Highly Efficient One-Pot Double-Wittig Approach to Unsymmetrical (1*Z*,4*Z*,7*Z*)-Homoconjugated Trienes

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Keywords: Wittig reactions / Homoconjugated trienes / Alkenes / Fatty acids / Pheromones

We describe a novel one-pot double-Wittig approach towards unsymmetrically substituted skipped trienes using the symmetrical (*Z*)-hex-3-ene-1,6-bis(triphenylphosphonium iodide) **(2)** as key reagent. Double alkenylation of the corresponding bis(ylide) **3** with sequentially added aldehydes gives (*Z*)-1,4,7-homoconjugated trienes in good yields. Dissymmetrization of the bis(ylide) **3** is feasible, since it displays enhanced reactivity compared to the monoylide resulting from the first olefination. Symmetrical products from statistical coupling of the bis(ylide) **3** can be drastically suppressed by slow release of the first aldehyde component through in situ thermal decomposition of an intermediate aluminate complex, generated by reduction of a methyl ester with DIBAL-H. The novel strategy is successfully applied to the one-pot synthesis of functionalized and isotopically labelled polyunsaturated fatty acids as well as to the synthesis of the geometrid moth pheromone (3Z,6Z,9Z)-nonadeca-1,3,6,9-tetraene **(6a)**. The dissymmetrization strategy was also found to be suitable for the synthesis of homoconjugated dienes from 1,3-propylbis(triphenylphosphonium bromide).

Introduction

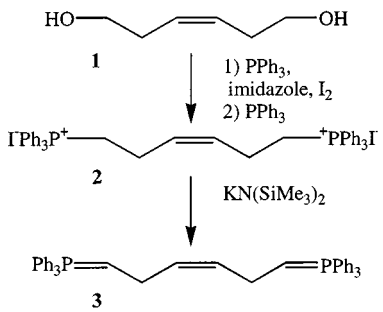
(*Z*)-1,4,7-Homoconjugated trienes are present in a wide range of natural products such as fatty acids,[1] leucotrienes,[2] or insect pheromones.[3,4] Due to the high biological importance of these metabolites, substantial effort has been invested in the synthesis of both the natural products and their isotopically labelled analogues. The first routes to (*Z*)-1,4,7-homoconjugated trienes mainly relied on the coupling of acetylenic building blocks,[3] followed by semi-hydrogenation. Later, Wittig-type approaches[5] were introduced as a powerful tool for *Z*-selective generation of methylene-bridged double-bond systems. Combinations of both approaches were also used widely[6] but, in all examples, multistep sequences were required for the formation of the repetitive methylene-bridged double-bond system. Only a very few approaches take advantage of the symmetrical nature of the homoconjugated double-bond units as pre-formed structural elements in the synthesis. Thus, mono-protected (*Z*)-hex-3-enedial[1] was used as a C6-homologating agent in the Wittig-reaction-based synthesis of polyunsaturated fatty acids. A related C9 1,4-dienoic phosphonium salt was used for the synthesis of a C22:6 fatty acid by Taber.[7] The most popular strategy following the concept of dissymmetrization of preformed homoconjugated double bonds in synthons involves the sequential coupling of allylic halides to di-*n*-butyl-1-stanna-2,5-cyclohexadiene resulting in homoconjugated dienes.[8]

In a previous communication, we introduced the bis(ylide) **3** for the enantioselective one-pot synthesis of protected 17-hydroxy linolenic acid.[9] The glutamine amide of this hydroxy acid, named volicitin, has recently attracted interest since it was found as a prominent metabolite in the regurgitant of caterpillars[10] and was demonstrated to be a potent elicitor of plant volatile biosynthesis.[11] Here we extend the scope of the concept and present an efficient and versatile one-pot synthesis of structurally diverse products, with homoconjugated trienoic structural units, from the key precursor **2**.

Results and Discussion

In the synthetic method we describe here, a one-pot procedure for the generation of all *cis* methylene-bridged trienes is used for the synthesis of functionalized and isotopically labelled polyunsaturated fatty acids, as well as for the geometrid moth pheromone (3*Z*,6*Z*,9*Z*)-nonadeca-1,3,6,9-tetraene (**6a**). The triene skeleton is readily assembled in a single operation starting from simple aldehyde precursors and the symmetric bifunctional Wittig salt **2**. Careful optimization of the reaction conditions allowed the nonstatistical dissymmetrization of the intermediate bis(ylide) **3**.

