A Flexible Route toward Polypropylene Model Compounds of Various Tacticities

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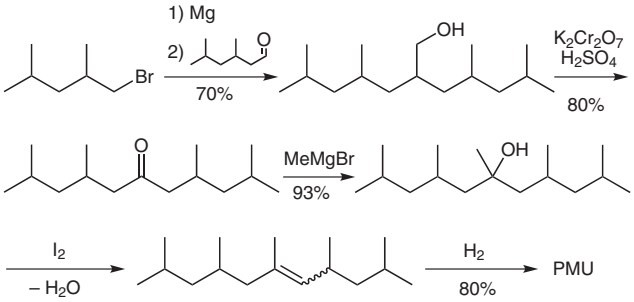
Abstract: This paper reports the flexible synthesis of 2,4,6,8,10-pentamethylundecane (PMU) as well as a chromatographic method for the separation of its diastereoisomers. This strategy offers a unique opportunity to accede to three model compounds of polypropylene (PP) of different tacticities (i.e., isotactic, syndiotactic, and atactic PP).

Key words: model hydrocarbons, polyolefins, total synthesis, HPLC, NMR

Isotactic polypropylene modifications (i.e., grafting of polar monomers, racemization, etc.) are very challenging industrial processes and the underlying chemical reactions are barely established.[2] The very high molecular weights of the polymers and the low graft contents make the identification of reaction products and intermediates very delicate. As a consequence, small oligomers are commonly used as model compounds to shed light on the functionalization mechanisms through the analytical tools of the organic chemist. This paper describes a flexible synthesis of 2,4,6,8,10-pentamethylundecane (PMU) and a chromatographic method for the separation of its diastereoisomers as a route to polypropylene model compounds with controlled tacticities.

PMU synthesis was initially described about 40 years ago and it has not been revisited since that time.[3] Reaction of 3,5-dimethylhexanal with the Grignard reagent from 1-bromo-2,4-dimethylpentane, followed by oxidation of the alcohol intermediate, led to 2,4,8,10-tetramethylundecan-6-one (Scheme 1). The central missing methyl group was then introduced by addition of methylmagnesium bromide, giving 2,4,6,8,10-pentamethylundecan-6-ol. Alcohol dehydration by distillation over iodine afforded a mixture of isomeric olefins that was hydrogenated in the presence of Raney nickel to yield PMU as a mixture of stereoisomers, separable by fractional distillation with low purity.

In our hands, this PMU synthesis was hardly reproducible on a multigram scale, mainly because a competitive side reaction that occurred during the first organometallic coupling, auto-condensation of the alkyl bromide. We tried to replace the aldehyde partner by the corresponding



Scheme 1 Synthesis of PMU according to Pino et al.[3]

Weinreb amide with a view to directly forming the ketone key intermediate, but without success. Therefore, we investigated another route to PMU based on Wittig-type coupling reactions and using a flexible intermediate, namely 2,4,8,10-tetramethyl-6-methyleneundecane, to furnish either a mixture of PMU stereoisomers, or the individual stereoisomers by chromatographic separation of more polar precursors.

Scheme 2 depicts the overall synthetic route to 2,4,6,8,10-pentamethylundecane (PMU, **7**) as a mixture of stereoisomers. The first two steps were performed according to known procedures.[4] The unsaturated ester **1** was synthesized from 4-methylpentan-2-one and triethyl phosphonoacetate, through a Horner–Wadsworth–Emmons (HWE) reaction, as a mixture of regio- and stereoisomers **1′**, all of them led to ethyl 3,5-dimethylhexanoate (**2**) upon catalytic hydrogenation; addition of methyl dimethylphosphonate in the presence of butyllithium led to the β-ketophosphonate **3**. The enone **4** was synthesized through a second HWE reaction between **3** and isovaleraldehyde. The subsequent addition of methylmagnesium bromide in the presence of copper iodide allowed the insertion of the missing methyl group in the polypropylene-like structure. A simple Wittig reaction from ketone **5** led to the exomethylene compound **6** as a key intermediate in the synthesis of the model compounds. Catalytic hydrogenation of **6** gave PMU **7** (mixture of isomers) with an overall yield of 42% for seven steps, including one purification by distillation (for **1**) and four purifications by flash chromatography (for **3**, **4**, **5**, and **6**). Synthesis of **6** on a 250-mmol scale was performed, without purification of the intermediates, in 65% yield for six steps (see Supporting Information).

