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Selective formation of α,ω–ester amides from the aminocarbonylation of castor oil derived methy 10-undecenoate and other unsaturated substrates†

Cristina Jiménez-Rodriguez,[a] Angel A. Núñez-Magro,[a] Thomas Seidensticker,[a] Graham R. Eastham,[b] Marc R. L. Furst[a] and David J. Cole-Hamilton*[a]

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Reaction of long chain alkenes with CO and aniline in the presence of palladium complexes of 1,2-*bis*–(di*tert*butylphosphinomethyl)benzene produces amides with high linear selectivity, with much higher rates and catalyst stability if 2–naphthol and sodium or potassium iodide are added; unsaturated esters including methyl 10-undecenoate from castor oil give α,ω–ester amides, whilst reactions in THF give *N*–phenylpyrrolidine.

Introduction

As part of a programme aimed at producing monomers for polyesters[1-3] and polyamides, we report the selective synthesis of terminal amides by aminocarbonylation reactions of alkenes, including methyl 10-undecenoate, which is available from castor oil.[4]

Amides are important industrial chemicals finding uses in detergents[5] and as thickeners.[6, 7] Diamides and ester amides have the potential for reduction, prefereably by hydrogenation,[8-11] to give useful monomer feedstocks for polyamides and polyester amides. Amides are usually prepared in the laboratory by the Schotten-Baumann reaction[12, 13] involving the condensation reaction of an amine with an acyl chloride, which is highly wasteful as chloride has to be introduced and then removed for disposal. It is also hazardous, because acyl chlorides are unstable on exposure to atmospheric or other moisture and produce fumes of HCl. Several amide syntheses have been developed over the past century, among them the Schmidt reaction[14] involving a ketone and an azide, the Ugi reaction[15] producing bis-amides by using a ketone (or an aldehyde), an isocyanide, a carboxylic acid and an amine, and the Chapman thermal rearrangement[16] of aryl imino ethers. More recently, Milstein and co-workers[17] developed a ruthenium-based catalyst for producing an amide directly from an alcohol and an amine. An interesting synthesis of amides involving the aminocarbonylation of alkenes has been developed, but has found use mainly in cyclisation reactions.[18-20]

We now report that the system involving palladium complexes of 1,2-*bis*(di*tert*butylphosphinomethyl)benzene (DTBPMB), which has been developed for the methoxycarbonylation of aromatic halides[21] unsaturated compounds,[3, 22-25] and fatty acids[1-3, 26-29] usually with very high selectivity towards the linear products, is also highly active for aminocarbonylation using aniline and other amines. The Pd/DTBPMB system has been shown to give very high terminal selectivity for the isomerising methoxycarbonylation of alkenes, wherever the double bond is in the chain.[1-3, 22, 26-29] Exceptionally, the same catalytic system also gives high branched selectivity to lactic acid precursors when used for the methoxycarbonylation of vinyl acetate.[23-25] In this paper we start by examining the selectivity of aminocarbonylation of simple alkenes, then move on to unsaturated esters before demonstrating the reaction on the naturally sourced methyl 10-undecenoate.

Results and discussion

Aminocarbonylation of alkenes

Table 1 Products from the aminocarbonylation of simple alkenes[a]

Entry	Substrate	T / °C	p_{CO} / bar	time / h	Conversion of **1** / %	isomers[b] / %	**3** / %	branched / %
1[c]	1–octene (**1**)	100	30	3	85	45	40	0
2	**1**	100	30	3	89	51	38	0
3	**1**	100	30	6	100	0	98	2
4	**1**	20	30	3	0	0	0	0
5	**1**	100	10	3	100	32	65	3
6	**1**	100	2	22	0	0	0	0
7	2–octene (**7**)	100	30	6	100	0	97	3
8	4–octene (**8**)	100	30	6	100	0	97	3
9	1–hexene (**4**)	100	30	3	100	0	99.9	0.1
10	2-M-1-P (**9**)	100	30	6	100	0	59[d]	41[e]
11	2-M-2-P (**10**)	100	30	6	100	0	85[d]	15[e]
12	3-M-1-P (**13**)	100	30	6	100	0	98	2

