, 2H), 1.58 (m, 4H), 1.48 (m, 4H), 1.32−0.93 (m, 26H), 0.88 (d, *J* 6.6, 3H), 0.87 (d, *J* 6.6, 3H), 0.86 (t, *J* 7.0, 3H), 0.85 (t, *J* 7.1, 3H), 0.82 (d, *J* 6.6, 3H), 0.810 (d, *J* 6.7, 3H), 0.807 (d, *J* 6.3, 3H), 0.803 (d, *J* 6.6, 3H), 0.79 (d, *J* 6.2, 3H), 0.78 (d, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 69.23, 69.16, 46.9, 46.1, 45.5, 44.7, 40.50, 40.46, 40.1, 39.0, 33.25, 33.21, 29.72, 29.67, 27.22, 27.21, 27.1, 27.0, 20.6, 20.4, 20.2, 20.1, 19.97, 19.94, 19.88, 19.4, 16.2, 16.1, 14.40, 14.35. This alcohol is a diastereomer of the fully characterized primary alcohol **38**.

e. 2,4,6,8-Tetramethylundecanal, 61 (*ssa* and *asa*). Alcohol *ssa*- and *asa*-**60** (43 mg, 0.19 mmol) was oxidized under Swern conditions (refer to Scheme 4 for details). The crude aldehyde was taken up in THF (0.5 mL), dried over 4 Å sieves for a few hours, and then used directly in the Wittig coupling.

f. 4,6,8,10,16-Pentamethyldocosanes, 63 (*ssa*) and 64 (*asa*). At −78 °C, ^{n}BuLi (0.6 M in hexane, 0.19 mL) was added to (5-methylundecyl)triphenylphosphonium iodide (68 mg, 0.12 mmol) in THF (1.5 mL) under a nitrogen atmosphere. The bright orange solution was stirred for 30 min. Half of the above aldehyde/THF solution was added, and the reaction was stirred overnight while the temperature rose gradually. Upon the addition of saturated NH_4Cl (3 mL), the solution was extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (4 mL), dried ($MgSO_4$), and concentrated. The corresponding alkenyl mixture (25 mg, 75%, containing ~40% of 7,16-dimethyldocosane formed from the dimerization of **62**) was isolated after flash chromatography (hexane). The alkenes were then reduced with Pd−C and H_2 to provide the pentamethyl alkanes **63** and **64**. Most of the Wittig dimer was removed by preparative GC. **63**: ^{1}H NMR (750 MHz): δ 1.57−1.43 (m, 4H), 1.36−1.17 (m, 26H), 1.11−0.93 (m, 4H), 0.86 (t, *J* 7.0, 6H), 0.82 (d, *J* 6.6, 6H), 0.80 (d, *J* 6.7, 3H), 0.798 (d, *J* 6.4, 3H), 0.791 (d, *J* 6.3, 3H). ^{13}C NMR (187 MHz): δ 46.18, 45.49, 44.46, 44.45, 39.02, 38.244, 38.239, 27.104, 27.098, 32.75, 31.96, 30.35, 30.34, 30.08, 30.04, 29.74, 29.70, 27.35, 27.27, 27.25, 27.174, 27.172, 27.117, 27.113, 27.05, 22.70, 20.72, 20.44, 20.38, 19.99, 19.44, 19.43, 14.43, 14.12. GCMS: *m/z* 337 ($M^+ - 43$, <1), 295 (1), 267 (<1), 253 (1), 239 (<1), 225 (1), 211 (1), 197 (2), 183 (2), 169 (2), 155 (6), 141 (3), 127 (6), 113 (11), 99 (13), 85 (31), 71 (59), 57 (94), 43 (100). **64**: ^{1}H NMR (750 MHz): δ 1.57−1.43 (m, 4H), 1.36−1.17 (m, 26H), 1.11−0.93 (m, 4H), 0.86 (t, *J* 7.0, 6H), 0.82 (d, *J* 6.6, 6H), 0.80 (d, *J* 6.5, 6H), 0.78 (d, *J* 6.5, 3H). ^{13}C NMR (187 MHz): δ 46.92, 44.82, 44.81, 44.76, 40.47, 38.135, 38.129, 37.105, 37.098, 32.75, 31.96, 30.08, 30.04, 29.70, 27.25, 27.142, 27.138, 27.05, 22.70, 20.14, 20.08, 20.07, 19.73, 19.72, 19.51, 19.50, 14.38, 14.12. GCMS: *m/z* 380 (M^+, <1), 365 (<1), 337 (<1), 295 (1), 267 (<1), 253 (1), 239 (<1), 225 (1), 211 (1), 197 (2), 183 (2), 169 (2), 155 (5), 141 (3), 127 (5), 113 (10), 99 (12), 85 (30), 71 (57), 57 (92), 43 (100).