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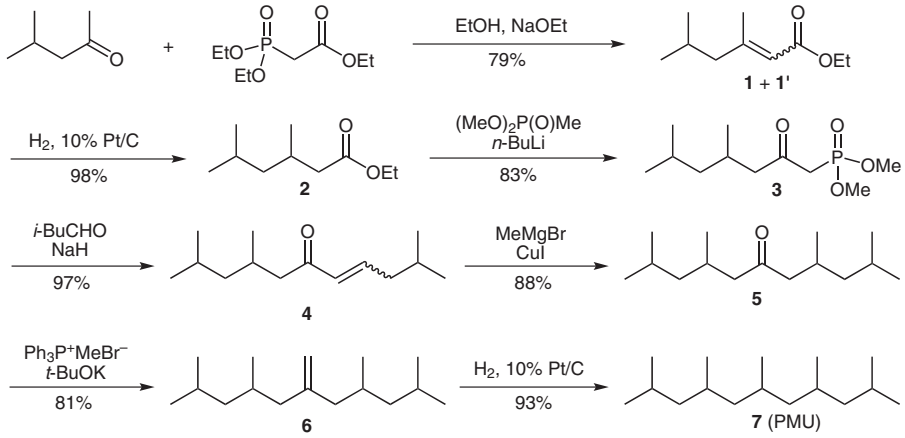


Scheme 2 High-yielding synthesis of PMU as a mixture of stereoisomers

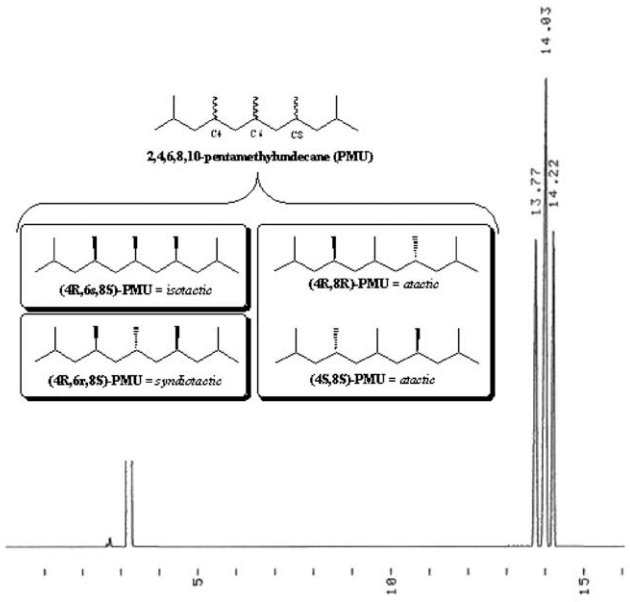


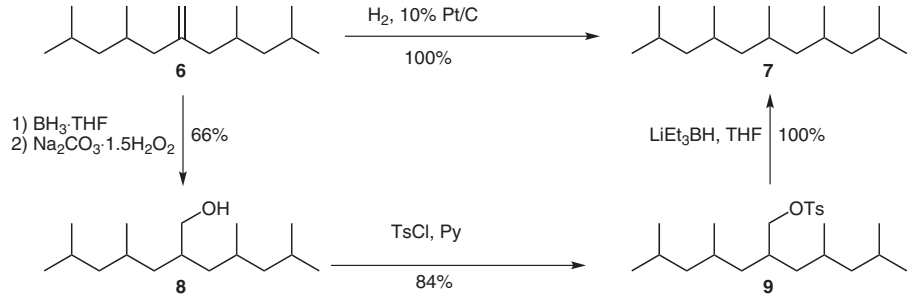
Figure 1 GC chromatogram of PMU synthesized as a mixture of stereoisomers according to Scheme 2; {(Supelco Fused Silica capillary column, SLB 5ms, 30 m × 0.25 mm × 0.25 mm): t_R =13.77 [(4*R*,6*s*,8*S*)-PMU], 14.03 [(4*R*,8*R*)- and (4*S*,8*S*)-PMU)], 14.22 min [(4*R*,6*r*,8*S*)-PMU)]}.

Figure 1 shows the GC chromatogram of the mixture of stereoisomers of PMU. It consists of three peaks in a 1:2:1 ratio. Since PMU has two asymmetric carbons (C4 and C8) and one pseudo-asymmetric carbon (C6), it was synthesized as a mixture of four stereoisomers in equivalent amounts, two of them being enantiomers to each other. The central peak of the chromatogram can unambiguously be assigned to the mixture of enantiomers but without further information it is impossible to ascribe the other peaks to either of the two remaining diastereoisomers. These must be isolated for accurate characterization. As no fraction of pure isomer could be retrieved by distillation, we turned to simple flash chromatography.

The chromatographic separation of hydrocarbons (and more specially stereoisomers) is very delicate as there are no functional groups to interact with the stationary phase. Scheme 3 shows how olefin **6** was derivatized to insert functional groups, i.e. a hydroxy **8** or a tosylate **9** group, onto the main chain. PMU was then recovered through the nucleophilic substitution of the tosylate moiety by hydride.