[a] Conditions: alkene (6 mmol), aniline (1 mL, 11 mmol), $PdCl_2$ (32 mg, 0.2 mmol), DTBPMB (98 mg, 0.25 mmol), diethyl ether (10 mL), 3–6 h. Conversions and selectivitiess are from GC-FID integrations using measured response factors; [b] double bond isomers of starting alkene; [c] aniline (2 mL, 22 mmol); [d] *N*–phenyl 5–methylhexanamide (**11**); [e] *N*–phenyl 3–methylhexanamide (**12**); [f] *N*-phenyl 4-methylhexanamide (**14**).

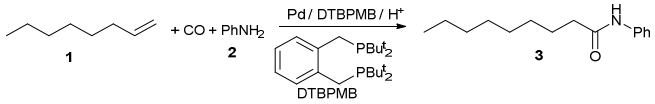

Fig. 1 Catalytic aminocarbonylation of 1–octene to linear amide

Aniline was used as the nucleophile since it is a liquid and is moderately nucleophilic. Carbonylation of 1–octene (**1**) in the presence of aniline (**2**) and a catalyst, prepared *in situ* from $PdCl_2$ and DTBPMB, at 100 °C under CO (30 bar) for 3 h produces the linear amide, *N*–phenyl nonanamide (**3**, Figure 1) as the only amide product in ~40 % yield regardless of the excess of aniline used (Table 1, entries **1** and **2**). There is also extensive isomerisation of the alkene and the catalyst solution is black at the end suggesting substantial catalyst decomposition. Extending the reaction time to 6 h allows quantitative conversion to amides (98 % linear, Table 1, entry **3**) perhaps suggesting that the catalyst decomposition occurs on cooling and/or decompression. Aminocarbonylation of 1–hexene (**4**) proceeded smoothly to yield the desired linear amide (**5**, > 99.9 %, Table 1, entry **9**). Lowering the temperature to ambient inhibited the reaction (and isomerisation) with 1–octene as the substrate (Table 1,entry **4**). Lowering the pressure to 10 bar increased the conversion in 3 h to 100 %, with rather poorer linearity (65 %, Table 1, entry **5**). Lowering the pressure (2 bar) still further inhibited the reaction despite an extended reaction time (Table 1, entry **6**). The fact that the linearity of the product is so high, despite extensive alkene isomerisation being observed when the reaction is incomplete, suggests that, as with methoxycarbonylation,[1-3, 22, 26-29] internal alkenes isomerise to terminal alkenes which are trapped by carbonylation. We have therefore investigated 2– (**7**) and 4–octene (**8**) as substrates. In both cases (Table 1, entries **7** and **8**), 100 % conversion to amides is observed with 97 % linearity.

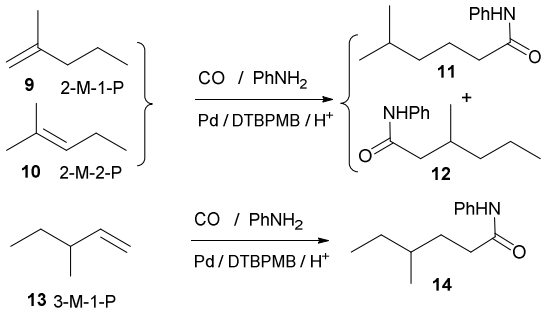

Fig. 2 Products from aminocarbonylation of methylpentenes

The effect of the position of the double bond in the chain was further investigated using methylpentenes. 2–Methyl–1–pentene (2-M-1-P, (**9**) Table 1, entry **10**) and 2–methyl–2–pentene (2-M-2-P, (**10**) Table 1,entry **11**) both gave predominantly *N*–phenyl 5–methylhexanamide (**11**), although the alternative product, *N*–phenyl 3–methylhexanamide (**12**) was also formed, especially from **9**. **11** is formed by carbonylation at the less sterically crowded end of the molecule, but **12** can be formed from **9** without the unfavoured double bond isomerisation past the quaternary centre occurring. 3–Methyl–1–pentene (3-M-1-P, **13**, Table 1, entry **12**) produced *N*–phenyl 4–methylhexanamide (**14**, 97.9 % linearity). These reactions are outlined in Figure 2 and Table 1.

