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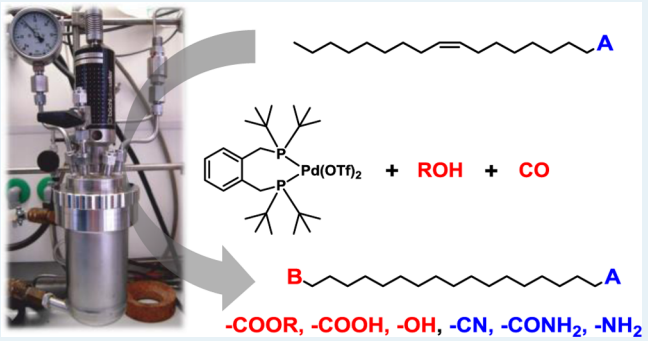
Unsymmetrical α,ω-Difunctionalized Long-Chain Compounds via Full Molecular Incorporation of Fatty Acids

Timo Witt, Florian Stempfle, Philipp Roesle, Manuel Häußler, and Stefan Mecking*

Department of Chemistry, University of Konstanz, Universitätsstraße 10, 78457 Konstanz, Germany

Supporting Information

ABSTRACT: α,ω-Difunctionalized long-chain compounds A-$(CH_2)_n$-B are valuable intermediates and monomers. Unsymmetrical compounds with two different functional groups (A ≠ B) are, however, only accessible by multistep traditional organic syntheses to date. We report on their generation in a single step by isomerizing alkoxycarbonylations of the double bond deep in the chain of oleic derivatives. The compatibility with amide, nitrile and imide functionalities in the substrate allows for the formation with high linear selectivities (ca. 90%) and conversions (70 to 96%) of unsymmetric diesters, ester−amides, ester-nitriles and ester-(*N*-imides) in which these functional groups are terminally attached to a ≥ 17 methylene unit chain. These products further provide access to carboxylic acid-esters, alcohol-esters and amino-esters, and polymers from these AB-monomers. Undesired transesterifications that scramble the A and B functionalities are suppressed completely (<0.1%) by the utilization of a Pd(II) catalyst precursor devoid of acid additives in the presence of amine base.



KEYWORDS: *Fatty acid functionalization, isomerizing alkoxycarbonylation, Long-chain α,ω-difunctional compounds, unsymmetric α,ω-difunctional compounds, isomerizing alkoxycarbonylation functional group tolerance*

INTRODUCTION

Long-chain compounds functionalized in α- and ω-position are relevant intermediates in organic and polymer synthesis.[1] Their long methylene chains, X−$(CH_2)_n$−Y, can in principle be generated by coupling of two shorter fragments, for example, of two alkyl bromides. However, these reactions are of limited practical utility, among others, because of their multistep natures. Fatty acids and their derivatives possess unique long-chain aliphatic sequences and already provide a functionality in the α-position, making them potential starting materials for more straightforward approaches. A selective further terminal ω-functionalization can be achieved by biotechnological ω-oxidation,[2] or chemical catalytic approaches such as isomerizing alkoxycarbonylation[3] or olefin self-metathesis[4] of unsaturated fatty acids (although in the latter case, half of the substrate is lost as the unsubstituted olefin).

To date, these and other approaches have been restricted largely to the generation of symmetric compounds. Toward the challenge of generating unsymmetric products (X ≠ Y) selectively, ω-hydroxylation of fatty acids by biotechnologically modified yeast strains has been developed. A limitation is the lack of compatibility of the carefully engineered strains with substrates of different chain lengths, and currently, high selectivities are restricted to C_{14} fatty acids.[5] Cross-metathesis of unsaturated fatty acid derivatives usually leads to equilibrium mixtures of products.[6] In addition, isomerization of the double bond can lead to a further increased number of different products. A more favorable concept is highly kinetically controlled isomerization/functionalization reactions. Isomerizing hydroboration of unsaturated fatty acid esters provides access to ω-borylated fatty acids, albeit yields and selectivities are low because of competitive hydrogenation during the process.[7] Isomerizing hydroformylation yields α,ω-formyl esters; however, competitive hydrogenation again is problematic, and the selectivity for linear vs branched products was moderate.[8] An isomerizing aminocarbonylation of fatty acids has recently been reported, although the selectivity toward the linear, terminal compound is still low.[9]

Compared with this scenario, isomerizing alkoxycarbonylation of unsaturated fatty acid esters offers the advantage of a high selectivity for linear (symmetric) α,ω-difunctionalized compound in combination with the absence of a significant competitive side reaction, such as hydrogenation.

Key mechanistic features of this reaction are a rapid isomerization by a series of olefin insertions into a metal hydride and β-hydride eliminations from the resulting alkyls.[10] Of all the possible alkyls, the linear terminal Pd alkyl is preferred, along with the branched alkyl stabilized by chelating coordination of the methyl oleate substrates' ester group (Scheme 1). CO inserts reversibly into these species (and into all other alkyls, although

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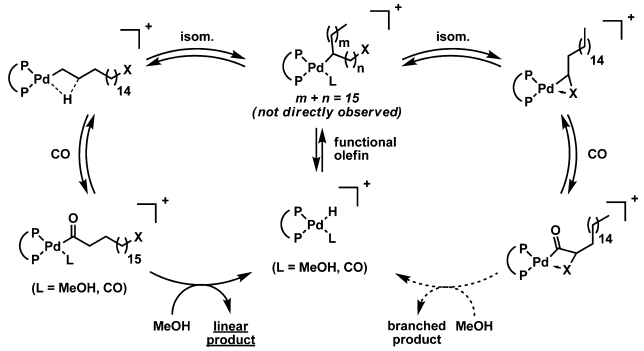
Scheme 1. Major Pathways of Isomerizing Methoxycarbonylation of Olefins, Containing a Functional Group X, As Observed by Low-Temperature NMR Studies for X = COOMe[a]



[a] P^P = tBu$_2$P(CH$_2$)$_3$PtBu$_2$.[10b]

they are present in only very low amounts). The key to the high terminal selectivity is methanolysis as the rate-determining step, which occurs with a significantly lower barrier for the terminal acyl due to the very bulky, electron-rich diphosphine ligand.[10b,c] This understanding provokes the question whether substrates with other potentially more strongly coordinating functional groups (X) will deactivate the catalyst or provide unfavorable thermodynamic sinks otherwise.

We now present an account of the utility of isomerizing alkoxycarbonylation reactions for the preparation of unsymmetric α,ω-difunctionalized compounds.

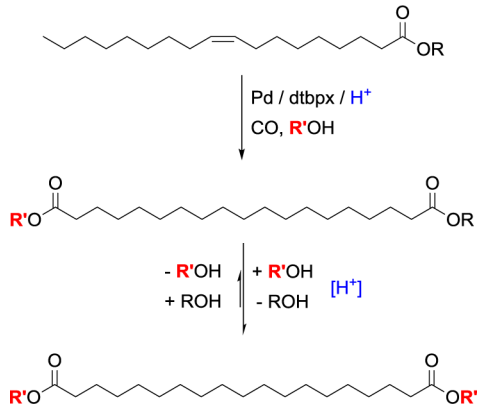
RESULTS AND DISCUSSION

Isomerizing Alkoxycarbonylation to Unsymmetrical α,ω-Dicarboxylates. The initially described catalyst system (which is derived from carbonylation processes for ethylene[11] or also butadiene and its derivatives[12]) for isomerizing methoxycarbonylation of internal olefins[13] and later on for (internally) unsaturated carboxylic acids[3] features a palladium source such as [Pd$^0_2$(dba)$_3$] or [Pd^{II}(OAc)$_2$], an excess of 1,2-bis{(di-*tert*-butylphosphino)methyl}benzene (dtbpx), and an excess of methanesulfonic acid required for the activation of the catalyst. Under these highly acidic conditions, a rapid transesterification of the substrates' ester groups with the alcohol reagent (and solvent) occurs (Scheme 2). This is detrimental for an approach to unsymmetric diesters.

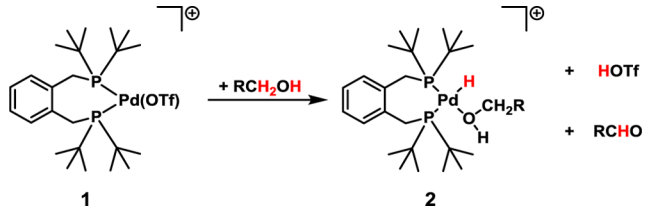
To this end, the defined catalyst precursor [(dtbpx)Pd(OTf)](OTf) (**1**) circumvents the requirements of an additional acid (and also of excess diphosphine ligand).[14] Hence, **1** was used as a catalyst precursor. Even under these "acid-free" conditions, a moderate acidity of the solution can be noted (estimated by placing a drop of the methanolic solution on a moist pH indicator paper, indicating a pH of ~4), probably as a result of the liberation of 1 equiv of acid in the formation of the catalytically active [Pd]−H species (**2**) in methanol (Scheme 3). Performing isomerizing methoxycarbonylation of methyl oleate in ethanol with this catalytic system (1.6 mol % of **1**, p = 20 bar of CO, T = 90 °C) results in the formation of the symmetrically diethyl-substituted compound. The desired ethyl methyl diester was not observed because of transesterification.