The key precursor **2** is readily accessible in a large-scale two-step synthesis (Scheme 1) from (*Z*)-hex-3-ene-1,6-diol



Scheme 1. Synthesis of the symmetrical bis(ylide) **3**

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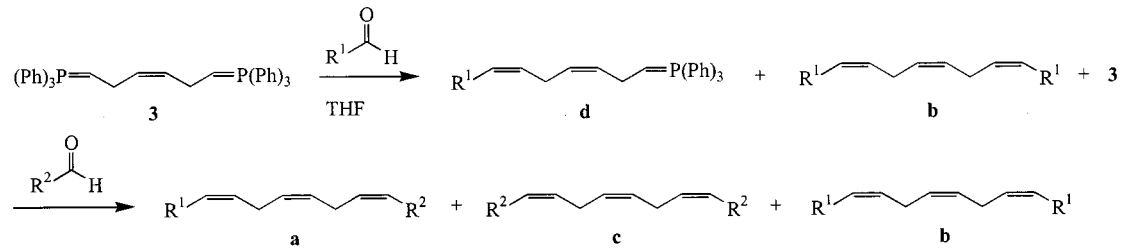
(**1**).[12] Halogenation of **1**, using triphenylphosphane, imidazole and iodine[13] is followed by conversion of the intermediate (*Z*)-hex-3-ene-1,6-diiodide into the crystalline phosphonium salt **2** (*Z*/*E* > 98:2 determined by ^{13}C NMR spectroscopy). Deprotonation with potassium bis(trimethylsilylamide) ensures a high (*Z*)-configurational purity of the resulting all-*cis* triene system.[15]

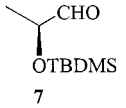
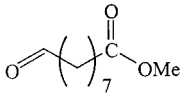
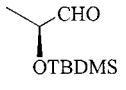
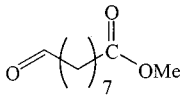
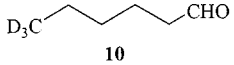
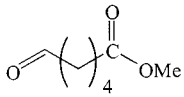
We investigated the scope and limitations of this novel procedure in detail using the synthesis of the geometrid moth pheromone (3*Z*,6*Z*,9*Z*)-nonadeca-1,3,6,9-tetraene (**6a**) as a model reaction. The double-Wittig approach allowed the one pot formation of **6a** through addition of decanal (**4**) and acrolein (**5**) to the bis(ylide) **3**. Addition of a 1:1 mixture of the aldehydes resulted in the expected statistical product ratio (**6a/6b/6c** ≈ 2:1:1). However, slow addition of decanal (**4**) to the bis(ylide) **3** followed by slow warming of the reaction mixture to 0 °C, before re-cooling and addition of acrolein (**5**), led to a preferential formation of **6a** (Table 1, entry 1). The nonstatistical product formation indicated that the initially generated bis(ylide) **3** was of higher reactivity than the monoylide **6d** resulting from the first olefination. This allowed an effective control of the reaction. We found that the yield of the desired cross-coupled product **6a** could be improved significantly if decanal (**4**) was not added in THF solution but generated in situ through slow decomposition of an aluminium alkoxide complex (**14**). The latter was added by transferring the cold reaction mixture resulting from DIBAL-H reduction of decanoic acid methyl ester to the ylide solution (Table 1, entry 2). Monodeprotonation of the double-Wittig salt and olefination followed by a second deprotonation/olefination sequence did not lead to the desired product formation.

During warm-up of the reaction mixture to room temperature, decanal (**4**) is presumably slowly released from the intermediate aluminium complex **14** and reacts, preferentially, with the more reactive bis(ylide) **3** instead of the intermediate monoylide **6d**. After 30 min at room temperature, the solution was re-cooled (to −78 °C) and 1.2 equivalents of acrolein (**5**) were added. Following workup, pure (3*Z*,6*Z*,9*Z*)-nonadeca-1,3,6,9-tetraene (**6a**) could be isolated in 58% yield after column chromatography. Only 12% of the symmetrical coupling product **6b** and 4% of **6c** were isolated (Table 1, entry 2). A ^{13}C NMR spectroscopic analysis revealed the configuration of the 3- and 9-double bonds to be > 95% (*Z*); the > 98% (*Z*) configuration of the Wittig salt was retained at the C-6 double bond of the coupling product.