The potential separation of the diastereoisomers of tosylate **9** was investigated using reverse-phase HPLC. Figure 2 shows that a satisfactory separation could be obtained, but the very long retention times (50–60 min) make it difficult to scale up the separation to preparative HPLC.

GC analysis of the fractions collected during the flash chromatography purification of alcohol **8** revealed that many of them contained only one diastereoisomer (single peak observed by GC whereas three peaks were observed for the crude product). Fractions containing only one of the three diastereoisomers were, therefore, collected sep-



Scheme 3 Derivatization of olefin **6** to introduce functional groups onto the PMU backbone for HPLC separation

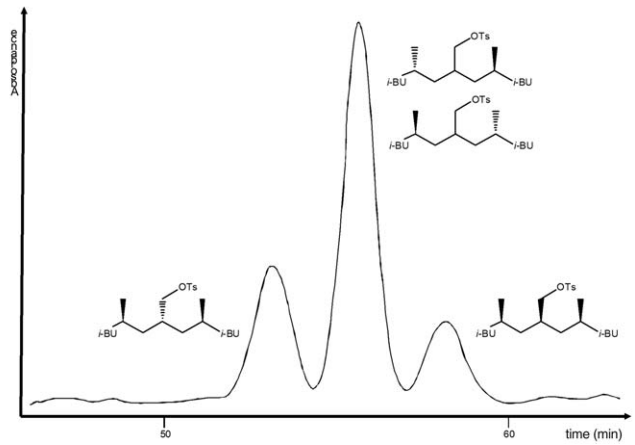


Figure 2 Chromatographic separation of tosylate **9** {(Xterra RP-18, 5 µm, MeOH–H_2O 85:15, 1 mL/min, 227 nm): t_R = 53.82 [(4*R*,6*r*,8*S*)-**9**], 56.15 [(4*R*,8*R*)- and (4*S*,8*S*)-**9**], 58.40 min [(4*R*,6*s*,8S)-**9**]}.

arately and converted into PMU **7** separately as well according to Scheme 3. The correct stereochemistry of the diastereoisomers of intermediates **8** and **9** was assigned *a posteriori* based on NMR data of each PMU stereoisomer independently prepared from their pure precursors.

As can be seen in Figure 3 (a) and (b), isotactic and syndiotactic polypropylene (iPP and sPP, respectively) can be differentiated in ^{1}H NMR on the basis of the chemical shifts of their CH_2 hydrogen atoms as their magnetic environment differs with respect to tacticity.[5,6] These hydrogen atoms are magnetically equivalent in sPP and hence have the same chemical shift at δ ~ 1.1 [Figure 3 (b)]. Conversely, the two CH_2 hydrogen atoms are magnetically non-equivalent in iPP and are exposed to different shielding. Therefore these two hydrogen atoms have two distinct chemical shifts at δ ~ 1.3 and 0.9 [Figure 3 (a)]. The same principle also applies for small oligomers of propylene and can, therefore, be used for the stereochemical assignment of the models. ^{1}H NMR spectra in Figure 3 (c) to (e) show the three stereoisomers of PMU **7**. Figure 3 (c) clearly exhibits one set of resonances at δ = 0.9–1.14, very similar to that observed in sPP, where-

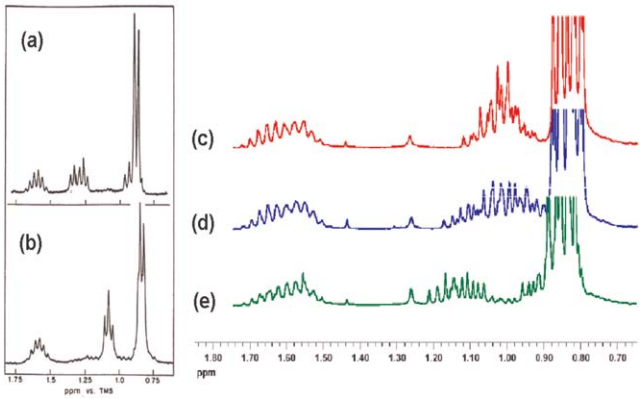


Figure 3 ^{1}H NMR spectra (δ) of (a) iPP, (b) sPP, (c) (4*R*,6*r*,8*S*)-PMU, (d) (4*R*,8*R*)- and (4*S*,8*S*)-PMU, (e) (4*R*,6*s*,8*S*)-PMU. *Conditions:* (a) and (b): *o*-dichlorobenzene, 150 °C, see ref. 6a; (c) to (e) $CDCl_3$, r.t.

as Figure 3 (e) exhibits two sets of chemical shifts at δ ~ 1.06–1.22 and δ ~ 0.95, such as those observed in iPP. Figure 3 (d) exhibits all the resonances simultaneously and is, therefore, coherent with the random conformation of atactic PP.