To suppress acid-promoted transesterification, an organic amine base was added to neutralize the generated acid and to adjust the acidity of the reaction mixture (also cf. Table S1 in the Supporting Information). Although triethylamine (5 equiv with

Scheme 2. Transesterification in Isomerizing Alkoxycarbonylation



Scheme 3. Formation of Catalytically Active [Pd]−H Species (2) from [(dtbpx)Pd(OTf)](OTf) (1) in an alcohol RCH$_2$OH and Assumed Organic Byproducts



respect to **1**) quenched the catalytic activity and yielded only unreacted starting material, pyridine (5 equiv with respect to **1**) resulted in formation of the desired ethyl methyl diester in moderate yields (conversion ~20% as determined by ^{1}H NMR spectroscopy) under typical reaction conditions (T = 90 °C, p = 20 bar, t = 22 h). The suppression of transesterification was further investigated in an isomerizing benzyloxycarbonylation of methyl oleate. Benzyl alcohol was chosen as an alcohol because the corresponding esters can be cleaved orthogonally to methyl esters under mild hydrogenolysis conditions. A formation of the catalytically active palladium hydride species **2** in benzyl alcohol was probed for by NMR spectroscopy. Full conversion of **1** occurred within seconds upon dissolution in benzyl alcohol to completely form a single hydride species (Figure 1).

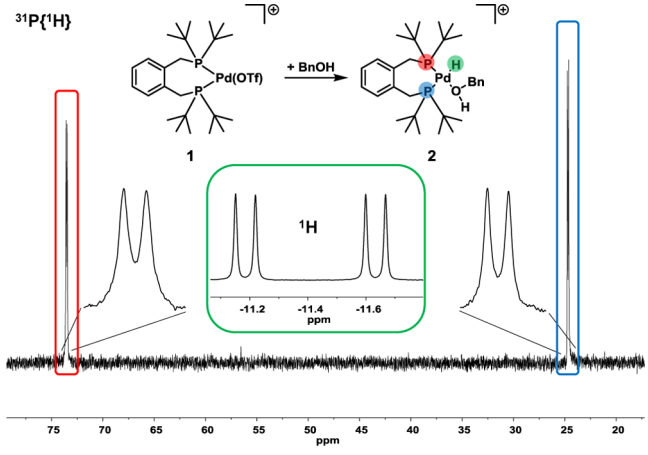


Figure 1. ^{31}P{^{1}H} NMR spectrum (25 °C) of **1** in CD$_2$Cl$_2$ after addition of benzyl alcohol. Inset: ^{1}H NMR region of Pd−H species.

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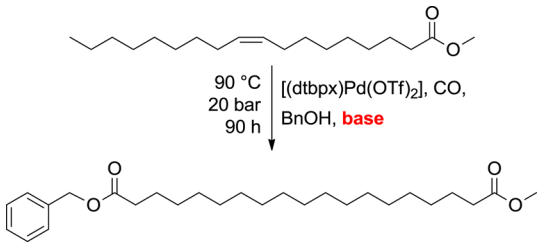
Isomerizing benzyloxycarbonylation of methyl oleate with addition of pyridine to inhibit a transesterification yielded the desired unsymmetrical disubstituted α,ω-dicarboxylic ester as the major product. Reducing the amount of base led to higher conversions, although below a certain threshold (1 equiv of base with respect to the catalyst), transesterification increased strongly (Table 1, entry 5). For an optimal conversion, equimolar

Table 1. Isomerizing Benzyloxycarbonylation of Methyl Oleate in the Presence of a Base[a]



entry	pyridine,[b] equiv	conv[c] [%]	sel[c] [%]	trans[c] [%]
1	5	7	73	<0.1
2	3	9	76	0.2
3	2	10	75	0.1
4	1	24	87	0.3
5	0.1	4	89	8

[a]Reaction conditions: 6.00 mmol of methyl oleate (technical grade), 8.0 mL of benzyl alcohol, 0.048 mmol of **1**, 20 bar of CO, stirred at 90 °C for 90 h. [b]Equivalents of base with respect to amount of catalyst precursor (**1**) used. [c]Determined by GC analysis.

amounts of pyridine were used, resulting in a conversion of 24% after a period of 90 h (entry 4). In general, selectivities appear to be higher for a lower concentration of base (entries 4 and 5), although at very low conversion, these differences in selectivity are close to the experimental error. Variation of reaction conditions further showed that higher carbon monoxide pressures accelerate the reaction, and lower temperatures seem to increase catalyst lifetime (cf. Table S2).

Further insights into the reaction rate were obtained by monitoring the reaction via periodically drawn samples. As a compromise of catalyst activity and lifetime, $T = 55$ °C and $p = 50$ bar were chosen (cf. Table S2). The catalyst exhibits a remarkably long lifetime, and even after reaction times as long as 340 h, the catalyst still shows significant activity to reach a final conversion of 86% (Figure 2). Notably, over the course of this experiment, only a minor extent of transesterification of 0.07% is observed, and selectivity for the desired linear product was between 88 and 90%. Considering all possible reaction products of isomerizing benzyloxycarbonylation of methyl oleate, the selectivity toward the linear terminal diester reveals a high preference for the alcoholysis of a terminal palladium acyl species by benzyl alcohol (cf. Scheme 1).

All products of isomerizing benzyloxycarbonylation (Scheme 4) were further identified and quantified by comparison with isomerizing methoxycarbonylation products. Hydrogenolysis of the benzyl ester according to standard procedures[15] and esterification with methanol was performed to yield the symmetric dimethyl ester. This procedure allows one to draw on existing assignments for methoxycarbonylation of methyl oleate (Figure 3).[16] Unambiguous GC assignment was achieved by crystallization of the linear diester, resulting in enrichment of the branched side products. As for methoxycarbonylation, all possible branched side products appear to form in small

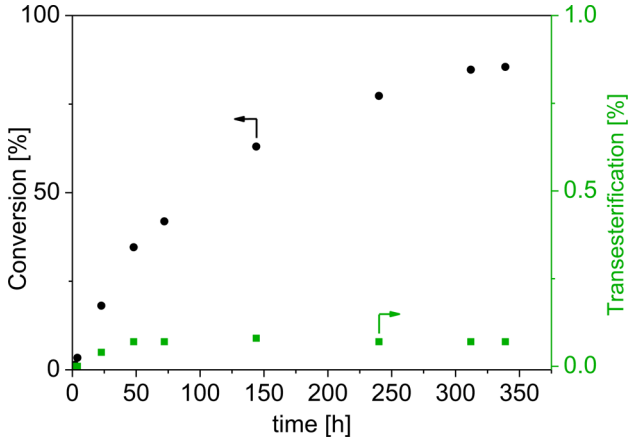
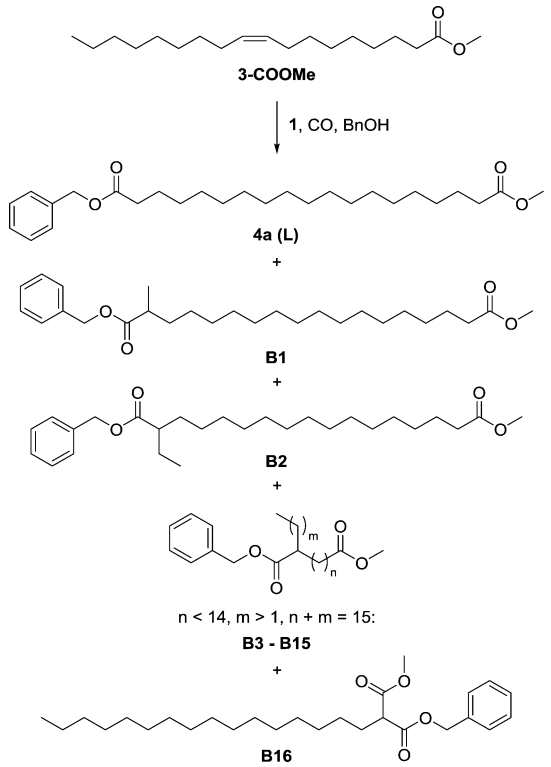


Figure 2. Conversion over time (black) and transesterification over time (green) of isomerizing benzyloxycarbonylation of methyl oleate (at 55 °C and 50 bar of CO).

Scheme 4. Possible Products of an Isomerizing Benzyloxycarbonylation of Methyl Oleate



amounts. However, the ratio of the side products is shifted toward the methyl branched ester (**B1**), probably because of the greater sterical hindrance of benzyl alcohol (Table 2). Notwithstanding this, the branched malonic diester (**B16**) still is observed in trace amounts.