The ability to perform an effective dissymmetrization of the initially formed bis(ylide) **3** is in agreement with our previous findings on the synthesis of TBDMS-protected 17-

Table 1. Double-Wittig reaction for the formation of (*Z*)-1,4,7-trienes



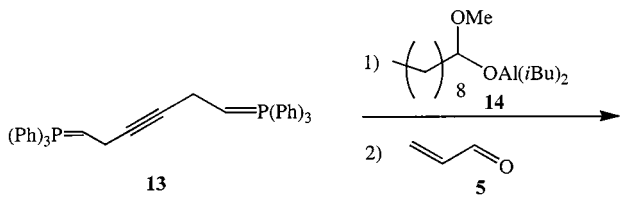
Entry	Aldehyde 1	Aldehyde 2	Method[a]	Yield[b] (a:b:c)[c]
1	$C_9H_{19}CHO$ (**4**)	acrolein (**5**)	B	32 % (**6a**) (1:0.37:0.12)[d]
2	$C_9H_{19}CHO$ (**4**)	acrolein (**5**)	A	58 % (**6a**) (1:0.21:0.07)
3	 **7**	 **8**	B	18 % (**9a**) (1:0.31:0.18)
4	 **7**	 **8**	A	42 % (**9a**) (1:0.14:0.1)
5	 **10** (0.7 eq.)	 **11**	A	51 % (**12a**) (1:0.1:0.15)[d]

[a] A: Reductive olefination protocol; B: nonreductive olefination protocol. – [b] Yield of unsymmetrical coupling product **a** after purification. – [c] The relatively lower yield of **c** compared to **b** can be explained through nonquantitative yields of the successive olefination reactions. – [d] Ratio determined by GLC.

hydroxylinolenic acid methyl ester **9a**. Sequential addition of the aldehydes **7** and **8** to the bis(ylide) **3** at −78 °C in combination with a carefully elaborated temperature program resulted preferentially in the formation of **9a**[9] (Table 1, entry 3). As described above, the best results were obtained after release of the first aldehyde equivalent through slow thermal decomposition of an intermediate aluminate derived from DIBAL-H-reduction of TBDMS-protected lactic acid methyl ester (Table 1, entry 4). Use of the configurationally stable aluminium complex had the additional advantage that the sensitive chiral C_3-aldehyde **7** reacted without racemisation under the basic Wittig conditions.

The concept of the three component reductive olefination reaction could be extended further to the generation of isotope-labelled fatty acids with efficient use of the labelled precursors. Thus, methyl [18,18,18-$^2H_3$]-(6*Z*,9*Z*,12*Z*)-octadeca-6,9,12-trienoate (**12a**), a versatile tool in our ongoing investigation of fatty acid metabolism, could be assembled in a single operation and 51% overall yield (referred to the labelled starting material), starting from [6,6,6-$^2H_3$]hexanoic acid methyl ester and 6-oxo-hexanoic acid methyl ester (**11**) (Table 1, entry 5). To guarantee a maximum efficiency for the transformation of the labelled precursor, a 1.5 molar excess of the bis(ylide) was used to lower the amount of **12b**. After slow decomposition of the aluminium complex of **10** in the ylide reaction mixture, re-cooling and addition of **11**, only 8.7% of the unwanted symmetrical **12b** could be detected along with the cross-coupled product which was separated efficiently from the by-products by column chromatography.

To further elucidate the structural requirements for the differential reactivity of symmetrical bis(ylides) of type **3** we investigated the transformation of hex-3-ynyl-1,6-bis(triphenylphosphonium iodide) (Scheme 2). Deprotonation with potassium bis(trimethylsilylamide) gave the bis(ylide) **13**, which was reacted with the decanoic acid methyl ester derived aluminate (**14**) and acrolein (**5**). In contrast to the above examples, the transformation of the ylide containing a triple bond (**13**) resulted in an almost statistical product ratio (**15a/15b/15c** = 1:0.44:0.3). In this example, the linear geometry of **13** precludes intramolecular interactions of the