2-Naphthol and NaI as promoters

Although the reactions described above produce amides with good conversion and good linear selectivity, the catalyst loadings are high (2-mol %), the reaction times long (3–6 h) and the catalyst is found to have decomposed when the autoclave is opened. Drent and coworkers have reported that the addition of phenol or naphthols and NaI allows the successful aminocarbonylation of **1** with 3-dimethylamino-1-propylamine (**15**), when using $Pd(OAc)_2$ in the presence of 1,2–P,P–*bis*(9–phosphabicyclo[3,3,1 or 4,2,1]nonyl)ethane as the catalyst precursor. Turnovers in 1 h can be as high as 1500 with linearities up to 98.5 %.[30] Using our catalytic system under similar conditions to those employed by Drent and toluene, one of Drent's favoured solvents, no conversion was obtained when using a catalyst loading of 0.2 mol % either with aniline or the more nucleophilic **15** in the absence of 2-naphthol (Table 2, entries **1** and **2**), but significant activities (31 % conversion for aniline (Table 2, entry **3**), 61 % for **15** (Table 2, entry **4**) with excellent linear selectivities (> 99 % for both amine substrates) were obtained for both substrates when both NaI and 2-naphthol were present. Omission of either 2–naphthol (Table 2, entries **1** and **2**) or NaI (Table 2, entry **6**) gave no conversion.Interestingly, the less acidic phenol was not effective in this type of reaction (Table 2, entry **11**), despite the fact that sodium phenoxide has been shown to be effective in exactly the way proposed in Figure 3 during the aminocarbonylation of aryl chlorides.[31] 1–naphthol was less effective than 2–naphthol (Table 2, entries **9** and **10**). These reactions were carried out in the presence of methanesulphonic acid, but the relatively acidic character of anilinium salts apparently allows generation of some hydridopalladium complex and hence some conversion in the absence of added MSA (Table 2, entry **7**). For the more basic 3–(dimethylamino)–1–propylamine (**15**), no conversion was obtained (Table 2, entry **8**) when MSA was omitted. The best results obtained with aniline, TON > 400 in 1 h, employed 0.75 equivalents of 2–naphthol (relative to 1–octene), a temperature of 140 °C and moderate pressure (10-20 bar, Table 2, entries **12** and **13**). Higher pressures inhibited the reaction (Table 2, entries **14** and **15**).

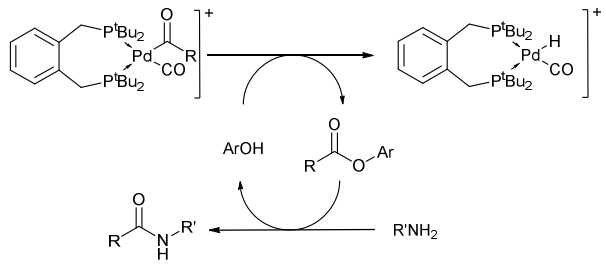

Fig. 3 Possible role of 2–naphthol in the aminocarbonylation of 1–octene. (R = 1-octyl; R' = Ph (**2**) or $Me_2N(CH_2)_3$- (**15**), Ar = 2-naphthyl)

It has been shown that, at least for methoxycarbonylation, the rate determining step of this kind of reaction is the attack of the nucleophile onto the acylpalladium species.[22, 32-34] Using imidazole as a nucleophilic promoter in the aminocarbonylation of halo aromatic compounds, Hallberg has proposed an initial attack of the promoter onto the acylpalladium species generating the corresponding amide, which undergoes transamidation to give the final product.[35] Thus, a plausible explanation for