g. 4,6,8,10,16,18-Hexamethyldocosanes, 14 (*asa*(*s*)) and 17 (*ssa*(*s*)). According to the above procedure, the aldehyde **61**/THF solution was added to ylide **25** (75 mg, 0.14 mmol), formed in situ by deprotonation of Wittig salt **44** with ^{n}BuLi (0.6 M in hexane, 0.19 mL) in THF (1 mL) at −78 °C. The corresponding alkenes (19 mg, 67%), together with 65% of the coupling dimer (which can be suppressed by oxygen exclusion and was demonstrated in the later part of the synthesis), were obtained after column chromatography (hexane). The alkenes were hydrogenated with Pd−C under hydrogen (refer to Scheme 4 for detailed procedure) to furnish the desired alkane mixture (18 mg, 98%). **14** and **17**: ^{1}H NMR (750 MHz, *J* in Hz): δ 1.55 (m, 8H), 1.45 (m, 8H), 1.32−1.16 (m, 24H), 1.01 (m, 2H), 0.88−0.78 [m, with 0.87 (t, *J* 7.1), 0.817 (d, *J* 6.5), 0.813 (d, *J* 6.6), 48H)]. The NMR and GCMS data of **17** were reported above. **14**: ^{13}C NMR (187 MHz): δ 46.923, 46.920, 45.23, 44.82, 44.81, 44.76, 40.47, 38.15, 38.13, 36.57, 30.38, 30.053, 30.048, 30.036, 30.01, 30.00, 29.98, 29.75, 29.74, 29.18, 27.25, 27.15, 27.14, 26.91, 23.07, 20.30, 20.14, 20.08, 20.06, 19.44, 19.43, 14.38, 14.18. GCMS: *m/z* 394 (M^+, <1), 309 (<1), 281 (<1), 267 (<1), 253 (<1), 239 (<1), 225 (1), 211 (1), 197 (1), 183 (2), 169 (2), 155 (4), 141 (3), 127 (6), 113 (9), 99 (12), 85 (27), 71 (42), 57 (76), 43 (100).

5. Syntheses of *aas*- and *aaa*-4,6,8,10,16-Pentamethyldocosanes, 84 and 85, and *aas*(*s*)- and *aaa*(*s*)-4,6,8,10,-16,18-Hexamethyldocosanes, 18 and 15 (Refer to Schemes 7 and 8). a. Methyl 6-(*tert*-Butyldimethylsilyloxy)-2,4-dimethylheptanoate. TBDMSCl (3.1 g, 20.4 mmol) was added in one portion to a solution of hydroxyester **29** (3.2 g,

17.0 mmol), DMAP (0.16 g, 1.4 mmol), and triethylamine (4.9 mL, 34.0 mmol) in toluene (8 mL) at 0 °C under an inert atmosphere. Instant precipitation of the amine salt was observed, and the mixture was stirred overnight, while the temperature gradually increased. After the addition of diethyl ether (40 mL), the mixture was filtered and the residue was washed thoroughly with more diethyl ether (3 × 10 mL). The combined ethereal extracts were washed with brine (15 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (10% diethyl ether in hexane) of the residue afforded the silyl ether (4.9 g) in 95% yield. ^{1}H NMR (400 MHz, *J* in Hz): δ 3.85 (ddq, *J* 8.8, 6.2, 4.1, 1H), 3.63 (s, 3H), 2.54 (m, 1H), 1.60 (m, 2H), 1.42 (ddd, *J* 13.5, 8.8, 4.1, 1H), 1.20−1.10 (m, 2H), 1.12 (d, *J* 7.0, 3H), 1.09 (d, *J* 6.2, 3H), 0.86 (d, *J* 6.5, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (100 MHz): δ 177.5, 66.0, 51.4, 47.1, 41.9, 37.1, 27.1, 25.9, 24.5, 19.5, 18.0, 17.6, −4.1, −4.9. GCMS: *m/z* 287 (M^+ − 15, 1), 271 (3), 245 (39), 213 (52), 159 (14), 143 (18), 121 (18), 103 (17), 89 (38), 75 (100), 55 (44), 41 (67). These data matched those reported.[13]

b. 6-(*tert*-Butyldimethylsilyloxy)-2,4-dimethylheptanoic Acid, 71. A mixture of LiOH (1.7 g, 75.5 mmol) and methyl 6-(*tert*-butyldimethylsilyloxy)-2,4-dimethylheptanoate (3.3 g, 11.0 mmol) in MeOH/H_2O (4:1 v/v, 60 mL) was refluxed gently for 21 h and then acidified with 1 M HCl. The acidic solution was extracted with dichloromethane (3 × 25 mL). The combined organic extracts were washed with brine (20 mL) and dried ($MgSO_4$), and solvent removal furnished acid **71** (3.0 g, 93%) as a yellowish oil. ^{1}H NMR (400 MHz, *J* in Hz): δ 3.85 (m, 1H), 2.55 (m, 1H), 1.65 (m, 2H), 1.43 (ddd, *J* 12.6, 8.8, 3.5, 1H), 1.17 (m, 1H), 1.15 (d, *J* 7.0, 3H), 1.09 (d, *J* 6.2, 3H), 1.04 (m, 1H), 0.88 (d, *J* 6.2, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (100 MHz): δ 183.5, 66.0, 47.0, 37.1, 27.0, 25.9, 24.5, 19.6, 18.0, 17.4, −4.1, −4.9. GCMS: *m/z* 273 (M^+ − 15, <1), 231 (6), 213 (24), 171 (3), 139 (15), 111 (28), 103 (8), 75 (100), 69 (88), 55 (42), 41 (46). These data matched those reported.[13]