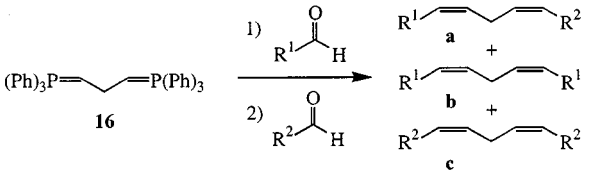


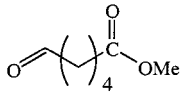
	R^1	R^2
15a	C_9H_{19}	C_2H_3
15b	C_9H_{19}	C_9H_{19}
15c	C_2H_3	C_2H_3

Scheme 2. Application of the Double-Wittig sequence to the formation of dieneynes

two reactive ylide positions. We therefore conclude that the enhanced reactivity of **3** compared to the monoylide of type **6d** might result from intramolecular interaction of the reactive ylide positions in a cyclic bis(ylide) intermediate with or without involvement of an aluminium species (e.g. by complexation).

Table 2. Double-Wittig reaction for the formation of (*Z*)-1,4-dienes



Entry	Aldehyde 1	Aldehyde 2	Method[a]	Yield[b] (a:b:c)[c]
1	$C_6H_{13}CHO$ **17**	acrolein (**5**)	A	traces (**18a**)
2	$C_6H_{13}CHO$ **17**	acrolein (**5**)	B	52 % (**18a**) (1 : 0.25 : 0.07)
3	$C_9H_{19}CHO$ **4**	 **11**	B	36 % (**19a**) (1 : 0.32 : 0.1)[d]

[a] A: Reductive olefination protocol; B: nonreductive olefination protocol. − [b] Yield of unsymmetrical coupling product **a** after purification. − [c] The relatively lower yield of **c** compared to **b** can be explained through nonquantitative yields of the successive olefination reactions. − [d] Ratio determined by GLC.

To challenge the potential of our method we tried to expand the concept of differential reactivities of bis(ylides) to the formation of methylene-bridged (*Z*)-1,4-double bond systems (Table 2). In contrast to **13**, the structure of the symmetrical bis(ylide) **16**[16] should allow intramolecular interaction of the two ylide centres. The use of **16** for the preparation of insect pheromones containing methylene-bridged diene systems as structural elements has been previously introduced by Bestmann et al.[17,18] Since, in these studies, two different aldehyde components were added as mixtures to the bis(ylide) **16**, no information was obtained on the reactivity of **16** compared to that of the intermediate monoylide. Surprisingly, only traces of dienes were obtained using the reductive olefination reaction as above. This suggests a substantial interference from the introduced aluminium species, or the required reaction conditions for the transformation of the bis(ylide) **16**. However, addition of heptanal (**17**) to **16** at −78 °C before slow (two hours) warming to room temperature, re-cooling and addition of acrolein (**5**) resulted in the formation of (3*Z*,6*Z*)-trideca-1,3,6-triene (**18a**) in 52% yield (Table 2, entry 2). The product ratio after workup was **18a/18b** = 1:0.25 and only traces of **18c** could be detected by GLC analysis. Similar results

were found for the preparation of methyl (6*Z*,9*Z*)-nonadeca-6,9-dienoate **(19a)** (Table 2, entry 3). In both examples, a carefully elaborated temperature program avoiding rapid reaction between the initially added aldehyde and the bis(ylide) gives a high selectivity. The ability to perform a dissymmetrization of the initially formed bis(ylide) **16** offers a universal tool for the efficient formation of dienes from a 1,3-dibromopropane derived precursor.

Conclusions

The novel sequential double-Wittig reactions described here exhibit an enormous potential for the short and efficient synthesis of homoconjugated dienes and trienes from simple precursors. The method proved suitable for preparation of a geometrid moth pheromone, stable isotopically labelled fatty acids and functionalized fatty acids. It tolerates the presence of protected hydroxy groups and, in addition, allows the formation of conjugated double bond systems adjacent to the homoconjugated triene system. The key intermediate Wittig salts required for the general synthesis are readily available and can be stored indefinitely.

Experimental Section

General: All reactions were carried out under argon in flame-dried glassware using a standard gas-tight syringe, cannula and septa. Solvents and reagents were dried prior to use. ^{1}H and ^{13}C NMR: Avance DRX 500 spectrometer; $CDCl_3$ or [D$_4$]MeOH as solvent. Chemical shifts (δ) (^{1}H, 500 MHz) were internally referenced to $CHCl_3$ (7.26 ppm) or MeOH (3.31 ppm) or (^{13}C, 125 MHz) to $CDCl_3$ (77 ppm) or [D$_4$]MeOH (49.1 ppm). Infrared (IR) spectroscopy was performed on a Bruker Equinox 55 FT-IR Spectrophotometer. GC-MS (70 eV): Finnigan GCQ, equipped with a fused silica column, coated with DB5 (15 m × 0.25 mm); helium served as carrier gas. HR-MS: Kratos MS 50. Column chromatographic separations were performed with silica gel (230−400 mesh, Merck).