Table 2 Aminocarbonylation reactions of 1-octene (**1**) in the presence of phenolic additives and NaI[a]

Entry	Amine	Additive	[Additive][b]	p_{CO} / bar	TON	Conversion / %	Selevtivity to **3** / %
1	$PhNH_2$ (**2**)	–	0.5	20	–	–	–
2	$Me_2N(CH_2)_3NH_2$ (**15**)	–	0.5	20	–	–	–
3	**2**	2–naphthol	0.5	20	158	31	> 99
4	**15**	2–naphthol	0.5	20	310	61	> 99
5	**–**	2–naphthol	0.5	20	5[c]	1[c]	> 99
6	**2**	2–naphthol[d]	0.5	20	–	–	–
7	**2**	2–naphthol[e]	0.5	20	40	8	> 99
8	**15**	2–naphthol[e]	0.5	20	–	–	–
9	**15**	1–naphthol	0.5	20	–	–	–
10	**2**	1–naphthol	0.5	20	95	19	> 99
11	**2**	PhOH	0.5	20	–	–	–
12	**2**	2–naphthol	0.75	10	433	85	> 99
13	**2**	2–naphthol	0.75	20	402	82	> 99
14	**2**	2–naphthol	0.75	40	350	67	> 99
15	**2**	2–naphthol	0.75	50	236	46	> 99

[a] Conditions: 1–octene (2 ml, 12.7 mmol), amine (12.74 mmol), [$Pd(OAc)_2$] (0.025 mmol), DTBPMB (25.1 mg, 0.064 mmol), MSA (10 μl, 0.15 mmol), additive (6.37 or 9.6 mmol), NaI (9.5 mg, 0.06 mmol), toluene (10 ml), 140 °C. Conversions and selectivities were determined by GC FID using measured response factors, 1 h; [b] Equivalents relative to 1–octene; [c] Naphthyl nonanoate; [d] No NaI was added; [e] No MSA was added.

the role of 2–naphthol in our system (Figure 3) involves the attack of the aryl alcohol onto the acylpalladium species to generate the aryl ester and the hydridopalladium complex which restarts the catalytic reaction. In order to prove this hypothesis we tried to run the reaction in the absence of amine; only a very low conversion to naphthyl nonanoate was obtained (Table 2, entry **5**). We note that iodide$^-$ is the best σ–donor of the halides,[35, 36] but its exact role in these reactions is unclear.

Aminocarbonylation of unsaturated esters

The goal is to achieve the aminocarbonylation of natural fatty acid esters for preparing a range of esteramides that could be reduced to esteramines or amino alcohols, precursors to bio-derived polyamides and polyesteramides. We therefore, studied shorter chain unsaturated esters to optimise the yields and the conversions to the desired linear products.

Initial reactions using methyl acrylate as the substrate, for which we changed the solvent to dioxane and the iodide source to KI so as to maximise its solubility, are reported in the ESI. These reactions were generally unsuccessful, with Michael addition of aniline being favoured over aminocarbonylation under all conditions studied. This may be due to the conjugation of the C=C bond with the C=O bond of the ester function preventing the reaction from occurring, although better results were obtained when using butyl acrylate or methyl methacrylate as substrates (See ESI Table S1 and Scheme S1).

Ethyl 3–hexenoate (**16**) does not have a conjugated double bond so aminocarbonylation reactions using it as substrate were attempted next (Figure 4). The reaction conditions previously used with methyl acrylate failed to produce the desired amidoester. Only low conversion, mainly to *N*-phenylhexenamide (**17**) by transamidation of the ester group was observed (Table 3, entry **1**). It seemed the conjugation of the double bond was not the source of the inefficiency of the reaction when using acrylate esters as substrates. Changing the solvent back from dioxane to toluene led to a marginally improved selectivity for some amidoester isomers (Table 3, entry **2**).