To further understand the decisive factors for reaction rates, ethylene was studied as a substrate. Ethylene is known to react much more rapidly than longer-chain olefins, and at 90 °C under 20 bar of carbon monoxide in methanol, ethylene is consumed within minutes to form methyl propionate (with a catalyst loading of 236 μmol for the conversion of 30 mmol of substrate).[10b] Under the determined optimal conditions of isomerizing benzyloxycarbonylation of methyl oleate ($T = 55$ °C, $p = 50$ bar), ethylene is converted significantly more slowly, and

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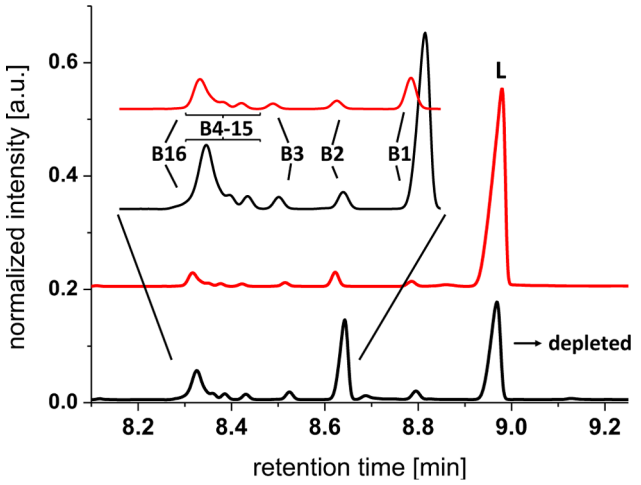


Figure 3. Comparison of gas chromatograms of isomerizing methoxycarbonylation and isomerizing benzyloxycarbonylation products. Red: isomerizing methoxycarbonylation of methyl oleate. Black: isomerizing benzyloxycarbonylation of methyl oleate with successive hydrogenation and esterification in methanol (linear product depleted by recrystallization).

Table 2. Comparison of Side Products of Isomerizing Benzyloxycarbonylation and Isomerizing Methoxycarbonylation[a]

alcohol	B1, %	B2, %	B3, %	B4−15, %	B16, %
BnOH	47.2	6.2	4.0	42.6	
MeOH[b]	39.1	9.1	5.5	43.6	2.7

[a]Product distribution of side products calculated from GC data. [b]Data from ref 16.

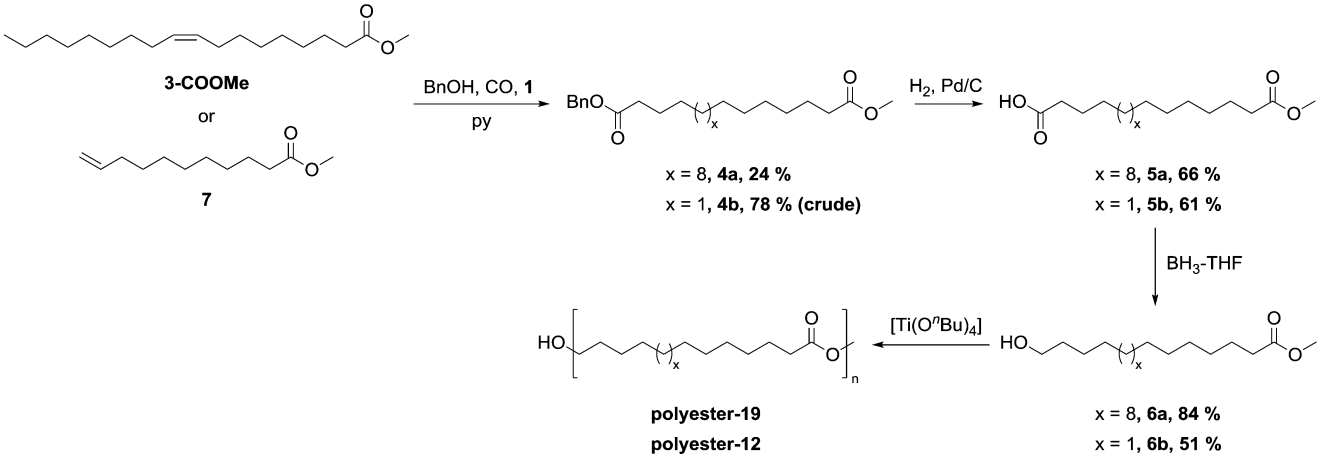
for a full consumption of ethylene (~30 mmol), more than 6 h is required. Interestingly, the presence of pyridine only has a minor effect on the reaction rate. Under otherwise identical conditions, ethylene is methoxycarbonylated in less than 3 h. These results clearly support that alcoholysis, as a rate-determining step,[10b,c] occurs at lower rates with the sterically more demanding benzyl alcohol. This was independently shown by a direct alcoholysis experiment of a ^{13}C-labeled acetyl chloro palladium(II) complex, [(dtbpx)Pd{^{13}C(═O)Me}Cl], prepared for this purpose. Compared with lower alcohols (methanol, ethanol, *n*-propanol, isopropyl alcohol),[10c] benzyl alcohol shows an alcoholysis rate between *n*- and isopropyl alcohol, accounting for the prolonged reaction times required in preparative pressure reactor experiments.

To verify the general applicability of this reaction scheme to unsymmetrical diesters, the industrial mid-chain material methyl 10-undecenoate (**7**) was used to prepare benzyl methyl C_{12}-diester **4b** (Scheme 5). Under the optimized conditions for the conversion of methyl oleate, compound **7** was benzyloxycarbonylated at 55 °C under 50 bar of CO. After a reaction time of 288 h, 95% of the starting material was converted into diesters with a selectivity for the linear diester **4a** of 90%. The overall extent of transesterification was only 0.9%.

Isomerizing Alkoxycarbonylation of *N*-Containing Substrates. On the basis of these findings, we approached the generation of unsymmetric α,ω-difunctional, long-chain compounds with one nitrogen-containing functionality. Amides are of interest for their own sake, but they may also serve as a precursor to amines, for exaple, for AB monomers for polyamides. Unlike amines, they are anticipated to coordinate less strongly to the catalysts' metal center. In the presence of 1 equiv of pyridine, isomerizing methoxycarbonylation of oleamide (**3**-CONH$_2$) led to the formation of methyl 18-carbamoyloctadecanoate (**9**) as the major product in moderate yields (~30% conversion of starting material under standard conditions: T = 90 °C, p = 20 bar of CO). In contrast, in the absence of a base, conversion dropped to ~13%, as determined by ^{1}H NMR spectroscopy.[17] Consequently, all further experiments were performed in the presence of pyridine.

Variation of the reaction conditions revealed the highest conversions were achieved for moderate temperatures and pressures (T = 50 °C, p = 10 bar; cf. Table S3). Higher temperatures resulted in lower conversion, and the limited solubility of the substrate did not allow for decreasing temperature further, albeit longer catalyst lifetime could be achieved. Under these optimized conditions, the course of the reaction over time was monitored by ^{1}H NMR spectra of periodically drawn samples (Figure 4). An apparent decrease in conversion occurs, stabilizing at ~42%. This is due to precipitation of the product from the reaction mixture, affecting the observed ratio of product to starting material. After reaching a critical conversion, the concentration of the product surpasses the saturation point, and amide ester **9** precipitates. This is

Scheme 5. Synthesis Approach for the Preparation of Polyester-19 and Polyester-12 via Isomerizing Benzyloxycarbonylation of Methyl Oleate (3-COOMe) and Methyl 10-Undecenoate (7)



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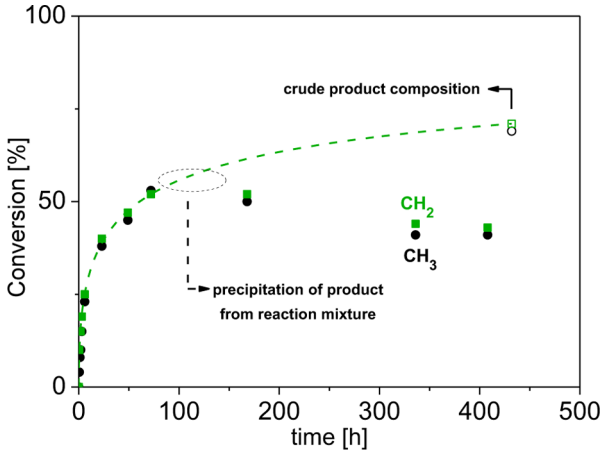

Figure 4. Conversion over time of isomerizing methoxycarbonylation of oleamide (3-$CONH_2$) at 50 °C and 10 bar of CO estimated by the ratio of methylene units adjacent to carboxylic functions (green) and the ratio of methyl groups of the starting material and product (black) in ^{1}H NMR spectroscopy, respectively. Dashed line to the open objects indicates conversion toward final reaction composition after workup.