(*Z*)-Hex-3-enyl-1,6-bis(triphenylphosphonium iodide) (2): A suspension of triphenylphosphane (2.6 g, 10 mmol) and imidazole (0.7 g, 10 mmol) in a mixture of ether and acetonitrile (3:1, 20 mL) was treated at 0 °C with iodine (2.5 g, 10 mmol).[13] After being stirred for 10 min at room temperature, the suspension was re-cooled to 0 °C and (*Z*)-hex-3-ene-1,6-diol (**1**)[12,14] (0.52 g, 4.5 mmol) in ether (2 mL) was added. After additional stirring for 3 h at room temperature, the reaction mixture was poured into saturated $NaHCO_3$. Extraction with petroleum ether, drying over Na_2SO_4 and evaporation of the solvent gave crude (*Z*)-1,6-diiodo-hex-3-ene which was transferred without further purification into a solution of triphenylphosphane (2.9 g, 11 mmol) in acetonitrile (50 mL). After refluxing for 4 h the mixture was poured into toluene (500 mL) and the resulting Wittig salt was filtered off. Recrystallization from methanol/diethyl ether afforded pure crystals of (*Z*)-hex-3-enyl-bis(triphenylphosphonium iodide) (**2**) (2.9 g, 3.3 mmol, 73%, *Z*/*E* > 98:2); m.p. 271−273 °C. − ^{1}H NMR ([D$_4$]MeOH, 500 MHz): δ = 2.32 (m, 4 H), 3.51 (m, 4 H), 5.57 (t, *J* = 4.73 Hz, 2 H), 7.69−7.81 (m, 24 H), 7.86−7.9 (m, 6 H). − ^{13}C NMR ([D$_4$]MeOH, 125 MHz): δ = 21.6 (d, *J* = 3.84 Hz, CH_2), 22.7 (d, *J* = 50.9 Hz, CH_2), 119.4 (d, *J* = 86.3, CH), 131.7 (d, *J* = 12.5 Hz, PC), 135.1 (d, *J* = 9.5 Hz, CH), 136.5 (d, *J* = 2.9 Hz, CH). − IR (KBr): ṽ 2880, 2861, 2783, 1481, 1437, 1109, 749 cm^{-1}. − $C_{42}H_{40}I_2P_2$ (860.53): calcd. C 58.62, H 4.68; found C 57.36, H 4.70.

Hex-3-ynyl-1,6-bis(triphenylphosphonium iodide): A mixture of hex-3-yne 1,6-ditosylate[19] (2.8 g, 6.5 mmol) and sodium iodide (3.9 g, 26.2 mmol) was stirred in acetone (25 mL) for 10 h at room temperature. Filtration and concentration of the filtrate in vacuum afforded crude 1,6-diiodo-hex-3-yne that was transferred directly into a solution of acetonitrile (60 mL) and triphenylphosphane (3.5 g, 13 mmol). After reflux for 6 h and workup as described for **2** hex-3-ynyl-1,6-bis(triphenylphosphonium iodide) (4.5 g, 5.3 mmol, 81%) was isolated as a pale yellow solid; m.p. 261−263 °C. − ^{1}H NMR ([D$_4$]MeOH, 500 MHz): δ = 2.43 (m, 4 H), 3.62 (dt, *J* = 7.2 Hz, 12.3 Hz, 4 H), 7.74−7.79 (m, 12 H), 7.8−7.89 (m, 18 H). − ^{13}C NMR ([D$_4$]MeOH, 125 MHz): δ = 13.75 (d, *J* = 6.9 Hz, CH_2), 22.45 (d, *J* = 51.8 Hz, CH_2), 81.6 (d, *J* = 13.4, C), 119.7 (d, *J* = 86.4, CH), 131.67 (d, *J* = 5.4 Hz, PC), 135.1 (d, *J* = 10.6 Hz, CH), 136.5 (d, *J* = 2.8 Hz, CH). − IR (KBr): ṽ 3049, 3025, 2885, 2857, 2792, 1440, 1334, 1110, 980 cm^{-1}. − $C_{42}H_{38}I_2P_2$ (858.52): calcd. C 58.76, H 4.46; found C 58.68, H 4.47.