^{13}C NMR was also used to ascertain the assignments made from ^{1}H NMR data as the chemical shifts of the methyl groups in polypropylenes are strongly dependent on the tacticity. It was reported that 3,5,7,[9-^{13}C],11,13,15-heptamethylpentadecane (HMHD) can be used to assign the triads centered on the ^{13}C-enriched methyl group.[7] The chemical shifts of the HMHD methyl triads were very close to those observed on polypropylene. 2,4,8,10-Tetramethyl-[6-^{13}C]-methylundecane (6-$^{13}CH_3$-PMU) was therefore synthesized from 6-($^{13}CH_2$)-**6** in order to identify the ^{13}C resonance of the central methyl group for each stereoisomer of PMU (see Supporting Information). Figure 4 (a) to (d) shows the ^{13}C spectra of (4*R*,6*s*,8*R*)-PMU, (4*R*,8*R*)- and (4*S*,8*S*)-PMU, (4*R*,6*r*,8*S*)-PMU, and 6-[$^{13}CH_3$]-PMU respectively.

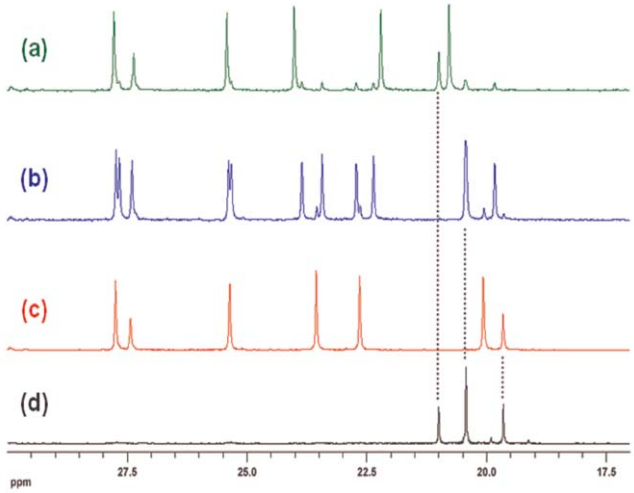


Figure 4 ^{13}C NMR spectrum (δ, $CDCl_3$, r.t.) of: (a) (4*R*,6*s*,8*S*)-PMU, (b) (4*R*,8*R*)- and (4*S*,8*S*)-PMU, (c) (4*R*,6*r*,8*S*)-PMU, (d) 6-[$^{13}CH_3$]-PMU.

Table 1 compares the chemical shifts of the methyl triads of PMU to those of HMHD[7] and polypropylene.[5] The rule of thumb 'δ isotactic > δ atactic > δ syndiotactic' commonly observed for propylene oligomers and polymers also applies in the case of PMU.

Each stereoisomer being clearly identified, it was therefore possible to assign the stereochemistry of each stereoisomer of intermediates **8** and **9** and to characterize them correctly (see experimental section). The two remaining peaks of PMU **7** of the GC chromatogram in Figure 1 could also be assigned accurately as reported in Table 2.

In conclusion, we have disclosed a practical and scalable synthesis of PMU, the model compound of PP. The isotactic stereoisomer could be isolated by flash chromatography separation of the primary alcohol intermediate **8**

Table 1 ^{13}C Chemical Shifts (δ) of Isotactic, Atactic, and Syndiotactic Triads in PMU **7**, HMHD, and PP

Structure	Isotactic triad	Atactic triad	Syndiotactic triad
(4*R*,6*s*,8*S*)-PMU	20.99	–	–
(4*R*,8*R*)- and (4S,8S)-PMU	–	20.43	–
(4*R*,6*r*,8*S*)-PMU	–	–	19.65
HMHD[7]	21.55	20.85	20.17
PP[5]	21.9–21.3	21.1–20.6	20.4–19.7

Table 2 GC/HPLC Retention Times (min) of Isotactic, Syndiotactic, and Atactic Stereoisomers of Intermediates **8**, **9**, and PMU

Isomer	GC **8**[a]	GC PMU **7**[a]	HPLC **9**[b]
Isotactic	21.6	13.8	58.4
Syndiotactic	22.0	14.2	53.8
Atactic (racemic mixture)	21.9	14.0	56.1

[a] Supelco fused silica capillary column, SLB 5ms, 30 m × 0.25 mm × 0.25 mm.
[b] Xterra RP-18, 5 mm, MeOH–H_2O 85:15, 1 mL/min, 227 nm.