Table 3 Products from the aminocarbonylation of ethyl 3–hexenoate (**16**) with aniline (**2**)

Entry[a]	T / °C	t / h	Conversion of **16** / %	**18** / %	**19** / %	**17** / %	**20** / %	Others / %
1[b]	85	16	46	0	0	28	1	17
2	85	16	52	2	1	20	1	28
3	115	16	68	1	0	38	1	28
4	115	64	90	27	1	29	6	27
5	140	16	89	21	18	22	6	22
6[c]	140	16	87	5	0	46	6	30
7	140	64	94	15	14	40	5	20

[a] Conditions: ethyl 3–hexenoate (2.02 mL, 12.7 mmol), aniline (1.16 mL, 12.7 mmol), [$Pd_2(dba)_3$] (114 mg, 0.0125 mmol), DTBPMB (251 mg, 0.0637 mmol), toluene (10 mL), MSA (10 µL), 2–naphthol (1.4 g, 9.5 mmol), KI (10 mg, 0.064mmol), p_{CO} = 50 bar. Conversions and selectivities were determined by GC FID using response factors calculated using a literature method[36] and an internal standard. "Others" are double bond isomers of the starting material and Michael addition product of **17**; [b] Dioxane was used instead of toluene; [c]Without 2-naphthol.

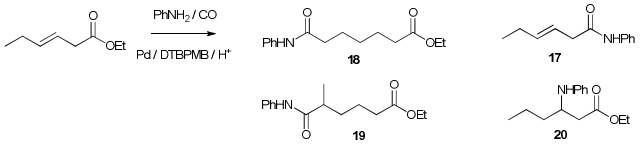

Fig. 4 Products from the aminocarbonylation of ethyl 3-hexenoate

Unfortunately, warming to 115 °C did not increase the conversion to the esteramides, **18** and **19**, but led to a higher conversion to the undesired **17** (Table 3, entry **3**). However, leaving the reaction running for 64 h increased the conversion to the esteramide, with increased selectivity to the desired linear product, **18** (27:1) (Table 3, entry **4**), although still producing a high yield of **17**. On raising the temperature to 140 °C, the conversion stayed the same, but the selectivity to **18** dropped dramatically (Table 3, entry **5**). A test reaction using no 2-naphthol promoter under the same conditions, dramatically decreased the conversion to **18** and **19**. (Table 3, entry **6**). Finally, a reaction with the promoter at high temperature gave a lower selectivity to **18** than at lower temperature (Table 3, entry **7**). Some Michael addition to the conjugated unsaturated ester formed by double bond isomerisation was observed in all of these reactions as product **20**.

Aminocarbonylation of methyl 10-undecenoate from castor oil

One possible problem with these reactions of ethyl 3-hexenoate (**16**) is that double bond isomerisation must precede aminocarbonylation if the terminal amide is to be formed. It has been shown for 1-octene that isomerisation is slow compared with methoxycarbonylation,[22] so direct amidation of the ester function will compete effectively with the desired isomerising aminocarbonylation. It has also been shown that methoxycarbonylation of terminal double bonds competes with isomerisation. We therefore investigated methyl 10–undecenoate (**21**), an unsaturated ester with a terminal double bond obtained from the thermal cracking of castor oil.[4] The potential products of aminocarbonylation are shown in Figure 5.

Following the conclusions obtained when using **16** as substrate (the higher the temperature the lower the conversion to the desired product, Table 3) we screened a range of temperatures between 60 and 140 °C (Table 5), finding that high temperatures promoted the amidation of the ester to **24** but some aminocarbonylation also occurred (Table 4, entry **1**). Although the conversion of the substrate decreased at 100 °C and 120 °C, the selectivity towards aminocarbonylation was significantly increased, becoming comparable to amidation. (Table 4, entries **2** and **3**). Increasing the amount of MSA from 10 to 100 µL, (Tables 5, entries **4-7**) did not significantly affect the conversion, but the selectivity towards esteramides, **22** and **23** was greatly increased especially at lower temperatures (Table 4, entries **6** and **7)** where amide formation became almost insignificant and the selectivity towards the desired linear amide, **22**, was 92 % at 80 °C (Table 4, entry **6**). Extending this reaction at 80 °C over a longer time (64 h instead of 16 h, Table 4, entry **10**) a significant increase in the conversion to the esteramide with good selectivity towards **22** was observed although **24** was again a product.