c. 7-(*tert*-Butyldimethylsilyloxy)-3,5-dimethyloctan-2-one, 73. To a solution of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl; 3.1 g, 10.3 mmol) and triethylamine (1.5 mL, 10.4 mmol) in dichloromethane (15 mL) was added acid **71** (3.0 g, 10.2 mmol) in dichloromethane (8 mL) under an inert atmosphere. After stirring for 5 min, 1-hydroxybenzotriazole hydrate (HOBT; 1.4 g, 10.4 mmol) was added in one portion at 0 °C. The solution was stirred at room temperature for 1 h, followed by the slow addition of a dichloromethane solution (15 mL) of *N*-methoxymethanamine hydrochloride (1.3 g, 13.3 mmol) and triethylamine (2.0 mL, 13.9 mmol). After 18 h of stirring, the reaction mixture was worked up by dichloromethane (50 mL) addition and washed with saturated $NaHCO_3$ (15 mL), NH_4Cl (15 mL), and brine (15 mL), respectively. The organic layer was dried ($MgSO_4$) and concentrated. Chromatography (25% EtOAc in hexane) of the crude oil furnished amide **72** (2.4 g) in 71% yield. [^{1}H NMR (400 MHz, *J* in Hz): δ 3.86 (m, 1H), 3.67 (s, 3H), 3.15 (s, 3H), 2.97 (m, 1H), 1.63 (m, 1H), 1.55 (m, 1H), 1.45 (m, 1H), 1.35 (m, 1H), 1.09 (d, *J* 6.1, 3H), 1.08 (d, *J* 6.8, 3H), 0.87 (d, *J* 6.7, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (100 MHz): δ 178.3, 66.1, 61.4, 41.6, 41.4, 27.1, 25.9, 24.5, 20.1, 18.0, 17.8, −4.1, −4.8. GCMS: *m/z* 316 (M^+ − 15, 1), 274 (59), 244 (5), 200 (6), 159 (9), 143 (7), 111 (25), 103 (12), 84 (18), 75 (94), 55 (37), 43 (100).] At 0 °C, MeMgI (1.3 M in diethyl ether, 11.0 mL) was added slowly to amide **72** (2.7 g, 8.2 mmol) in THF (20 mL), and the resulting mixture was stirred for 2 h. The reaction was quenched by anhydrous acetone (5 mL) and then saturated NH_4Cl (15 mL) with 5 min between the two additions. The heterogeneous solution was stirred for another 10 min while warming to room temperature. After separation of the layers, the organic fraction was washed with another portion of saturated NH_4Cl (10 mL). The combined aqueous solutions were re-extracted with more diethyl ether (3 × 15 mL). The combined ethereal solutions were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. After column chromatography (10% EtOAc in hexane), ketone **73** (2.0 g, 88%) was obtained. ^{1}H NMR (400 MHz, *J* in Hz): δ 3.85 (ddq, *J* 7.9, 6.2, 3.5, 1H), 2.59 (s, *J* 7.0, 1H), 2.10 (s, 3H), 1.58 (m, 1H), 1.55 (q, *J* 7.1, 1H), 1.43 (dd, *J* 8.8, 3.5, 1H), 1.12 (m, 1H), 1.09 (d, *J* 6.2, 3H), 1.05 (d, *J* 7.0, 3H), 0.98 (m, 1H), 0.86 (d, *J* 6.5, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (100 MHz): δ 212.9, 66.0, 46.9, 44.8, 40.9, 27.8, 26.9, 25.8, 19.9, 18.0, 16.6, −4.1, −4.8. GCMS: *m/z* 271 (M^+ − 15, <1), 229 (15), 173 (2), 159 (90), 129 (2), 119 (9), 115 (8), 95 (16), 75 (100), 55 (26), 43 (69). These data matched those reported.[13]

d. 6-(*tert*-Butyldimethylsilyloxy)-4-methylheptan-2-ol, 74. To a suspension of *m*CPBA (70%, 1.9 g, 7.7 mmol) and $NaHCO_3$ (0.68 g, 8.1 mmol) in dichloromethane (30 mL) was added ketone **73** (2.0 g, 7.0 mmol). The mixture was stirred for 1 day, and fresh *m*CPBA (70%, 1.0 g, 3.9 mmol) and $NaHCO_3$ (0.29 g, 3.6 mmol) in dichloromethane (8 mL) were added. After stirring for another day, more *m*CPBA (0.20 g, 0.81 mmol) and $NaHCO_3$ (80 mg, 0.95 mmol) in dichloromethane (1 mL) were added, and the resulting mixture was left to stir for a further 2 days. The precipitate was then filtered and washed thoroughly with diethyl ether/hexane (1:3, 40 mL). The organic solution was washed with 5% Na_2SO_3 (2 × 20 mL), saturated $NaHCO_3$ (2 × 20 mL), and brine (20 mL). After drying ($MgSO_4$) and concentration, the required ester was mixed with some *m*-chlorobenzoic acid after column chromatography (10% diethyl ether in hexane). [GCMS: *m/z* 245 (M^+ − 57, <1), 201 (<1), 185 (1), 159 (10), 135 (18), 117 (84), 87 (3), 69 (100), 55 (23).] The above ester (2.4 g, together with the *m*-chlorobenzoic acid) was then stirred with K_2CO_3 (1.8 g, 13.0 mmol) in MeOH (30 mL) for 1 day. After the addition of H_2O (50 mL), the homogeneous solution was concentrated and extracted with dichloromethane (3 × 25 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (20% diethyl ether in hexane) to afford alcohol **74** (1.3 g) in 69% over two steps. ^{1}H NMR (400 MHz, *J* in Hz): δ 3.87 (m, 2H), 1.74 (m, 1H), 1.45 (dd, *J* 8.5, 5.3, 1H), 1.40 (dd, *J* 8.5, 5.9, 1H), 1.38 (m, 1H), 1.20 (dd, *J* 8.2, 4.7, 1H), 1.17 (s, 1H), 1.16 (d, *J* 6.2, 3H), 1.10 (d, *J* 5.9, 3H), 0.89 (d, *J* 6.4, 3H), 0.86 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (100 MHz): δ 66.4, 66.1, 47.6, 47.4, 26.2, 25.9, 24.5, 24.0, 19.9, 18.1, −4.2, −4.7. GCMS: *m/z* 203 (M^+ − 57, <1), 201 (2), 185 (3), 159 (12), 143 (3), 119 (25), 111 (19), 101 (9), 75 (80), 69 (100), 55 (20). These spectral data matched those reported.[13]