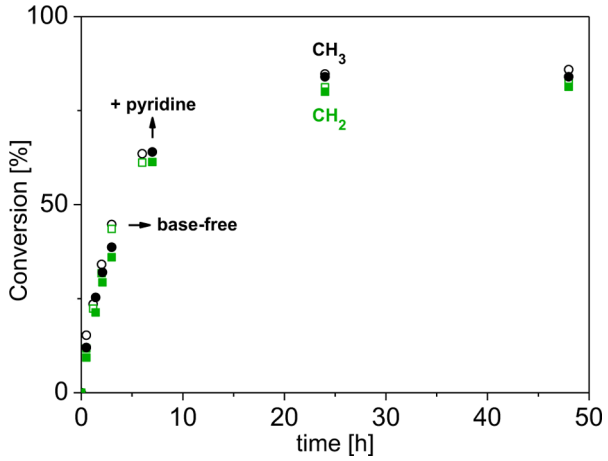

Figure 5. Conversion over time of isomerizing methoxycarbonylation of *N*-oleylphthalimide (3-CH_2NPhth) at 80 °C and 20 bar of CO in the presence of pyridine (solid objects) and without pyridine (open objects) estimated by the ratio of methylene units adjacent to functionalities (green) and the ratio of methyl groups of the starting material and product in ^{1}H NMR spectroscopy (black), respectively.

supported by the final composition of the crude product after workup, revealing a significantly higher conversion of 70% after 430 h. This value is clearly lower than observed for isomerizing methoxycarbonylation of methyl oleate. To account for this observation, the effect of added nonolefinic amides was studied. Isomerizing methoxycarbonylation of methyl oleate in the presence of acetamide as a model compound at standard conditions (T = 90 °C, p = 20 bar, t = 90 h, 6.00 mmol of acetamide) was found to result in a conversion below 10%, independently of the presence or absence of pyridine. This indicates an unfavorable interaction of the amides with the catalyst under reaction conditions, leading to a lower productivity.

As an alternative approach to ω-functionalized long-chain primary amines, oleylamine protected as the phthalimide was studied as a substrate. For this purpose, *N*-oleylphthalimide (3-CH_2NPhth) was prepared from technical grade oleylamine (3-CH_2NH_2) (~70% unsaturated compound).[18] Optimizing reaction conditions showed relatively high temperatures (T = 80 °C) are favorable for a high conversion. A pressure dependency of the reaction was not observed in the range studied (Table S4). In all cases, ^{1}H NMR spectra of the crude product revealed no olefinic signals present, indicating full consumption of 3-CH_2NPhth. Experiments in the absence of pyridine further showed that a base was not required for the stability of the protecting group.

The conversion over time of the isomerizing methoxycarbonylation of 3-CH_2NPhth at T = 80 °C and p = 20 bar was monitored by samples periodically drawn from the pressure reactor (Figure 5). The influence of pyridine on the reaction rate was found to be negligible, and a final conversion of 84% after 48 h was reached in both experiments. Remarkably, in contrast to oleamide, 3-CH_2NPhth is nearly quantitatively methoxycarbonylated within the first 24 h, indicating a more favorable compatibility of the phthalimide functionality.

An alternative functional group of interest is nitriles. Among others, they can serve as a precursor to amines. Nitriles are known to coordinate to transition metals, and they are ubiquitous ligands. This raises the question whether nitrile groups of free or inserted substrates will block catalysis by binding to the metal center. Preliminary experiments using methyl oleate (3-COOMe) in an isomerizing methoxycarbonylation in the presence of acetonitrile (T = 90 °C, p = 20 bar, 6.00 mmol of MeCN) revealed promising results in that no additional side products were formed, and the reaction rate was not significantly lowered by the nitrile present. First experiments with oleonitrile (3-CN) at standard conditions showed that a base is not required for a successful conversion to the desired methyl 18-cyanooctadecanoate (**13**), as determined by GC analysis. Note that other than 3-$CONH_2$ and 3-CH_2NPhth, oleonitrile is compatible with GC analysis, facilitating the determination of selectivity and conversion.

Under the determined optimal reaction conditions (T = 70 °C, p = 50 bar; cf. Table S5), the progress of the reaction was monitored by GC analysis of periodically drawn samples (Figure 6). The selectivity of the reaction stays around 89%, independent of the given conversion and reaction time. Oleonitrile, as well as 3-CH_2NPhth, is consumed more rapidly than oleamide (and methyl oleate in benzyloxycarbonylation). Compared with

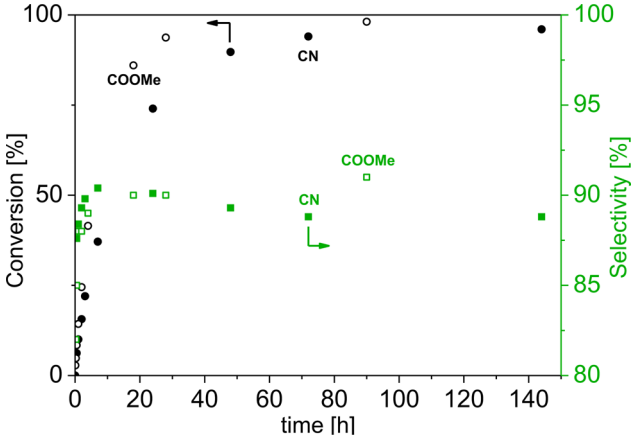

Figure 6. Conversion over time of isomerizing methoxycarbonylation of oleonitrile (3-CN, solid objects) and methyl oleate (3-COOMe, open objects) at 70 °C and 50 bar of CO and without pyridine estimated by GC analysis.

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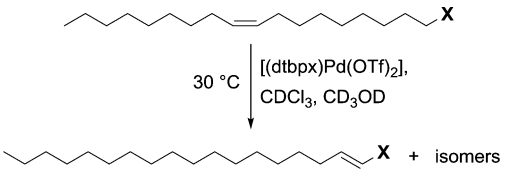
methyl oleate methoxycarbonylation, oleonitrile consumption is slower. Notwithstanding this, a final conversion of 96% is reached after 144 h.

The substantially different reaction rates observed for the various substrates show that the functional group of the substrate decisively impacts the reaction. To identify a possible bottleneck, limiting the reaction rate, the isomerization of the substrates was studied further. Exposure of methyl oleate, oleamide, *N*-oleylphthalimide, and oleonitrile to 1 mol % of complex **1** in the presence of methanol resulted in rapid isomerization within minutes, as observed by ^{1}H NMR spectroscopy. The portion of the α,β-unsaturated compound in the thermodynamic mixture of isomers varies, depending on the substrate functionality (Table 3). The preference for the α,β-unsaturated isomer is similar for esters and amides, whereas nitrile **3**-CN shows nearly no preference for this isomer. In addition, this is the only substrate in which both stereoisomers (*E* and *Z*) could be observed in similar ratios. In all other cases, no *Z* isomers were present, potentially because of sterical reasons. The α,β-unsaturated phthalimide was observed only at a very low ratio of 0.4%. Essentially, the formation of a particular stable olefin isomer, which could present a rate-limiting energetic sink, is not observed for any of the substrate functional groups studied here.

Table 3. Ratio of α,β-Unsaturated Compounds in Thermodynamically Driven Mixture of Isomers of the Different Substrates[a]



entry	substrate	(*E*)-α,β-unsat.,[b] %	(*Z*)-α,β-unsat.,[b] %
1	**3**-COOMe	5.1	n.d.
2	**3**-$CONH_2$	5.9	n.d.
3	**3**-CH_2NPhth	0.4	n.d.
4	**3**-CN	0.3	0.2

[a]Reaction conditions: 0.13 mmol of oleic acid derivative (**3**-COOMe, **3**-$CONH_2$, **3**-CH_2NPhth, or **3**-CN, respectively), 1.3 μmol of **1**, 0.3 mL of $CDCl_3$, 0.2 mL of CD_3OD, T = 30 °C. [b]Determined by ^{1}H NMR spectroscopy by comparison of the unsaturated CH signals.

Further Conversion of the Unsymmetrically α,ω-Difunctionalized Compounds. With unsymmetrically α,ω-difunctionalized compounds readily available on preparative scales, new approaches to intermediates from plant oils are possible. Mid- to long-chain aliphatic benzyl methyl α,ω-diesters **4a** and **4b**, isolated in 24% (99% purity) and 78% (crude product), respectively, are readily cleaved via hydrogenolysis to afford the α-carboxylic acid ω-esters in yields of 66% and 61% (after recrystallization), respectively (Scheme 5). The resulting monoesters **5a** and **5b** could be reduced selectively to the corresponding ω-hydroxy esters **6a** and **6b** by applying BH_3·THF.[19] After column chromatography, the compounds could be obtained in high purity in yields of 84% and 51%, respectively. As an example of the utility of these compounds, they can be used as AB-type monomers in a titanium(IV) alkoxide-catalyzed reaction to synthesize polyesters, such as long-chain polyester-19 (Table 4).