[obtained in 43% overall yield for 7 steps; recovery of (4*R*,6*s*,8*S*)-**8** = 30% of the initial content for the first run] followed by tosylation and reduction with lithium triethylborohydride (yield of 84% for 2 steps). Knowing that the initial content in (4*R*,6*s*,8*S*) stereoisomer is only 25% and that the compound of interest has the highest retention time, the final recovery of 6% of pure isotactic-PMU from the initial mixture is acceptable. Moreover, the other diastereoisomers are also accessible in pure forms. In the particular case of PMU, a molecule devoid of functional group, our stereochemically noncontrolled synthesis was preferred over asymmetric synthesis using the catalytic methods recently developed in the field of biologically relevant compounds featuring polydeoxypropionate chains.[8]

All commercially available reagents were purchased from either Aldrich or Acros Organics and used without further purification. Unless specified, all solvents used in chemical reactions were of p.a. grade, whereas solvents used for flash chromatography were technical grade. HPLC solvents were of HPLC grade. Technical petroleum ether (PE) was the fraction boiling in the range 40–65 °C. Deuterated solvents were purchased from ROCC S.A. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance II 300 MHz spectrometer. ^{31}P NMR spectra were recorded on a Bruker Avance 500 MHz spectrometer. FTIR spectra were recorded on a BioRad FTS-135 spectrophotometer. Mass spectra (APCI) were recorded on a Finnigan LCQ Ion Trap. HRMS analyses were performed at the 'Laboratoire de spectrometrie de masse de l'Université de Mons-Hainaut' (Prof. Flammang).

Ethyl (*E*)- and (*Z*)-3,5-Dimethylhex-2-enoate (1)
To a 3-neck round-bottomed flask under argon was added NaOEt (53 mL, 21 wt% in EtOH, 142 mmol)), anhyd EtOH (100 mL), and $(EtO)_2P(O)CH_2CO_2Et$ (32.83 g, 142 mmol) at r.t. After 5 min, 4-methylpentan-2-one (14.29 g, 0.142 mmol) was added in 1 portion and an exothermic reaction occurred. After 50 min, the mixture was heated under reflux for 1.5 h. The mixture was then distilled under atmospheric pressure to remove EtOH until the temperature of the vapor reached 90 °C. The mixture was finally cooled to r.t and Et_2O (100 mL) and cold H_2O (60 mL) were added. The aqueous layer was extracted with Et_2O (2 × 30 mL). The combined organic layers were washed with H_2O (3 × 50 mL) and dried ($MgSO_4$). The crude product was distilled under vacuum as a colorless oil; yield: 19.135 g (112.4 mmol, 79%).

The ^1H NMR spectrum is very complicated because four isomers were synthesized simultaneously. Only olefinic protons are presented. Full ^1H NMR assignment was done after catalytic hydrogenation (*vide infra*, ethyl 3,5-dimethylhexanoate).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.63 (s, 1 H, *E*-α,β), 5.71 (s, 1 H, *Z*-α,β), 5.10 (d, *J* = 9 Hz, 1 H, *E*-β,γ), 5.15 (d, *J* = 9 Hz, 1 H, *Z*-β,γ).

Ethyl 3,5-Dimethylhexanoate (2)
To a 3-neck round-bottomed flask was added the mixture of isomers of unsaturated ester **1** (3.226 g, 18.9 mmol) and 10% Pt/C (1.221 g, 60 μmol). The atmosphere in the flask was purged with argon (3 ×) and H_2 (3 ×). The mixture was stirred vigorously at 30 °C under a H_2 atmosphere (~1 bar) for 30 h. The catalyst was then filtered and washed with PE (3 × 50 mL). The pure product was recovered by distillation of the solvent as a colorless oil; yield: 3.198 g (18.6 mmol, 98%).

^1H NMR (300 MHz, $CDCl_3$): δ = 4.13 (q, *J* = 7 Hz, 2 H), 2.19–2.33 (m, 1 H), 1.93–2.12 (m, 2 H), 1.63 (m, 1 H), 1.26 (t, *J* = 7 Hz, 3 H), 1.01–1.18 (m, 2 H), 0.91 (d, *J* = 6 Hz, 3 H), 0.87 (2d, *J* = 6 Hz, 6 H).

Dimethyl 4,6-Dimethyl-2-oxoheptylphosphonate (3)
A 2-neck flask under argon containing 2.5 M BuLi in hexanes (9.3 mL, 23.2 mmol) and anhyd THF (13 mL) was cooled to –78 °C (dry ice/*i*-PrOH). $(MeO)_2P(O)Me$ (2.881 g, 23.2 mmol) was then added dropwise over 5 min; the colorless soln turned into a white gel. The mixture was stirred at –78 °C for 30 min. A soln of ethyl 3,5-dimethylhexanoate (**2**, 1 g, 5.8 mmol) in anhyd THF (3 mL) was added dropwise; the mixture turned into a colorless liquid again. The temperature was then allowed to rise to –20 °C over 2 h. 18% aq HCl (5 mL) was added to the mixture, the aqueous layer was separated, and $NaHCO_3$ was added until pH 8. The aqueous layer was extracted with CH_2Cl_2 (15 mL). The organic layers were washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, CH_2Cl_2–*i*-PrOH, 95:5, R_f = 0.6) to give a colorless liquid; yield: 1.2 g (4.8 mmol, 83%).