General Procedure for the Sequential Double-Wittig Olefination: A cold (−78 °C) suspension of the respective Wittig salt (1 mmol) in dry THF (20 mL) was treated with $KN(SiMe_3)_2$ in hexane (4.4 mL of a 0.5 M solution, 2.2 mmol). The reaction mixture was allowed to warm to room temperature, stirred for 30 min and re-cooled (−78 °C).

A) Reductive Olefination: An ethereal solution of the aluminate was prepared as follows.[20] To a cold (−78 °C) solution of the respective methyl ester (1 mmol) in ether (5 mL) was added dropwise pre-cooled (−78 °C) DIBAL-H (1 mL of a 1 M solution in hexane, 1 mmol). After being stirred for 10−60 min (GLC control) the cold (−78 °C) aluminate was transferred quickly to the bis(ylide) reaction mixture with a pre-cooled cannula. The mixture was allowed to warm to room temp. over a period of 90 min, and stirring was continued for 30 min to 1 h (GLC control) before re-cooling to −78 °C. Then, a solution of the aldehyde component (1.2 mmol in 1 mL THF) was added, the mixture was allowed to reach room temperature and stirred for 30 min. Hydrolysis with HCl (2 N), extraction with ether, drying over Na_2SO_4, and flash chromatography on silica gel yielded the (1*Z*,4*Z*,7*Z*)-homoconjugated trienes or **15**.

B) Nonreductive Olefination: A solution of the first aldehyde component (1 mmol) in THF (2 mL) was added slowly with a syringe pump at −78 °C to the bis(ylide) and the reaction mixture was warmed over a period of 2 hours to 0 °C. Stirring was maintained at this temperature for 30 min before re-cooling to −78 °C. Then, a solution of the second aldehyde (1.2 mmol in 1 mL THF) was added, the mixture was allowed to reach room temperature and stirred for 30 min. Hydrolysis with HCl (2 N), extraction with ether, drying over Na_2SO_4, and flash chromatography on silica gel yielded the (1*Z*,4*Z*)-homoconjugated dienes or (1*Z*,4*Z*,7*Z*)-homoconjugated trienes.

(3*Z*,6*Z*,9*Z*)-Nonadeca-1,3,6,9-tetraene (6a): Prepared from methyl decanoate (186 mg, 1 mmol), reduced with DIBAL-H (1 mmol), **2** (860 mg, 1 mmol), and acrolein (**5**) (67 mg, 1.2 mmol) following procedure **A**. Flash chromatography on silica gel (petroleum ether, R_f = 0.4) gave the product **6a** separated from the symmetrical by-products as a colourless oil in 58% yield [151 mg, 0.58 mmol; (*E*/*Z*)-3/(*E*/*Z*)-9 > 95:5; (*E*/*Z*)-6 > 98:2]. Alternatively, it could be prepared from decanal (**4**) (156 mg, 1 mmol), **2** (860 mg, 1 mmol), and acrolein (**5**) (67 mg, 1.2 mmol) following procedure **B** [83 mg, 0.32 mmol, 32%; (*E*/*Z*)-3/(*E*/*Z*)-9 > 95:5; (*E*/*Z*)-6 > 98:2]. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.87 (t, *J* = 6.94 Hz, 3 H), 1.26 (m,

14 H), 2.04 (q, J = 6.94 Hz, 2 H), 2.8 (t, J = 6.62 Hz, 2 H), 2.96 (t, J = 6.6 Hz, 2 H), 5.11 (d, J = 10.1 Hz, 1 H), 5.2 (d, J = 17.1 Hz, 1 H), 5.38 (m, 5 H), 6.0 (t, J = 10.7 Hz, 1 H), 6.66 (m, 1 H). These data are in agreement with Jain et al.[3]