Unsymmetrically disubstituted compounds containing a nitrogen atom (**9**, **11**, **13**, isolated by recrystallization in 27%, 48% and 58%, respectively) offer the potential for the preparation of long-chain ω-amino esters (Scheme 6), which can serve, among others, as monomers for long-chain aliphatic polyamides. Although hydrogenation of nitrile ester **13** and hydrazinolysis[20] of phthalimide ester **11** will result in the formation of methyl 19-amino nonadecanoate (**12**), transformation of amide ester **9** into the latter compound by catalytic hydrogenation is rather challenging. A selective reduction of the amide functionality could not be achieved because of lower reactivity of the amide compared with the ester functionality. A more convenient route to an ω-amino ester is the Hofmann rearrangement to methyl 18-amino octadecanoate (**10**) using hypervalent iodine(III) species.[21] Although one methylene unit is lost during the process, the toleration of ester functionalities in this approach is beneficial. The selective hydrogenation of nitriles is achieved by applying a Grubbs catalyst in combination with a strong base, not only allowing for hydrogenation in the presence of esters but also suppressing formation of secondary amines, common side products in nitrile hydrogenations.[22] The amino compounds were purified by recrystallization of the corresponding HCl adducts from ethyl acetate. Hydrazinolysis of **11** yielded **12** in 91% yield, hydrogenation of **13** yielded the same compound in 74% yield, and Hofmann rearrangement of **9** yielded compound **10** in 71% yield.

Polymers from Unsymmetrically α,ω-Difunctionalized Compounds. Monomers **6a**, **10**, and **12** were utilized for polycondensation reactions (Table 4). Polyester-19 was prepared from ω-hydroxy ester **6a** under vacuum at elevated temperatures using $Ti(O^nBu)_4$ as a catalyst. Polyamides were prepared from ω-amino esters at elevated temperatures without added catalyst in a 20 mL stainless steel pressure reactor in vacuo.

The polyester-19 prepared exhibits molecular weights of around 20 000 g mol^{-1} (determined by GPC and ^{1}H NMR spectroscopy end group analysis) and a melting point of T_m = 103 °C. This agrees with the reported data for polyester-19 prepared by ROP of nonadecalactone,[23] and polyester-19,19 prepared by polycondensation of dimethyl 1,19-nonadecanedioate and 1,19-nonadecanediol.[24]

Table 4. Properties of Prepared Polymers

entry	T_m1,[a] °C	T_m2,[a] °C	T_c,[a] °C	ΔH_m, J g^{-1}	$M_{n,NMR}$, g mol^{-1}	$M_{n,GPC}$,[b] g mol^{-1}	M_w/M_n[b]
polyester-19	103	n.d.	84	164	17.0×10^3	19.8×10^3	2.0
polyamide-19[c]	154	160	139	112	3.5×10^3	n.d.	n.d.
polyamide-19[d]	152	158	138	113	2.7×10^3	n.d.	n.d.
polyamide-18[e]	157	163	141	107	4.4×10^3	n.d.	n.d.

[a]Determined by DSC with a heating/cooling rate of 10 K min^{-1}. [b]GPC at 160 °C in trichlorobenzene versus polyethylene standards. [c]Polyamide prepared by polycondensation of methyl 19-aminononadecanoate (**12**) prepared from phthalimide (**11**). [d]Polyamide prepared by polycondensation of methyl 19-aminononadecanoate (**12**) prepared from nitrile (**13**). [e]Polyamide prepared by polycondensation of methyl 18-aminooctadecanoate (**10**) prepared from amide (**9**).

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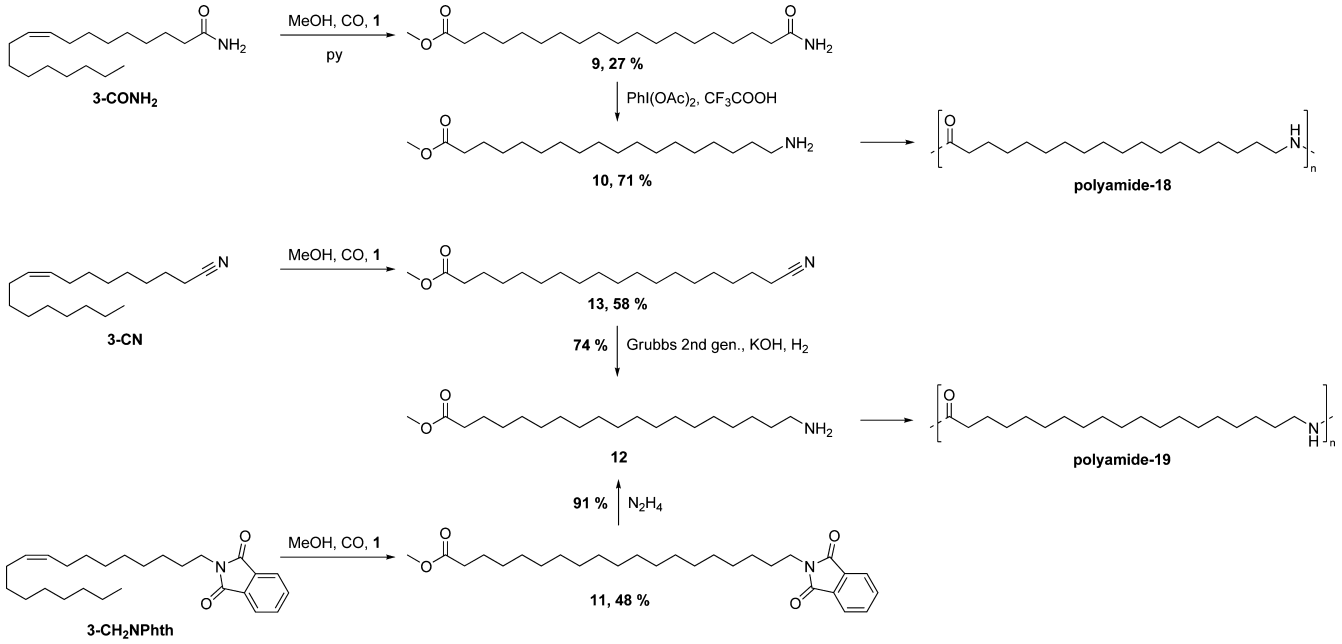
Scheme 6. Synthesis Approach for the Preparation of Polyamide-18 and Polyamide-19 via Isomerizing Methoxycarbonylation of Oleamide (3-$CONH_2$), Oleonitrile (3-CN), and *N*-Oleylphthalimide (3-CH_2NPhth)



Polyamide-18 and polyamide-19 were found to possess relatively low molecular weights around 3000 g mol^{-1} (as determined by ^1H NMR spectroscopy). In general, polyamide-18 shows an undefined melting transition at 163 °C with a minor melting peak at 157 °C. Polyamide-19, prepared from **11** as well as from **13**, again showed two transitions, located between 152 and 154 °C (minor peak) and 158 and 160 °C (major peak). Multiple melting transitions are known for polyamides due to their hydrogen-bonding-dominated multiple crystal morphologies.[25] Compared with previously reported properties of polyamide-18 (T_m = 158 °C)[25b] and polyamide-18,18 (T_m = 162−164 °C),[25c] the material reported in this work shows similar thermal properties.

CONCLUSIONS

In summary, isomerizing alkoxycarbonylation of fatty acid derivatives is a general approach to long-chain unsymmetric α,ω-difunctional compounds, as illustrated for a number of substrates. This provides access in one step and with high selectivities to unsymmetric diesters, ester-amides, ester-nitriles, and ester-(*N*-imides) in which these functional groups are terminally attached to a ≥17 methylene unit chain. These products can be further converted conveniently to carboxylic acid esters, alcohol esters and amino esters. The utility of these intermediates was exemplified by the preparation of long-chain AB-type polyesters and polyamides.

Remarkably, despite the rapid isomerization of the catalytically active sites along the chain as an inherent feature of this approach, which brings them into close proximity to the functional groups in the intermediates occurring intermittently, catalysis is compatible with a range of *N*-containing functional groups. The overall reactions are relatively slow because of the barrier for alcoholysis, but due to the outstanding stability of the catalyst over time, eventually high or virtually complete conversions can be achieved with uncompromised selectivity.

EXPERIMENTAL SECTION

Materials and General Considerations. All reactions and manipulation of moisture and air-sensitive substances were performed under an inert gas atmosphere using standard Schlenk or glovebox techniques. Solvents were dried under an inert atmosphere as follows: Toluene was distilled from sodium prior to use. CH_2Cl_2 and DMF were distilled from CaH_2, THF was distilled from blue sodium/benzophenone and MeOH was distilled from magnesium turnings. Anhydrous benzyl alcohol was purchased from Sigma-Aldrich and degassed prior to use. All dry and degassed solvents were stored under an inert atmosphere. Carbon monoxide (3.7 grade, 99.97% pure) and ethylene (3.5 grade, 99.95%) were supplied by Air Liquide. Methyl oleate (**3**-COOMe, Dakolub MB9001 high oleic sunflower oil with 92.5% methyl oleate) supplied by Dako AG was degassed prior to use. Oleic acid (**3**-COOH, technical grade) and oleyl amine (**3**-CH_2NH_2, technical grade) were purchased from Sigma-Aldrich and used as received. Oleamide (**3**-$CONH_2$) was prepared according to a procedure by Fong et al. and recrystallized from heptanes prior to use.[26] Methyl undecenoate (**7**) was synthesized from undecenoic acid and methanol following a procedure by Vijai Kumar Reddy et al. and used without further purification.[27] [(dtbpx)Pd(OTf)]OTf (**1**) was prepared by a reported procedure.[14] All deuterated solvents for NMR spectroscopy were supplied by Euriotop.