IR (film): 2850–3000, 1716, 1469, 1386, 1259, 1032, 813, 545 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.79 (d, *J* = 11 Hz, 6 H), 2.98–3.18 (m, 2 H), 2.52–2.62 (dd, *J* = 5, 17 Hz, 1 H), 2.36–2.47 (dd, *J* = 8, 17 Hz, 1 H), 2.09 (m, 1 H), 1.62 (m, 1 H), 1.00–1.16 (m, 2 H), 0.84–0.90 (m, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.6, 52.9 (d, *J* = 6 Hz), 51.8, 46.3, 41.8 (d, *J* = 128 Hz), 26.7, 25.3, 23.2, 22.2, 19.8.

^{13}P NMR (200 MHz, $CDCl_3$, external reference: H_3PO_4 at δ = 0): δ = 23.49.

MS (APCI): *m*/*z* = 251 $[M + H]^+$.

2,8,10-Trimethylundec-4-en-6-one (4)
NaH (0.80 g, 20 mmol, 60% in mineral oil) was washed in a 2-neck flask under argon with PE (3 × 20 mL) and dried under vacuum. Anhyd DME (20 mL) was then poured onto NaH and cooled down to 0 °C. Phosphonate **3** (5 g, 20 mmol) was then added dropwise over 15 min. When all the NaH had been consumed (NaH is not sol-

uble into DME), isovaleraldehyde (2.2 mL, 20 mmol) was slowly added to the mixture. The mixture was stirred at 0 °C for 15 min. H_2O (40 mL) and Et_2O (40 mL) were then added, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine (3 × 20 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, EtOAc, R_f = 0.9) to give a colorless liquid; yield: 4.069 g (19.3 mmol, 97%). A fraction of the product still contained an impurity that was removed on a short flash chromatography (silica gel, CH_2Cl_2, R_f = 0.7).

IR (film): 2930–2956, 2872–2902, 1696, 1671, 1629, 1457–1468, 1367–1386, 982 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.79 (dt, J = 7.5, 15 Hz, 1 H), 6.09 (dd, J = 2, 15 Hz, 1 H), 2.44–2.52 (dd, J = 6, 15 Hz, 1 H), 2.27–2.36 (dd, J = 7.5, 15 Hz, 1 H), 2.00–2.18 (m, 3 H), 1.78 (m, 1 H), 1.62 (m, 1 H), 1.01–1.8 (m, 2 H), 0.93 (d, J = 7 Hz, 6 H), 0.85–0.90 (m, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.7, 146.1, 131.9, 48.2, 46.9, 41.9, 28.1, 27.8, 25.5, 23.5, 22.6, 22.4, 20.2.

HRMS (CI): m/z $[M + H]^+$ calcd for $C_{14}H_{27}O$: 211.2062; found: 211.2069.

2,4,8,10-Tetramethylundecan-6-one (5)

CuI (0.146 g, 0.8 mmol) and anhyd Et_2O (10 mL) were added to a 3-neck flask under argon. The flask was then cooled to 0 °C and 3.0 M MeMgBr in Et_2O (5.0 mL, 15.0 mmol) was added dropwise over 10 min. The mixture was stirred at 0 °C for 30 min and then a soln of enone **4** (1.530 g, 7.3 mmol) in anhyd Et_2O (30 mL) was added dropwise over 30 min. The mixture was stirred at 0 °C for a further 1 h and then aq 1 M HCl (10 mL) and H_2O (60 mL) were added and a white solid appeared. The aqueous layer was extracted with Et_2O (3 × 50 mL). The organic layers were washed with H_2O (2 × 50 mL) and brine (3 × 50 mL). The white solid then disappeared. The crude product was recovered after drying ($MgSO_4$), filtration, and evaporation of the solvent. The crude product was purified by flash chromatography (silica gel, CH_2Cl_2, R_f = 0.8) to give a colorless liquid; yield: 1.46 g (6.4 mmol, 88%).

IR (film): 2931–2958, 2875–2900, 1711, 1454–1466, 1362–1385 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.28–2.37 (dd, J = 5, 15 Hz, 2 H), 1.99–2.21 (m, 4 H), 1.61 (m, 2 H), 0.98–1.14 (m, 4 H), 0.83–0.90 (m, 18 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 211.3, 51.4, 51.3, 46.7, 46.6, 27.0, 25.4, 23.4, 22.3, 20.1.

HRMS (CI): m/z $[M + H]^+$ calcd for $C_{15}H_{31}O$: 227.237491; found: 227.237145.