Methyl (9*Z*,12*Z*,15*Z*)-17-*tert*-Butyldimethylsiloxy-octadeca-9,12,15-trienoate (9a): Prepared from 2-(*tert*-butyldimethylsiloxy)-propionic acid methyl ester (202 mg, 1 mmol), reduced with DIBAL-H (1 mL of a 1 M solution, 1 mmol), **2** (860 mg, 1 mmol), and 9-oxo-nonanoic acid methyl ester (**8**) (186 mg, 1 mmol) following procedure **A**. The main product **9a** [177 mg, 0.42 mmol, 42%; (*E*/*Z*)-9/(*E*/*Z*)-15 > 95:5; (*E*/*Z*)-12 > 98:2] was separated from the symmetrical by-products by flash chromatography on silica gel (petroleum ether/ether 95:5, R_f = 0.3). Alternatively, it could be prepared from 2-(*tert*-butyldimethylsiloxy)propionaldehyde (**7**) (172 mg, 1 mmol), **2** (860 mg, 1 mmol), and 9-oxo-nonanoic acid methyl ester (**8**) (186 mg, 1 mmol). The main product **9a** (76 mg, 0.18 mmol, 18%) was isolated following procedure **B**. See Pohnert et al.[9] for spectroscopic data.

Methyl [18,18,18-$^2H_3$]-(6*Z*,9*Z*,12*Z*)-Octadeca-6,9,12-trienoate (12a): Prepared from [6,6,6-$^2H_3$]hexanoic acid methyl ester (100 mg, 0.75 mmol), DIBAL-H (0.75 mmol), **2** (860 mg, 1 mmol), and 6-oxo-hexanoic acid methyl ester (**11**) (216 mg, 1.5 mmol) following procedure **A**. The product **12a** [113.8 mg, 0.38 mmol, (*E*/*Z*)-6/(*E*/*Z*)-12 > 95:5; (*E*/*Z*)-9 > 98:2] could be isolated in 51% yield (with respect to [6,6,6-$^2H_3$]hexanoic acid methyl ester) after flash chromatography on silica gel (petroleum ether/ether 90:10, R_f = 0.35). − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.28 (m, 4 H), 1.38 (m, 4 H), 1.64 (quint., J = 7.8 Hz, 2 H), 2.06 (m, 4 H), 2.3 (t, J = 7.4 Hz, 2 H), 2.79 (m, 4 H), 3.65 (s, 3 H), 5.35 (m, 6 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 12.58 (CD_3), 22.29 (CH_2), 24.57 (CH_2), 25.62 (CH_2), 26.84 (CH_2), 27.21 (CH_2), 29.09 (CH_2), 29.21 (CH_2), 29.33 (CH_2), 31.43 (CH_2), 33.97 (CH_2), 51.44 (OCH_3), 127.58 (CH), 128.06 (CH), 128.33 (CH), 128.44 (CH), 129.52 (CH), 130.44 (CH), 174.1 (COO). − IR (KBr): ṽ 3012, 2925, 2858, 1740, 1437, 1201 cm^{-1}. − MS (70 eV): m/z = 295 (10, M^+), 262 (11), 194 (12), 153 (10), 107 (52), 93 (54), 80 (48), 79 (100), 67 (78). − HRMS ($C_{19}H_{29}{}^2H_3O_2$): calcd. 295.2591; found 295.2593.

(3*Z*,9*Z*)-Nonadeca-1,3,9-trien-6-yne (15a): Prepared from methyl decanoate (186 mg, 1 mmol), DIBAL-H (1 mmol), hex-3-ynyl-1,6-bis(triphenylphosphonium iodide) (858 mg, 1 mmol), and acrolein (**5**) (67 mg, 1.2 mmol) following procedure **A**. The product (**15a**) was obtained as a colourless oil in 18% yield [46 mg, 0.18 mmol, (*E*/*Z*)-3/(*E*/*Z*)-9 > 95:5] after separation of the symmetrical by-products by flash chromatography on silica gel (petroleum ether, R_f = 0.4). − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.87 (t, J = 6.9 Hz, 3 H), 1.25 (m, 14 H), 2.02 (quint., J = 7.4 Hz, 2 H), 2.95 (m, 4 H), 5.01 (d, J = 10 Hz, 1 H), 5.2 (d, J = 16.7 Hz, 1 H), 5.43 (m, 3 H), 6.02 (t, J = 10.7 Hz, 1 H), 6.58 (dt, J = 16.7 Hz, J = 10.7 Hz, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.09 (CH_3), 22.67 (CH_2), 27.11 (CH_2), 27.13 (CH_2), 29.26 (CH_2), 29.31 (CH_2), 29.38 (CH_2), 29.52 (CH_2), 29.58 (CH_2), 29.69 (CH_2), 31.9 (CH_2), 78.88 (C), 80.85 (C), 118.31 (CH), 124.58 (CH), 126.98 (CH), 131.57 (CH), 131.59 (CH), 136.45 (CH). − IR (KBr): ṽ 2924, 2854, 1466, 1261, 1003, 905, 799 cm^{-1}. − MS (70 eV): m/z = 258 (5, M^+), 159 (12), 145 (55), 131 (88), 117 (71), 105 (47), 91 (100), 79 (55), 67 (57), 55 (48). − HRMS ($C_{19}H_{30}$): calcd. 258.2348; found 258.2354.