Organic syntheses were monitored by TLC on Merck TLC silica gel 60 F254 plates on plastic sheets with F254 fluorescent indicator. The TLC plates were stained in an ethanolic phosphomolybdic acid solution for spot analysis. NMR spectra were recorded on a Varian Inova 400 or a Bruker Avance 400 spectrometer. ^1H and ^{13}C chemical shifts were referenced to the solvent signals. NMR spectroscopy of polymers was performed in 1,1,2,2-tetrachloroethane-d_2 at 130 °C. GPC analyses of polymers were performed with a Polymer Laboratories GPC220 instrument equipped with PLgel Olexis columns using the refractive index detector. Molecular weights were determined by

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calibration with PE standards at 160 °C in 1,2,4-trichlorobenzene (flow rate: 1.0 mL min^{-1}).

GC analyses were performed using a PerkinElmer Clarus 500 instrument with an autosampler equipped with an Elite-5 crossbond 5% diphenyl/95% dimethyl polysiloxane column of 30 m length, 0.25 mm i.d., and 0.25 μm film thickness. The temperature of the oven was kept at 100 °C for 1 min, then heated from 100 to 300 °C with a heating rate of 15 °C per minute. The final temperature was held for 5 min. The injector was kept at 270 °C, and the detector, at 280 °C. The injection volume was 1.0 μL. Analysis of the retention times and peak areas were performed using the TotalChrom software of PerkinElmer.

LC/MS analyzes were conducted on a LCMS-2020 instrument from Shimadzu (pumps LC-20 AD, autosampler SIL-20AT HAT, column oven CTO-20AC, UV−vis detector SPD-20A, controller CBM-20, APCI detector and software LCMS-solution) with an EC 125/4 Nucleodur C18, 3 μM column (Machery-Nagel). A binary gradient of acetonitrile (with 0.1% formic acid) in water (with 0.1% formic acid) was used at a flow rate of 0.4 mL min^{-1}.

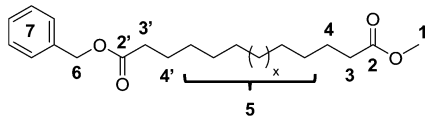
Analytical high performance liquid chromatography (HPLC) was conducted on a LC-20A prominence system (pumps LC-20AT, auto sampler SIL-20A, column oven CTO-20AC, diode array detector SPD-M20A, ELSD-LT II detector, controller CBM-20A and software LC-solution) from Shimadzu using an EC 125/4 Nucleodur C18, 3 μM column (Machery-Nagel).

DSC analysis was performed on a Netzsch DSC 204 F1 at a heating rate of 10 °C per minute in a temperature range from −50 to 160 °C. All data reported are from second heating cycles. All elemental analyzes were performed on an Elementar vario MICRO cube elemental analyzer by the in-house Microanalysis Service.

Synthetic Procedures. Carbonylation reactions were run in stainless steel pressure reactors (Büchi miniclave (300 mL) with a mechanical stirrer and a heating/cooling mantle controlled by a temperature sensor dipping directly into the reaction mixture) or in 20 mL stainless steel pressure reactors equipped with a heating jacket, glass inlay, and magnetic stir bar.

General Procedure for Unsymmetrical Isomerizing Benzyloxycarbonylation Experiments. The reactor was evacuated and purged with argon several times. In a glovebox, the catalyst precursor **1** (38.4 mg, 0.048 mmol) was weighed in a Schlenk tube equipped with a magnetic stir bar. The Schlenk tube was removed from the glovebox, and 6.00 mmol (1.78 g, 2.03 mL) of methyl oleate (Dakolub MB 9001), 8.0 mL of benzyl alcohol, and 0.048 mmol (3.8 mg, 3.9 μL) of pyridine were added using standard Schlenk techniques. The stirred mixture was cannula-transferred into the reactor in an argon counter stream. The reactor was then pressurized with carbon monoxide and heated to the desired temperature. After a reaction time of 90 h, the reactor was cooled to room temperature and vented. The mixture was diluted with dichloromethane, filtered over a silica plug, and dried in vacuo. Conversion, selectivity, and the extent of transesterification were determined by GC or NMR analysis. Isolation of pure linear, unsymmetric, 1,19-disubstituted benzyl methyl diester was achieved by recrystallization from heptanes to yield the desired compound in high purity (>99% as determined by GC analysis) in 24% yield. Mid-chain benzyl methyl diester **4b** could be purified by recrystallization from methanol at −10 °C to a purity >99% in 11% yield.[28]

4a (x = 8): ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ = 7.38−7.27 (m, 5H, H-7), 5.11 (s, 2H, H-6), 3.65 (s, 3H, H-1), 2.34 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3′), 2.29 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3), 1.68−1.57

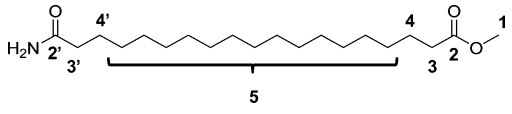


(m, 4H, H-4, H-4′), 1.35−1.21 (m, 26H, H-5) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C) δ = 174.3 (C-2), 173.7 (C-2′), 136.2−128.2 (C-7), 66.1 (C-6), 51.4 (C-1), 34.4 (C-3′), 34.2 (C-3), 29.7−29.2 (C-5), 25.0 (C-4, C-4′) ppm. Elemental analysis (%) calcd: 74.96 (C), 10.25 (H). Found: 74.64 (C), 10.43 (H). APCI-MS (m/z): 433.1 $[M + H]^+$.

4b (x = 1): ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ = 7.38−7.27 (m, 5H, H-7), 5.10 (s, 2H, H-6), 3.65 (s, 3H, H-1), 2.34 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3′), 2.29 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3), 1.68−1.56 (m, 4H, H-4, H-4′), 1.34−1.22 (m, 12H, H-5) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C) δ =174.3 (C-2), 173.7 (C-2′), 136.2−128.2 (C-7), 66.1 (C-6), 51.4 (C-1), 34.4 (C-3′), 34.1 (C-3), 29.4−29.2 (C-5), 25.0 (C-4, C-4′) ppm. Elemental analysis (%) calcd: 71.82 (C); 9.04 (H). Found: 72.01 (C), 8.94 (H). APCI-MS (m/z): 335.0 $[M + H]^+$.

General Procedure for Unsymmetrical Isomerizing Methoxycarbonylation Experiments. In the case of solid fatty acid derivatives, 6.00 mmol of the corresponding substrate (**3**-$CONH_2$ or **3**-CH_2NPhth) was weighed in the reactor glass inlay. The reactor was assembled, evacuated, and purged with argon several times. In a glovebox, the catalyst precursor **1** (38.4 mg, 0.048 mmol) was weighed in a Schlenk tube equipped with a magnetic stirring bar. The Schlenk tube was removed from the glovebox. In the case of utilization of liquid fatty acid substrates, 6.00 mmol of these was added at this point (**3**-COOMe or **3**-CN) along with 8.0 mL of methanol and 0.048 mmol (3.8 mg, 3.9 μL) of pyridine using standard Schlenk techniques. The stirred mixture was cannula-transferred into the reactor in an argon counter stream. The reactor was then pressurized with carbon monoxide and heated to the desired temperature. After a reaction time of 90 h, the reactor was cooled to room temperature and vented. The mixture was diluted with dichloromethane, filtered over a silica plug to remove residual catalyst and palladium black and dried in vacuo. Conversion was determined by ^{1}H NMR analysis or by GC, if possible.

Purification of the crude ester amide **9** was achieved by multiple recrystallizations from heptanes/*i*PrOH (9/1), and a white solid was obtained in 27% yield in a purity >99% (as determined by HPLC).



9: ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ = 5.36 (s, br, 2H, NH_2), 3.66 (s, 3H, H-1), 2.30 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3), 2.22 (t, $^3J_{HH}$ = 7.6 Hz, 2H, H-3′), 1.67−1.56 (m, 4H, H-4, H-4′), 1.37−1.20 (m, 26H, H-5) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 100 MHz, 25 °C) δ = 174.4 (C-2), 51.5 (C-1), 42.3 (C-8), 34.3 (C-3), 33.8 (C-7), 29.8−29.3 (C-5), 27.0 (C-6), 25.1 (C-4) ppm. Elemental analysis (%) calcd: 70.34 (C), 11.51 (H), 4.10 (N). Found: 70.21 (C), 11.53 (H), 4.21 (N). APCI-MS (m/z): 342.3 $[M + H]^+$.

From the resulting crude product, pure phthalimide ester **11** was isolated by repetitive recrystallization from heptanes/*i*PrOH (9/1) in 48% yield in a purity >99% (determined by HPLC).