2,4,8,10-Tetramethyl-6-methyleneundecane (6)

$MePh_3P^+Br^-$ (7.148 g, 20.0 mmol) and 1.0 M *t*-BuOK in THF (20 mL,20.0 mmol) were added to a 3-neck round-bottomed flask under argon; the mixture was stirred at r.t. for 7 min. Ketone **5** (2.264 g, 10.0 mmol) was then added dropwise. The mixture was stirred at r.t. for 2 h and then quenched by the addition of H_2O (30 mL). The aqueous layer was then extracted with EtOAc (2 × 60 mL). The combined organic layers were washed with H_2O (2 × 30 mL) and brine (2 × 30 mL), dried ($MgSO_4$), filtered, and concentrated. The crystallization of Ph_3PO occurred during evaporation of the solvent. The solid was then triturated in pentane (40 mL) and filtered. This procedure was repeated several times. The combined filtrates were concentrated to give crude product (2.125 g). The remaining solid was ground into a powder, poured into pentane (150 mL) and stirred overnight. Additional crude product (0.25 g) was recovered after filtration and distillation of the solvent. The crude product was purified by flash chromatography (silica gel, PE, R_f = 0.9) to give a colorless liquid; yield: 1.822 g (8.1 mmol, 81%).

IR (film): 3071, 2913–2956, 2839–2869, 1641, 1437–1466, 1361–1383, 892 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.71 (s, 2 H), 1.90–2.08 (m, 2 H), 1.58–1.80 (m, 6 H), 0.79–1.18 (m, 22 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.6, 111.9, 111.8, 47.2, 46.8, 44.5, 44.2, 28.4, 28.3, 25.4, 23.7, 23.6, 22.5, 22.3, 20.1, 19.8.

HRMS (EI): m/z $[M + H]^+$ calcd for $C_{16}H_{33}$: 224.250401; found: 224.249788.

6-(Hydroxymethyl)-2,4,8,10-tetramethylundecane (8)

A 2-neck round-bottomed flask under argon containing **6** (0.561 g, 2.5 mmol) was cooled to 0 °C. 1 M BH_3·THF in THF (7.5 mL, 7.5 mmol) was then added dropwise and the mixture stirred at r.t. for 2 h. The mixture was then cooled again to 0 °C and H_2O (7.5 mL) was slowly added to neutralize the excess of hydride. Sodium percarbonate (2.777 g, ~13% H_2O_2 w/w, ~22.3 mmol H_2O_2) was slowly added, and the mixture stirred at 50 °C for 1 h and at r.t. for 48 h. The aqueous layer was then separated and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, PE–EtOAc 95:5, R_f = 0.21–0.55) as a colorless liquid; yield: 0.402 g (1.7 mmol, 66%, all isomers considered).

(4*R*,6*r*,8*S*)-8

^1H NMR (300 MHz, $CDCl_3$): δ = 3.51 (d, J^3 = 5 Hz, 2 H), 1.46–1.72 (m, 5 H), 1.22–1.36 (m, 4 H), 0.89–1.16 (m, 4 H), 0.78–0.89 (m, 18 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 65.91, 47.31, 40.20, 35.29, 27.89, 25.38, 23.74, 22.38, 20.47.

(4*R*,6*s*,8*S*)-8

^1H NMR (300 MHz, $CDCl_3$): δ = 3.51 (d, J = 5 Hz, 2 H), 1.48–1.75 (m, 5 H), 0.91–1.30 (m, 8 H), 0.74–0.91 (m, 18 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.97, 47.21, 40.10, 35.47, 27.96, 25.39, 23.77, 22.33, 20.51.

(4*R*,8*R*)-8 and (4*S*,8*S*)-8

^1H NMR (300 MHz, $CDCl_3$): δ = 3.50–3.60 (dd, J^3 = 4.8 Hz, J^2 = 10.5 Hz, 1 H), 3.39–3.49 (dd, J^3 = 5.7 Hz, J^2 = 10.5 Hz, 1 H), 1.45–1.74 (m, 5 H), 0.74–1.34 (m, 26 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.47, 47.67, 47.56, 40.41, 39.30, 35.41, 27.93, 27.70, 25.35, 23.63, 23.59, 22.47, 20.22, 20.18.

2,4,8,10-Tetramethyl-6-(tosyloxymethyl)undecane (9)

A 2-neck round-bottomed flask under argon containing **8** (0.292 g, 1.2 mmol) and anhyd pyridine (3.6 mL) was cooled to 0 °C. TsCl (1.144 g, 6.0 mmol) was added and the mixture stirred at r.t. for 48 h. H_2O (8 mL) was then added and the aqueous layer was separated and extracted with Et_2O (3 × 8 mL). The combined organic layers were washed with 10% aq HCl (3 × 5 mL) and H_2O (8 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, $CHCl_3$–cyclohexane, 60:40, R_f = 0.40–0.71) to give a colorless liquid; yield: 0.401 g (1.0 mmol, 84%).