e. Methyl 6-Hydroxy-2,4-dimethylheptanoate. Alcohol **74** (1.8 g, 6.9 mmol) was mesylated under standard mesylation conditions (refer to Scheme 1) to afford the required sulfonate ester. [GCMS: *m/z* 323 (M^+ − 15, <1), 309 (1), 243 (<1), 227 (2), 185 (47), 153 (57), 141 (21), 111 (27), 99 (24), 75 (100), 69 (63), 55 (15).] The mesylate was displaced by cyanide (refer to Scheme 2 for detailed procedures) to furnish nitrile **75** (1.2 g, 66%). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.86 (m, 1H), 2.63 (s, *J* 7.04, 1H), 1.81 (m, 1H), 1.62−1.37 (m, 4H), 1.27 (d, *J* 7.0, 3H), 1.11 (d, *J* 5.9, 3H), 0.90 (d, *J* 6.8, 3H), 0.87 (s, 9H), 0.039 (s, 3H), 0.036 (s, 3H). ^{13}C NMR (100 MHz): δ 123.4, 65.9, 46.8, 42.2, 41.9, 27.1, 25.9, 24.6, 23.1, 19.2, 18.0, −4.1, −4.8. GCMS: *m/z* 268 (M^+ − 1, <1), 254 (3), 212 (52), 168 (44), 159 (7), 138 (4), 115 (6), 101 (19), 75 (100), 59 (21), 45 (25). Nitrile **75** (1.2 g, 4.5 mmol) was hydrolyzed to its methyl ester (0.58 g, 70%) under acidic conditions (refer to Scheme 2 for procedure details). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.86 (m, 1H), 3.65 (s, 3H), 2.52 (s, *J* 7.04, 1H), 1.65 (m, 1H), 1.55 (dd, *J* 13.5, 7.0, 1H), 1.46 (ddd, *J* 13.3, 9.1, 4.1, 1H), 1.40 (m, 1H), 1.32 (ddd, *J* 13.7, 7.6, 6.2, 1H), 1.12 (m, 1H), 1.17 (d, *J* 6.2, 3H), 1.11 (d, *J* 6.8, 3H), 0.88 (d, *J* 7.0, 3H). ^{13}C NMR (100 MHz): δ 177.5, 65.6, 51.6, 46.7, 41.6, 37.1, 27.3, 24.4, 19.2, 17.0. GCMS: *m/z* 173 (M^+ − 15, <1), 141 (8), 129 (4), 113 (7), 111 (7), 101 (100), 88 (51), 69 (68), 55 (40). This methyl ester is a diastereomer of ester **29**, which was fully characterized.

f. 2,4-Dimethyl-6-(tetrahydropyran-2-yloxy)heptan-1-ol. The hydroxyl group in the above hydroxyester, methyl

6-hydroxy-2,4-dimethylheptanoate (0.55 g, 2.9 mmol), was protected as a THP ether (0.60 g, 85%, two diastereomers) under conditions mentioned earlier (refer to Scheme 1). [GCMS: Two GC peaks were observed. First diastereomer: *m/z* 171 ($M^+ - 85$, 11), 139 (16), 111 (17), 101 (7), 85 (100), 69 (45), 55 (42), 41 (68). Second diastereomer: 171 ($M^+ - 85$, 14), 139 (21), 111 (22), 101 (8), 85 (100), 69 (54), 55 (49), 41 (79).] The above ester (0.60 g, 2.2 mmol) was reduced by the LAH protocol (refer to Scheme 1) to furnish the desired alcohol (0.50 g, 93%, two diastereomers). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.69 (t, *J* 3.8, 1H), 4.59 (dd, *J* 5.0, 2.9, 1H), 3.90 (m, 3H), 3.77 (m, 1H), 3.49−3.37 (m, 6H), 1.82−1.47 (m, 18H), 1.21 (d, *J* 6.5, 3H), 1.15 (m, 2H), 1.08 (d, *J* 6.2, 3H), 0.88 (d, *J* 6.8, 6H), 0.86 (d, *J* 6.8, 3H), 0.85 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 99.5, 95.2, 72.8, 69.0, 68.9, 68.7, 62.9, 62.4, 35.7, 41.1, 40.1, 33.11, 33.09, 31.3, 31.2, 26.54, 26.47, 25.6, 25.5, 22.4, 20.1, 19.8, 19.7, 19.6, 19.5, 16.6, 16.4. GCMS: Only one broad GC peak was observed. *m/z* 211 ($M^+ - 33$, 1), 143 (11), 125 (5), 101 (7), 85 (100), 69 (56), 55 (62), 41 (85). This monoprotected alcohol is a diastereomer of the fully characterized alcohol **30** described earlier.