(3*Z*,6*Z*)-Trideca-1,3,6-triene (18a): Prepared from heptanal (**17**) (114 mg, 1 mmol), propyl-1,3-bis(triphenylphosphonium bromide) (726 mg, 1 mmol), and acrolein (**5**) (67 mg, 1.2 mmol) following procedure **B**. The product (**18a**) could be isolated as a colourless oil in 52% yield [92.6 mg, (*E*/*Z*)-3/(*E*/*Z*)-6 > 95:5] after flash chromatography on silica gel (petroleum ether, R_f = 0.4). − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.9 (t, J = 7.3 Hz, 3 H), 1.3 (m, 8 H), 2.07 (quint., J = 7.2 Hz, 2 H), 2.95 (t, J = 7.3 Hz, 2 H), 5.12 (d, J = 10.2 Hz, 1 H), 5.23 (d, J = 16.7 Hz, 1 H), 5.4 (m, 3 H), 6.02 (t, J = 10.8 Hz, 1 H), 6.68 (dt, J = 16.8 Hz, J = 10.6 Hz, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.07 (CH_3), 22.63 (CH_2), 26.09 (CH_2), 27.25 (CH_2), 28.96 (CH_2), 29.57 (CH_2), 31.76 (CH_2), 117.19 (CH), 125.29 (CH), 127.03 (CH), 130.78 (CH), 130.83 (CH), 137.84 (CH). − IR (KBr): ṽ 2957, 2926, 2855, 1466, 1434, 1261, 995, 903 cm^{-1}. − MS (70 eV): m/z = 178 (12, M^+), 136 (25), 121 (15), 107 (35), 91 (75), 79 (100), 67 (75), 55 (50). − HRMS ($C_{13}H_{22}$): calcd. 178.1722; found 178.1722.

Methyl (6*Z*,9*Z*)-nonadeca-6,9-dienoate (19a): Prepared from decanal (**4**) (156 mg, 1 mmol), propyl-1,3-bis(triphenylphosphonium bromide) (726 mg, 1 mmol), and 6-oxo-hexanoic acid methyl ester (**11**) (180 mg, 1.25 mmol) following procedure **B**. The product (**19a**) could be isolated as a colourless oil in 36% yield [111 mg, (*E*/*Z*)-6/(*E*/*Z*)-9 > 95:5] after flash chromatography on silica gel (petroleum ether/ether 90:10, R_f = 0.35). − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.87 (t, J = 6.9 Hz, 3 H), 1.28 (m, 18 H), 1.63 (quint., J = 7.8 Hz, 2 H), 2.05 (m, 4 H), 2.3 (t, J = 7.8 Hz, 2 H), 3.66 (s, 3 H), 5.36 (m, 4 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.09 (CH_3), 22.67 (CH_2), 24.57 (CH_2), 25.62 (CH_2), 26.83 (CH_2), 27.24 (CH_2), 29.11 (CH_2), 29.32 (CH_2), 29.55 (CH_2), 29.59 (CH_2), 29.66 (CH_2), 31.89 (CH_2), 32.55 (CH_2), 33.97 (CH_2), 51.43 (OCH_3), 127.73 (CH), 128.53 (CH), 129.36 (CH), 130.32 (CH), 174.12 (COO). − IR (KBr): ṽ 3010, 2925, 2854, 1745, 1458, 1436, 1200, 1172, 721 cm^{-1}. − MS (70 eV): m/z = 308 (6, M^+), 276 (8), 207 (8), 163 (11), 150 (19), 135 (25), 109 (39), 95 (52), 81 (73), 67 (73), 41 (100). − HRMS ($C_{19}H_{36}O_2$): calcd. 308.2715; found 308.2726.

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