(4*R*,6*r*,8*S*)-9

^1H NMR (300 MHz, $CDCl_3$): δ = 7.78 (d, J^3 = 8 Hz, 2 H), 7.33 (d, J^3 = 8 Hz, 2 H), 3.91 (d, J^3 = 4.5 Hz, 2 H), 2.44 (s, 3 H), 1.75 (m, 1 H), 1.57 (m, 2 H), 1.42 (m, 2 H), 1.18–1.30 (m, 2 H), 0.85–1.05 (m, 6 H), 0.74–0.85 (m, 18 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.75, 133.32, 129.96, 128.07, 73.13, 47.09, 39.77, 32.62, 27.57, 25.25, 23.63, 22.32, 21.81, 20.09.

(4*R*,6*s*,8*S*)-9

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78 (d, J^3 = 8 Hz, 2 H), 7.33 (d, J^3 = 8 Hz, 2 H), 3.87 (d, J^3 = 5 Hz, 2 H), 2.44 (s, 3 H), 1.75 (m, 1 H), 1.58 (m, 2 H), 1.39 (m, 2 H), 0.86–1.20 (m, 8 H), 0.83 (d, J^3 = 6 Hz, 6 H), 0.76 (d, J^3 = 6 Hz, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.75, 133.21, 129.90, 128.07, 74.01, 46.64, 39.49, 32.54, 27.55, 25.20, 23.68, 22.07, 21.71, 20.18.

(4*R*,8*R*)- and (4*S*,8*S*)-9

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78 (d, J^3 = 9 Hz, 2 H), 7.33 (d, J^3 = 9 Hz, 2 H), 3.83–3.95 (m, 2 H), 2.44 (s, 3 H), 1.75 (m, 1 H), 1.57 (m, 2 H), 1.39 (m, 2 H), 0.85–1.25 (m, 8 H), 0.72–0.85 (m, 18 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.75, 133.28, 129.84, 127.97, 73.57, 47.29, 46.90, 39.87, 38.73, 32.52, 27.50, 27.28, 25.11, 23.51, 23.42, 22.30, 22.16, 21.67, 19.82, 19.74.

2,4,6,8,10-Pentamethylundecane (7)

From **6***:* To a 3-neck round-bottom flask was added **6** (0.617 g, 2.7 mmol) and 10% Pt/C (~0.5 g, ~24.5 μmol). The atmosphere in the flask was purged with argon (3 ×) and H_2 (3 ×). The mixture was stirred vigorously at 25 °C under H_2 (~1 atm) for 48 h. The catalyst was then filtered and washed with PE (3 × 50 mL). The pure product was recovered after distillation of the solvent as a colorless liquid; yield: 0.577 g, (2.5 mmol, 93%). NMR spectra are of mixtures of isomers.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45–1.75 (m, 5 H), 0.75–1.22 (m, 29 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.08, 47.80, 47.13, 46.75, 46.20, 46.10, 45.01, 27.68–27.80, 27.40–27.43, 25.34–25.43, 24.00, 23.85, 23.54, 23.43, 22.72, 22.64, 22.37, 22.21, 21.01, 20.79, 20.43–20.46, 20.07, 19.85, 19.65.

From **9***:* In a 2-neck round-bottomed flask under argon atmosphere containing **9** (0.086 g, 0.22 mmol) was added 1.0 M $LiEt_3BH$ in THF (0.7 mL, 0.7 mmol) at r.t. The mixture was then stirred at 67 °C for 6 h. Aq 3 M NaOH (1.4 mL) was then added dropwise at r.t. The aqueous layer was then separated and extracted with PE (2 × 5 mL). The combined organic layers were washed with H_2O (1 mL) and brine (1 mL), dried ($MgSO_4$), filtered, and concentrated to give a colorless liquid; yield: 0.051 g (0.22 mmol, 100%). GC and NMR measurements revealed that the product was pure and did not need to be further purified.

(4*R*,6*r*,8*S*)-7

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48–1.74 (m, 5 H), 0.90–1.13 (m, 8 H), 0.78–0.90 (m, 21 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.80, 46.19, 27.74, 27.42, 25.35, 23.55, 22.65, 20.70, 19.65.

(4*R*,6*s*,8*S*)-7

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.47–1.74 (m, 5 H), 0.79–1.22 (m, 29 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.69, 46.06, 27.76, 27.35, 25.41, 24.01, 22.19, 20.98, 20.78.

(4*R*,8*R*)- and (4*S*,8*S*)-7

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.47–1.74 (m, 5 H), 0.76–1.20 (m, 29 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.06, 47.10, 46.73, 44.97, 27.72, 27.65, 27.39, 25.38, 25.32, 23.85, 23.42, 22.72, 22.36, 20.44, 19.83.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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