g. 2-(6-Iodo-1,3,5-trimethylhexyloxy)tetrahydropyran, 77. Iodination of 2,4-dimethyl-6-(tetrahydropyran-2-yloxy)-heptan-1-ol (0.44 g, 1.8 mmol) was achieved by the procedure described earlier (refer to Scheme 2) in obtaining iodide **77** (0.62 g, 97%, two diastereomers). ^{1}H NMR (400 MHz, *J* in Hz): δ 4.70 (t, *J* 3.5, 1H), 4.59 (dd, *J* 5.3, 3.9, 1H), 3.88 (m, 3H), 3.74 (m, 1H), 3.49 (m, 2H), 3.19 (dq, *J* 9.7, 4.7, 2H), 3.17 (dq, *J* 9.7, 7.6, 2H), 1.83−1.47 (m, 20H), 1.21 (d, *J* 6.2, 3H), 1.17 (m, 2H), 1.12 (m, 2H), 1.08 (d, *J* 5.9, 3H), 0.94 (d, *J* 6.5, 3H), 0.93 (d, *J* 6.2, 3H), 0.88 (d, *J* 6.6, 3H), 0.86 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 99.9, 95.0, 73.1, 68.4, 62.9, 62.3, 45.2, 44.4, 32.01, 31.96, 31.3, 31.2, 26.8, 26.7, 25.6, 25.5, 20.5, 19.9, 19.7, 19.61, 19.58, 18.6, 18.5. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 353 ($M^+ - 1$, <1), 312 (<1), 253 (5), 211 (3), 183 (5), 169 (9), 125 (8), 101 (6), 85 (100), 69 (24), 55 (33). Second diastereomer: 353 ($M^+ - 1$, <1), 312 (<1), 253 (7), 211 (3), 183 (5), 169 (9), 125 (7), 101 (7), 85 (100), 69 (28), 55 (43). This iodide is a diastereomer of the one fully described and characterized within Scheme 2.

h. 2-(4,6-Dimethylnonan-2-yloxy)tetrahydro-2*H*-pyran. Iodide **77** (0.60 g, 1.7 mmol) was alkylated under Grignard's conditions (refer to Scheme 2 for procedure details) to afford the corresponding THP ether (0.30 g, two diastereomers) in 70% yield. ^{1}H NMR (400 MHz, *J* in Hz): δ 4.72 (t, *J* 3.8, 1H), 4.60 (dd, *J* 5.0, 2.6, 1H), 3.88 (m, 3H), 3.76 (m, 1H), 3.48 (m, 2H), 1.84−1.01 (m, 32H), 1.21 (d, *J* 6.26, 3H), 1.08 (d, *J* 6.2, 6H), 0.86 (t, *J* 7.0, 6H), 0.81 (d, *J* 6.5, 3H), 0.79 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 99.4, 95.0, 72.8, 68.6, 62.9, 62.1, 46.0, 45.6, 45.1, 45.0, 40.24, 40.21, 31.2, 29.69, 29.67, 26.6, 25.6, 25.5, 20.14, 20.07, 19.52, 19.50, 19.46, 19.4, 14.38, 14.36. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 213 ($M^+ - 43$, <1), 198 (<1), 155 (6), 129 (3), 113 (3), 99 (9), 85 (100), 71 (24), 57 (30). Second diastereomer: 213 ($M^+ - 43$, <1), 198 (<1), 155 (4), 129 (5), 113 (2), 99 (7), 85 (100), 71 (22), 57 (31). This THP ether is a diastereomer of the one fully characterized and described within Scheme 2.

i. 4,6-Dimethylnonan-2-ol, 78. Deprotection of the above THP ether (0.30 g, 1.2 mmol) was carried out under standard conditions (refer to Scheme 1) to give alcohol **78** (0.20 g, 99%). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.89 (ddq, *J* 8.8, 6.2, 4.1, 1H), 1.68 (m, 1H), 1.48 (m, 1H), 1.41 (ddd, *J* 13.8, 8.8, 5.0, 1H), 1.33−0.97 (m, 8H), 1.17 (d, *J* 6.2, 3H), 0.86 (t, *J* 6.8, 3H), 0.85 (d, *J* 6.8, 3H), 0.81 (d, *J* 6.8, 3H). ^{13}C NMR (100 MHz): δ 65.8, 47.7, 45.4, 40.2, 29.7, 26.8, 24.3, 20.1, 19.4, 19.1, 14.4. GCMS: *m/z* 157 ($M^+ - 15$, 1), 139 (1), 125 (1), 112 (39), 97 (10), 85 (60), 69 (100), 55 (69). This secondary alcohol is a diastereomer of **32**, which was fully characterized and described within Scheme 2.