11: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 7.80 (dd, $^3J_{HH}$ = 5.4, 3.1 Hz, 2H, H-1′)−7.66 (dd, $^3J_{HH}$ = 5.4, 3.1 Hz, 2H, H-1′), 3.64 (t, $^3J_{HH}$ = 7.3 Hz, 2H, H-3′), 3.63 (s, 3H, H-1), 2.26 (t, $^3J_{HH}$ = 7.3

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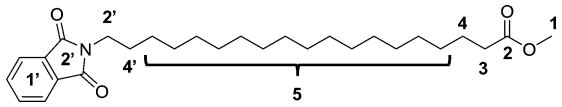
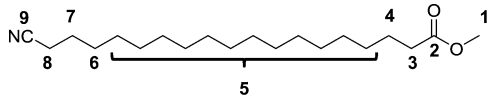


Hz, 2H, H-3), 1.68−1.53 (m, 4H, H-4, H-4′), 1.35−1.16 (m, 28H, H-5) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C) δ 174.4 (C-2), 168.6 (C-2′), 133.9−123.2 (C-1′), 51.5 (C-1), 38.2 (C-3′), 34.2 (C-3), 29.8−27.0 (C-‘4, C-5), 25.1 (C- 4) ppm. Elemental analysis (%) calcd: 73.49 (C), 9.47 (H), 3.06 (N). Found: 73.81 (C), 9.66 (H), 3.38 (N). APCI-MS (m/z): 458.1 $[M + H]^+$.

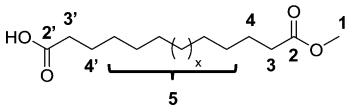
From the crude product, the desired linear nitrile ester **13** was isolated by repetitive recrystallization from methanol to yield the pure 1,19-difunctional compound in a purity >99% in 58% yield (as determined by GC analysis).



13: ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 3.64 (s, 3H, H-1), 2.31 (t, $^3J_{HH}$ = 7.2 Hz, 2H, H-8), 2.28 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3), 1.67−1.57 (m, 4H, H-4, H-7), 1.45−1.39 (m, 2H, H-6), 1.33−1.18 (m, 24H, H-5) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C) δ 174.4 (C-2), 119.9 (C-9), 51.5 (C-1), 34.2 (C-3), 29.7−28.8 (C-5, C-6), 25.5 (C-7), 25.1 (C-4), 17.2 (C-8), ppm. Elemental analysis (%) calcd: 74.25 (C), 11.53 (H), 4.33 (N). Found: 74.46 (C), 11.53 (H), 4.44 (N). APCI-MS (m/z): 324.1 $[M + H]^+$.

General Procedure for Isomerizing Alkoxycarbonylation with Monitoring over Time. In the case of solid fatty acid substrates, the starting material (150.00 mmol)[29] was weighed in, and the assembled reactor was evacuated and purged with argon several times. In a glovebox in a Schlenk tube equipped with a magnetic stir bar, the catalyst precursor **1** (958.9 mg, 1.20 mmol) was weighed in. Another Schlenk tube was charged with 120 mL of alcohol and 96.9 μL of pyridine (94.9 mg, 1.20 mmol). In the case of utilization of liquid fatty acid derivative starting materials, 150.00 mmol of substrate was also added at this point. The mixture was cannula-transferred into the preheated reactor in an argon counter stream. Successively, the catalyst precursor was dissolved in 20 mL of the alcohol and cannula-transferred into the reactor. The reactor was pressurized with carbon monoxide and stirred at the desired temperature. For the alkoxycarbonylation of ethylene, the reactor was pressurized with 5 bar of ethylene prior to CO addition. Samples of ∼4 mL were retrieved via a sampling valve at the bottom of the reactor at certain points in time, diluted with dichloromethane, and filtered over a silica plug. The solvent was removed in vacuo, and the residue was analyzed by GC or ^1H NMR spectroscopy.

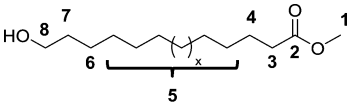
General Procedure for the Cleavage of Benzyl Esters. The hydrogenolysis of benzyl methyl esters was typically performed according to a standard procedure for hydrogenolysis of benzyl esters.[15] In a round-bottom flask with an argon inlet, benzyl methyl ester and 0.1 wt % Pd/C (10 wt %) were suspended in 50 mL of dry THF. The flask was purged with hydrogen and closed with a septum stopper. A balloon with hydrogen was attached to the flask, and the slurry was stirred at room temperature overnight. The mixture was filtered over a silica plug with CH_2Cl_2/THF, 7/3. After the solvent was removed by rotary evaporation, the crude product was used without further purification.



5a (x = 8): ^1H NMR ($CDCl_3$, 400 MHz, 25 °C) δ = 11.08 (s, br. 1H, COOH), 3.66 (s, 3H, H-1), 2.34 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3′), 2.30 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3), 1.67−1.57 (m, 4H, H-4, H-4′), 1.38−1.22 (m, 26H, H-5) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C) δ = 179.4 (C-2′), 174.6 (C-2), 51.6 (C-1), 34.3 (C-3), 34.1 (C-3′), 29.8−29.2 (C-5), 25.1 (C-4), 24.8 (C-4′) ppm. Elemental analysis (%) calcd: 70.13 (C), 11.18 (H). Found: 70.18 (C), 11.20 (H). APCI-MS (m/z): 343.1 $[M + H]^+$.

5b (x = 1): ^1H NMR ($CDCl_3$, 400 MHz, 25 °C) δ = 11.52 (s, br. 1H, COOH), 3.65 (s, 3H, H-1), 2.33 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3′), 2.28 (t, $^3J_{HH}$ = 7.6 Hz, 2H, H-3), 1.66−1.56 (m, 4H, H-4, H-4′), 1.36−1.22 (m, 26H, H-5) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C) δ = 180.2 (C-2′), 174.5 (C-2), 51.6 (C-1), 34.2 (C-3), 34.2 (C-3′), 29.5−29.1 (C-5), 25.1 (C-4), 24.8 (C-4′) ppm. Elemental analysis (%) calcd: 63.91 (C); 9.90 (H). Found: 63.68 (C), 10.13 (H). APCI-MS (m/z): 245.0 $[M + H]^+$.

General Procedure for the Synthesis of ω-Hydroxy Esters. According to a procedure by Gorczynski et al.,[19] the monoester was dissolved in dry THF in a flame-dried round-bottom flask with argon inlet and cooled to 0 °C. Over a period of 45 min, 1.1 equiv of BH_3·THF complex (1.0 M in THF) was added dropwise to the cooled solution. The reaction mixture was stirred at 0 °C for 30 min and then was stirred for 14 h at room temperature. The resulting slurry was quenched with 100 mL of water, the water phase was saturated with K_2CO_3, and the phases were separated. The water phase was washed with Et_2O, and the combined organic layer was washed with brine and dried over $MgSO_4$. The crude product obtained after removal of the solvent by rotary evaporation was purified by column chromatography using CH_2Cl_2/EtOAc, 8/2, to yield the desired compounds as a white solid in 84% (**6a**) and 51% (**6b**), respectively.



6a (x = 8): ^1H NMR ($CDCl_3$, 400 MHz, 25 °C) δ = 3.66 (s, 3H, H-1), 3.64 (t, $^3J_{HH}$ = 6.6 Hz, 2H, H-8), 2.28 (t, $^3J_{HH}$ = 7.6 Hz, 2H, H-3), 1.66−1.52 (m, 4H, H-4, H-7), 1.39−1.20 (m, 28H, H-5, H-6) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 100 MHz, 25 °C) δ = 174.5 (C-2), 63.2 (C-8), 51.6 (C-1), 34.3 (C-3), 33.0 (C-7), 29.8−29.3 (C-5), 25.9 (C-6), 25.1 (C-4) ppm. Elemental analysis (%) calcd: 73.12 (C), 12.27 (H). Found: 73.10 (C), 12.25 (H). APCI-MS (m/z): 329.1 $[M + H]^+$.

6b (x = 1): ^1H NMR ($CDCl_3$, 400 MHz, 25 °C) δ = 3.65 (s, 3H, H-1), 3.62 (t, $^3J_{HH}$ = 6.6 Hz, 2H, H-8), 2.30 (t, $^3J_{HH}$ = 7.6 Hz, 2H, H-3), 1.65−1.50 (m, 4H, H-4, H-7), 1.46 (s, br, 1H, OH), 1.37−1.23 (m, 14H, H-5, H-6) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 100 MHz, 25 °C) δ = 174.5 (C-2), 63.1 (C-8), 51.5 (C-1), 34.2 (C-3), 32.9 (C-7), 29.7−29.2 (C-5), 25.9 (C-6), 25.1 (C-4) ppm. Elemental analysis (%) calcd: 67.79 (C), 13.38 (H). Found: 67.97 (C), 11.22 (H). APCI-MS (m/z): 230.9 $[M + H]^+$.

General Procedure for the Preparation of Polyamides. In a 20 mL stainless steel pressure reactor, a glass inlay was charged with 1.00 g of ω-amino ester and 4.00 mL of distilled water. The reactor was closed and degassed prior to pressurizing with 10 bar of nitrogen. After heating to 190 °C for 3.5 h, the pressure was slowly released, and vacuum was applied for 4 h.

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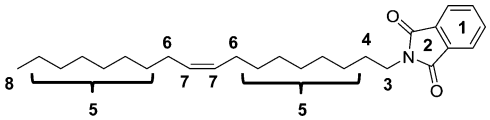
The cooled reactor was vented and opened, to yield a light yellow material that was further analyzed.