j. Methyl 2,4,6-Trimethylnonanoate. Alcohol **78** (0.20 g, 1.2 mmol) was mesylated to yield the sulfonate ester (refer to Scheme 1 for experimental details). [GCMS: *m/z* 154 ($M^+ -$ 15, 2), 139 (1), 123 (9), 111 (53), 97 (14), 85 (47), 79 (23), 69 (100), 55 (68).] The crude mesylate was displaced with cyanide (refer to Scheme 2 for experimental details) to give nitrile **79** (0.13 g, 62% over two steps). [^{1}H NMR (400 MHz, *J* in Hz): δ 2.66 (m, 1H), 1.82 (m, 1H), 1.28 (d, *J* 7.0, 3H), 0.88 (d, *J* 6.6, 3H), 0.86 (t, *J* 7.1, 3H), 0.83 (d, 6.6, 3H). ^{13}C NMR (100 MHz): δ 123.3, 43.8, 42.4, 40.3, 29.7, 28.2, 23.2, 20.1, 19.4, 19.2, 18.3, 14.3. GCMS: *m/z* 180 ($M^+ - 1$, 1), 166 (15), 152 (25), 138 (41), 124 (14), 110 (32), 96 (86), 69 (73), 55 (100).] Nitrile **79** (0.12 g, 0.65 mmol) was then hydrolyzed under acidic conditions (refer to Scheme 2 for details) to afford the required methyl ester (0.11 g, 74%). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.63 (s, 3H), 2.52 (s, *J* 7.0, 1H), 1.52−1.02 (m, 10H), 1.09 (d, *J* 7.0, 3H), 0.84 (t, *J* 7.2, 3H), 0.79 (d, *J* 6.2, 3H), 0.78 (d, *J* 6.2, 3H). ^{13}C NMR (100 MHz): δ 177.7, 51.4, 44.5, 42.0, 40.2, 37.1, 29.6, 27.9, 20.0, 19.3, 19.2, 17.2, 14.3. GCMS: *m/z* 214 (M^+, <1), 183 (1), 129 (6), 111 (3), 101 (63), 88 (100), 73 (8), 69 (30), 55 (34), 43 (67). This methyl ester is a diastereomer of **34**, which was fully characterized and described within Scheme 2.

k. 2,4,6-Trimethylnonan-1-ol. The above methyl 2,4,6-trimethylnonanoate (0.10 g, 0.41 mmol) was reduced to the title alcohol in quantitative yield (83 mg, 100%) with LAH. ^{1}H NMR (400 MHz, *J* in Hz): δ 3.44 (dd, *J* 10.4, 5.7, 1H), 3.35 (dd, *J* 10.4, 6.7, 1H), 1.89 (br s, 1H), 1.71−0.97 (m, 11H), 0.86 (d, *J* 6.6, 3H), 0.84 (t, *J* 7.2, 3H), 0.79 (d, *J* 6.6, 3H), 0.78 (d, *J* 6.5, 3H). ^{13}C NMR (100 MHz): δ 68.8, 45.6, 41.4, 40.0, 33.1, 29.6, 27.1, 20.0, 19.5, 19.1, 16.4, 14.3. GCMS: *m/z* 153 ($M^+ -$ 33, <1), 139 (<1), 125 (17), 111 (19), 97 (12), 83 (66), 69 (62), 57 (100). This primary alcohol is a diastereomer of the one fully characterized and described within Scheme 2.

l. Ethyl 2,4,6,8-Tetramethylundec-2-enoate. Under Swern conditions, the above 2,4,6-trimethylnonan-1-ol (83 mg, 0.45 mmol) was oxidized to provide its aldehyde, which was then coupled with Wittig ylide **36** (refer to Scheme 2 for details) to furnish the title ester (76 mg, 64% over two steps). ^{1}H NMR (400 MHz, *J* in Hz): δ 6.51 (dq, *J* 10.1, 1.4, 1H), 4.16 (q, *J* 7.1, 2H), 2.58 (m, 1H), 1.82 (d, *J* 1.4, 3H), 1.28 (t, *J* 7.1, 3H), 0.95 (d, *J* 6.6, 3H), 0.85 (t, *J* 7.2, 3H), 0.80 (d, *J* 6.6, 3H), 0.75 (d, *J* 6.6, 3H). ^{13}C NMR (100 MHz): δ 168.5, 148.5, 125.7, 60.4, 45.2, 44.5, 40.4, 30.7, 29.7, 27.9, 20.1, 20.0, 19.9, 19.3, 14.4, 14.3, 12.5. GCMS: *m/z* 268 (M^+, 1), 223 (2), 183 (2), 155 (3), 142 (3), 127 (4), 115 (30), 102 (14), 83 (22), 69 (28), 55 (23), 43 (100), 41 (66). This unsaturated ethyl ester is a diastereomer of **37**, which was fully characterized and described within Scheme 2.