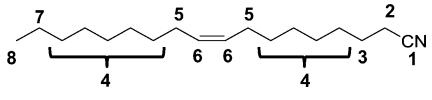
General Procedure for the Preparation of Polyesters. Polycondensations of ω-hydroxy esters were performed in a 100 mL, two-necked Schlenk tube equipped with a mechanical stirrer. The monomer was degassed at 110 °C, and a solution of $Ti(O^nBu)_4$ (5 mol %) in dry toluene was added. The temperature was increased stepwise to 200 °C and vacuum was applied. After 22 h, the resulting highly viscous polymer melt was cooled to 100 °C, dissolved in toluene, and precipitated from methanol.

Synthesis of *N*-Oleylphthalimide (3-CH_2NPhth). In a 500 mL, round-bottom flask, 50.0 g (0.187 mol) of oleylamine and 27.7 g (0.187 mol) of phthalic anhydride were heated to 150 °C and stirred for 18 h under vacuum. The brown mixture was cooled to room temperature and dissolved in dichloromethane. After the organic phase was washed with saturated aqueous Na_2CO_3 solution, water, and brine, the solution was dried over $MgSO_4$ and filtered over a short silica plug. The solvent was removed by rotary evaporation, and the crude product was recrystallized from ethanol at 4 °C in 63% yield (74.5 g) as a mixture of E/Z isomers and the corresponding saturated compound (ratio unsaturated vs saturated: ~3:1).



^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 7.85−7.66 (m, 4H, H-1), 5.40−5.27 (m, 2H, H-7), 3.66 (t, $^3J_{HH}$ = 7.4 Hz, 2H, H-3), 2.03−1.90 (m, 4H, H-6), 1.70−1.61 (m, 2H, H-4), 1.36−1.21 (m, 22H, H-5), 0.86 (t, $^3J_{HH}$ = 6.9 Hz, 3H, H-8) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C) δ 168.5 (C-2), 133.9 (C-1), 132.2 (C-1), 130.7−129.9 (C-7), 123.2 (C-1), 38.2 (C-3), 32.7−22.8 (C-4, C-5, C-6), 14.2 (C-8) ppm.

Synthesis of Oleonitrile (3-CN). In a 1 L, round-bottom flask, 260.0 g (0.924 mol) of oleamide and 335 mL (550.0 g, 4.62 mol) of thionyl chloride were stirred at 80 °C for 4 h. Excessive thionyl chloride was removed under reduced pressure, and the brown mixture was dissolved in petrol ether and washed with 0.5 N aqueous NaOH, water, and brine. After the organic phase was dried over $MgSO_4$ and filtered over a short silica plug, the solvent was removed by rotary evaporation, and the crude product was distilled in vacuo, affording a slightly yellow oil in 60% (145.5 g) yield.



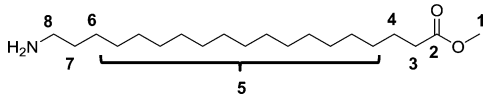
^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 5.40−5.28 (m, 2H, H-6), 2.31 (t, $^3J_{HH}$ = 7.2 Hz, 2H, H-2), 2.04−1.92 (m, 4H, H-5), 1.69−1.59 (m, 2H, H-3), 1.48−1.22 (m, 20H, H-4. H-7), 0.86 (t, $^3J_{HH}$ = 6.9 Hz, 3H, H-8) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C) δ 130.2, 129.6 (C-6), 119.9 (C-1), 32.0−28.8 (C-4), 27.3, 27.2 (C-5), 25.5 (C-3), 22.7 (C-7), 17.2 (C-2), 14.2 (C-8) ppm.

Synthesis of Methyl 18-Amino Octadecanoate (10). In a 1 L, round-bottom flask, 3.00 g (8.78 mmol) of amide ester **9** was dissolved in 600 mL of THF and cooled in an ice/water bath, then 60 mL of a water/trifluoroacetic acid mixture (1:1 v/v) and 3.63 g (11.41 mmol) of diacetoxyiodobenzene were added, and the flask was closed with a bubble counter. The mixture was allowed to warm to room temperature slowly, while stirring in the dark. After 23 h, the solvent was removed in vacuo, and the brown residue was dissolved in ethyl acetate. A 20 mL portion of a 2 N etherous HCl solution was added, and a white precipitate was formed that was filtered off. The precipitate was washed with ethyl acetate, acetone, and water subsequently and dissolved in chloroform. After washing thoroughly with 0.1 N NaOH solution, the solution was washed with brine and dried over magnesium sulfate, and the solvent was removed. ω-Amino ester **9** was obtained as a pale yellow powder in 71% (1.96 g) and was used without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ = 3.66 (s, 3H, H-1), 2.66 (t, $^3J_{HH}$ = 7.0 Hz, 2H, H-8), 2.30 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3), 1.66−1.55 (m, 2H, H-4), 1.47−1.38 (m, 2H, H-7), 1.35−1.21 (m, 26H, H-5, H-6, H-5) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 100 MHz, 25 °C) δ = 174.4 (C-2), 51.5 (C-1), 42.4 (C-8), 34.2 (C-3), 34.0 (C-7), 29.8−29.4 (C-5), 27.0 (C-6), 25.1 (C-4) ppm. Elemental analysis (%) calcd: 72.79 (C), 12.54 (H), 4.47 (N). Found: 72.77 (C), 12.15 (H), 4.56 (N). APCI-MS (m/z): 314.0 $[M + H]^+$.

Synthesis of Methyl 19-Amino Nonadecanoate (12). *Hydrazinolysis of **11**.* In a 500 mL, round-bottom flask, 5.00 g (10.93 mmol) of phthalimide **11** and 2.73 g (54.63 mmol) hydrazine hydrate were stirred in 400 mL of MeOH at 80 °C for 5 h. After the solvent was removed in vacuo, the residue was dissolved in chloroform, washed with aqueous NaOH, brine, and dried over magnesium sulfate. A white solid was obtained in 91% (1.96 g) that was used without further purification.

*Hydrogenation of **13**.* A 0.10 g (1.80 mmol) portion of KOH was degassed in a 20 mL stainless steel pressure reactor at 80 °C, and 1.94 g (6.00 mmol) of nitrile ester **13** and 50.9 mg (0.06 mmol) of Grubbs second generation catalyst were degassed in a Schlenk tube and dissolved in 8 mL of dry toluene. The solution was cannula-transferred into the reactor under inert gas atmosphere, and the reactor was closed and pressurized with 20 bar of hydrogen. After 40 h of stirring at 80 °C, the reaction was stopped, and the reactor was opened. The yellow suspension was dissolved in methanol, and an excess of trifluoroacetic acid was added. After stirring the mixture for 3 h at 80 °C to esterify saponified ester groups, the solvent was removed. The residue was dissolved in hot ethyl acetate, and an excess of 2 N etherous HCl was added. The white precipitate was filtered off; washed with EtOAc, acetone, and water; dissolved in chloroform; washed thoroughly with aqueous NaOH and brine; and dried over $MgSO_4$. A white solid was obtained in 74% (1.45 g) and used without further purification.



^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ =3.64 (s, 3H, H-1), 2.66 (t, $^3J_{HH}$ =7.0 Hz, 2H, H-8), 2.28 (t, $^3J_{HH}$ = 7.5 Hz, 2H, H-3), 1.65−1.54 (m, 2H, H-4), 1.50−1.38 (m, 2H, H-7), 1.35−1.19 (m, 28H, H-5, H-6) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 174.4 (C-2), 51.5 (C-1), 42.3 (C-8), 34.3 (C-3), 33.8 (C-7), 29.8−29.3 (C-5), 27.0 (C-6), 25.1 (C-4) ppm. Elemental analysis (%) calcd: 73.34 (C), 12.62 (H), 4.28 (N). Found: 73.02 (C), 11.93 (H), 4.35 (N). APCI-MS (m/z): 328.1 $[M + H]^+$.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b00825.

Characterization of products and experimental details of (isomerizing) alkoxycarbonylation experiments (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: stefan.mecking@uni-konstanz.de.

Notes

The authors declare no competing financial interest.

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(17) GC analysis of oleamide methoxycarbonylations could not be performed because of irreproducible results, probably due to degradation of the compounds at elevated temperatures on the GC column. Note that for NMR spectroscopy, no estimation of selectivity is possible. For a detailed description for the estimation of the conversion by ^{1}H NMR spectroscopy, compare with Supporting Information.

(18) Note that the **3**-CH_2NPhth prepared revealed a double bond content of 75%, as determined by ^{1}H NMR spectroscopy. The remaining saturated analog was not removed, and the mixture was used as obtained after recrystallization.

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(28) On a larger scale, direct hydrogenolysis of the crude **4b** was found to be a more convenient approach. Subsequent recrystallization of the higher melting acid ester compound **5b** allows for a better isolation and, hence, is more feasible.

(29) In case of **3**-NPhth, only 100 mmol was used because of the high molecular weight and the resulting higher volume of the substrate. Amounts of catalyst and pyridine were adjusted to the quantity of material used.

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