m. 2,4,6,8-Tetramethylundecan-1-ol, 66 (*aaa*) and 67 (*aas*). The above ethyl 2,4,6,8-tetramethylundec-2-enoate (69 mg, 0.26 mmol) was reduced successively with Mg and LAH (refer to Scheme 2 for details) to furnish the primary alcohols **66** and **67** (36 mg, 61% over two steps, two diastereomers). ^{1}H NMR (400 MHz, *J* in Hz): δ 3.50 (dd, *J* 10.6, 5.3, 1H), 3.46 (dd, *J* 10.6, 5.9, 1H), 3.38 (dd, *J* 10.3, 6.8, 1H), 3.35 (dd, *J* 10.3, 6.8, 1H), 1.71 (m, 2H), 1.56 (m, 4H), 1.47 (m, 2H), 1.31 (br s, 2H), 1.34−0.92 (m, 22H), 0.90 (d, *J* 6.8, 3H), 0.88 (d, *J* 6.8, 3H), 0.85 (t, *J* 7.0, 6H), 0.83 (d, *J* 6.8, 3H), 0.800 (d, *J* 6.5, 3H), 0.798 (d, *J* 6.5, 3H), 0.795 (d, *J* 6.5, 3H), 0.78 (d, *J* 6.5, 3H), 0.77 (d, *J* 6.8, 3H). ^{13}C NMR (100 MHz): δ 69.1, 68.5, 45.9, 45.5, 41.3, 40.2, 40.1, 33.2, 33.0, 29.7, 29.6, 27.32, 27.27, 27.24, 27.1, 20.4, 20.07, 20.05, 19.6, 19.2, 17.1, 16.4, 14.4. This primary alcohol is a diastereomer of **38**, which was fully characterized and described within Scheme 2.

n. 2,4,6,8-Tetramethylundecanal, 81 (*aaa* and *aas*). Under Swern conditions, the title aldehyde was prepared from alcohols **66** and **67** (26 mg, 0.11 mmol). The crude aldehyde was redissolved in THF (0.5 mL) with a few 4 Å sieves and purged with N_2, making it ready for the Wittig reaction. GCMS: Two GC peaks were observed. First diastereomer: *m/z* 168 ($M^+ - 57$, 2), 137 (1), 123 (3), 111 (93), 99 (6), 95 (6), 85 (12), 71 (28), 57 (51), 43 (100). Second diastereomer: 168 ($M^+ -$ 57, 2), 137 (1), 123 (4), 111 (3), 99 (7), 95 (6), 85 (13), 71 (32), 57 (52), 43 (100).

o. 4,6,8,10,16-Pentamethyldocosanes, 84 (*aaa*) and 85 (*aas*). (5-Methylundecyl)triphenylphosphonium iodide (53 mg, 95 μmol) in THF (1 mL) was purged with a gentle stream of N_2 for 10 min before cooling to −78 °C. ^{n}BuLi (2.2 M in hexane, 36 μL) was quickly added in one portion, followed by the above aldehydes (*aas* and *aaa*) in THF (0.25 mL). The mixture was stirred for 15 h, and the reaction was quenched by saturated NH_4Cl (5 mL). The aqueous layer was separated and extracted with diethyl ether (3 × 6 mL). The combined organic fractions were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. The crude paste was purified by column chromatography (hexane) to give two alkenes (6 mg, 34%), *aas*- and *aaa*-**83**, in an approximately 1:1 ratio, together with some minor isomers. [GCMS: Two GC peaks were observed. First diastereomer: *m/z* 378 (M^+, <1), 252 (1), 225 (<1), 210 (<1), 168 (1), 153 (2), 139 (2), 125 (7), 111 (20), 97 (14), 85 (20), 83 (20), 71 (27), 69 (45), 57 (62), 55 (49), 43 (100). Second diastereomer: 378 (M^+, <1), 252 (1), 225 (<1), 210 (<1), 169 (1), 153 (2), 139 (2), 125 (6), 111 (19), 97 (15), 85 (20), 83 (20), 71 (27), 69 (45), 57 (62), 55 (49), 43 (100).] Alkenes, *aas*- and *aaa*-**83**, in hexane (1.5 mL) were reduced to the title hydrocarbons, **84** (*aaa*) and **85** (*aaa*), in quantitative yield (6 mg, 100%) under standard reduction procedures (refer to Scheme 4 for experimental details). **85** (*aas*): ^{1}H NMR (750 MHz, *J* in Hz): δ 1.56−0.95 (m, 70H), 0.862 (t, *J* 7.1, 6H), 0.855 (t, *J* 7.4, 6H), 0.818 (d, *J* 6.6, 6H), 0.809 (d, *J* 6.6, 6H), 0.800 (d, *J* 6.6, 6H), 0.796 (d, *J* 6.6, 6H), 0.77 (d, *J* 6.6, 6H). ^{13}C NMR (187 MHz): δ 45.951, 45.947, 45.84, 45.55, 40.15, 37.114, 37.106, 36.984, 36.976, 32.76, 31.97, 30.41, 30.39, 29.900, 29.894, 29.71, 29.69, 27.34, 27.304, 27.297, 27.13, 27.12, 26.944, 26.934, 22.71, 20.36, 20.201, 20.198, 20.07, 19.730, 19.726, 19.62, 19.33, 14.39, 14.13. GCMS: *m/z* 323 (M^+ − 57, <1), 309 (<1), 295 (<1), 253 (<1), 225 (<1), 211 (1), 197 (1), 183 (1), 169 (1), 155 (3), 141 (2), 127 (5), 113 (6), 99 (10), 85 (27), 71 (52), 57 (96), 43 (100). **84** (*aaa*): ^{1}H NMR (750 MHz, *J* in Hz): δ 1.57−0.97 (m, 70H), 0.862 (t, *J* 7.1, 6H), 0.855 (t, *J* 7.4, 6H), 0.817 (d, *J* 6.6, 6H), 0.800 (d, *J* 6.6, 6H), 0.798 (d, *J* 6.6, 12H), 0.77 (d, *J* 6.6, 12H). ^{13}C NMR (187 MHz): δ 46.55, 45.58, 45.57, 45.55, 40.23, 37.893, 37.889, 37.114, 37.106, 32.76, 31.97, 30.36, 30.35, 30.006, 30.004, 29.72, 29.71, 27.122, 27.117, 27.08, 27.06, 20.36, 20.09, 19.733, 19.726, 19.653, 19.649, 19.59, 19.57, 19.56, 14.39, 14.13. GCMS: *m/z* 380 (M^+, <1), 295 (<1), 253 (1), 225 (<1), 211 (1), 197 (1), 183 (1), 169 (1), 155 (3), 141 (2), 127 (4), 113 (7), 99 (10), 85 (27), 71 (52), 57 (97), 43 (100).

p. 4,6,8,10,16,18-Hexamethyldocosanes, 15 (*aaa*(*s*)) and 18 (*aaa*(*s*)). According to the above procedure, alkenes **82** (*aas* and *aaa;* 10 mg, 57%, approximately 1:1 ratio) resulted by reacting the aldehydes *aaa*- and *aas*-**81** (0.25 mL) and the dimethyl Wittig ylide **25**, generated from deprotonation of **44** (55 mg, 95 μmol), with ^{n}BuLi (2.2 M in hexane, 36 μL) in THF (1 mL). Extreme care was taken in excluding moisture and molecular oxygen. [GCMS: Two GC peaks were observed, indicating complete suppression of the formation of the Wittig dimer. First diastereomer: *m/z* 354 (M^+ − 38, <1), 181 (1), 167 (1), 153 (2), 139 (2), 125 (8), 111 (14), 97 (11), 85 (18), 69 (36), 57 (52), 43 (100). Second diastereomer: 377 (M^+ − 15, <1), 181 (1), 167 (1), 153 (2), 139 (2), 125 (8), 111 (12), 97 (10), 85 (17), 69 (37), 57 (51), 43 (100).] Reduction of alkenes *aaa*- and *aas*-**82** under standard conditions furnished the title hydrocarbons (10 mg, 100%). **18** (*aas*(*s*)): ^{1}H NMR (750 MHz, *J* in Hz): δ 1.63−0.89 (m, 74H), 0.869 (t, *J* 7.1, 6H), 0.856 (t, *J* 7.4, 6H), 0.813 (d, *J* 6.6, 12H), 0.811 (d, *J* 6.6, 6H), 0.801 (d, *J* 6.6, 6H), 0.796 (d, *J* 6.6, 6H), 0.77 (d, *J* 6.6, 6H). ^{13}C NMR (187 MHz): δ 45.95, 45.84, 45.55, 45.54, 45.23, 40.15, 36.99, 36.96, 36.89, 36,87, 36.58, 30.42, 30.39, 30.01, 30.00, 29.98, 29.900, 29.888, 29.69, 29.18, 27.34, 27.30, 26.96, 26.95, 26.93, 23.07, 20.36, 20.35, 20.30, 20.19, 20.07, 19.61, 19.33, 14.39, 14.18. GCMS: *m/z* 394 (M^+, <1), 309 (<1), 267 (<1), 225 (<1), 183 (1), 169 (1), 155 (3), 127 (4), 111 (3), 99 (9), 85 (25), 71 (39), 69 (14), 57 (72), 43 (100). **15** (*aaa*(*s*)): ^{1}H NMR (750 MHz, *J* in Hz): δ 1.57−0.97 (m, 74H), 0.869 (t, *J* 7.1, 6H), 0.856 (t, *J* 7.47, 6H), 0.813 (d, *J* 6.6, 12H), 0.800 (d, H 6.6, 6H), 0.799 (d, *J* 6.6, 12H), 0.774 (d, *J* 6.6, 6H). ^{13}C NMR (187 MHz): δ 46.541, 46.538, 45.58, 45.57, 45.55, 45.23, 40.23, 37.891, 37.880, 36.884, 36.871, 36.58, 30.37, 30.35, 30.003, 29.995, 29.985, 29.71, 29.70, 29.18, 27.299, 27.292, 27.074, 27.069, 26.95, 26.93, 20.30, 20.08, 19.651, 19.648, 19.59, 19.57, 19.55, 14.39, 14.18. GCMS: *m/z* 393 (M^+ − 1, <1), 267 (<1), 225 (<1), 183 (1), 169 (1), 155 (3), 127 (4), 111 (3), 99 (8), 85 (25), 71 (38), 69 (12), 57 (74), 43 (100).

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Supporting Information Available: Capillary GC traces of the natural C28 lipid, the mixture of **15** and **18**, and the corresponding co-injection; mass spectral data for the natural and all the synthetic C27 and C28 hydrocarbons; preparative GC traces demonstrating the separation of the three synthetic mixtures of the C28 hydrocarbon; high field NMR spectra (^{1}H, 750 MHz; ^{13}C, 187 MHz) for compounds **14**−**18**, **63**, **64**, **84**, and **85**. This material is available free of charge via the Internet at http://pubs.acs.org.

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