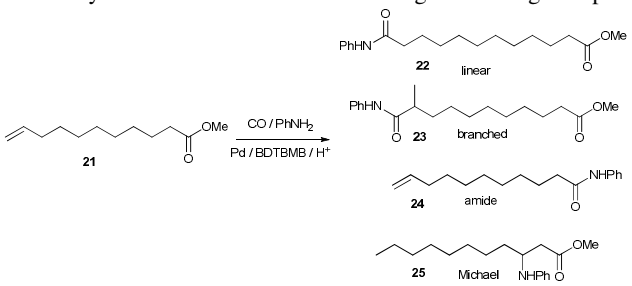

Fig. 5 Products from the aminocarbonylation of methyl 10-undeconate

The most dramatic improvement came when the reaction was carried out in diethyl ether rather than toluene over 64 h. The conversion to the esteramides was more than 99 %, with 96 % selectivity to **22**. (Table 4, entry **11**).

It seemed that diethyl ether was the key solvent for the reaction, but the reaction time was very long (64 h). The temperature and the amount of potassium iodide (KI) were varied in order to try to speed up the reaction (Table 5). Screening a range of temperatures between 90 and 110 °C while increasing the amount of KI from 0.06 (Table 4) to 0.2 equivalents was carried out. Using 0.1 equivalent, the optimal temperature (95 °C) gave a 70 % selectivity to **22** (Table 5, entry **2**).

Table 4 Aminocarbonylation of methyl 10–undecenoate (**20**) with aniline (**2**)

Entry[a]	T / °C	t / h	MSA / µL	Conversion of **20** / %	**21** / %	**22** / %	**23** / %	**24** / %
1	140	16	10	51	7	1	41	2
2	120	16	10	32	12	1	17	2
3	100	16	10	34	15	2	18	0
4	120	16	100	38	10	1	26	1
5	100	16	400	48	20	1	26	1
6	80	16	100	38	35	1	2	0
7	60	16	100	29	26	1	2	0
8	100	16	100	38	7	3	26	2
9[b]	100	16	100	15	9	0	6	0
10	80	64	100	74	62	2	10	1
11[c]	80	64	100	>99	96	3	0	0

[a] Conditions: methyl 10–undecenoate (1.42 mL, 6.35 mmol), aniline (1.16 mL, 12.7 mmol), [Pd(dba)$_2$] (115 mg, 0.2 mmol), DTBPMB (99 mg, 0.25 mmol), toluene (10 mL), 2–naphthol (1368 mg, 9.5 mmol), KI (10 mg, 0.06 mmol), p_{CO} = 50 bar. Conversions and selectivities were determined by GC FID using response factors calculated using a literature method[36] and an internal standard; [b] Solvent: dimethyl sulfoxide; [c] Solvent: diethyl ether

Table 5 Aminocarbonylation of methyl 10–undecenoate (**21**) with aniline in Et_2O

Entry[a]	T / °C	KI / equiv	**22** / %
1	90	0.1	10
2	95	0.1	70
3	110	0.1	21
4	95	0.2	91
5	110	0.2	99[b]

[a] Conditions: methyl 10–undecenoate (1.42 mL, 6.35 mmol), aniline (1.16 mL, 12.7 mmol), DTBPMB (395 mg, 1 mmol), Et_2O (10 mL), MSA (100 μL), $[Pd_2(dba)_3]$ (92 mg, 0.1 mmol), 2–naphthol (1368 mg, 9.5 mmol), KI (17 mg, 0.1mmol or 33mg, 0.2 mmol), p_{CO} = 30 bar, 16 h. Conversions and selectivities were determined by GC FID using response factors calculated using a literature method[36] and an internal standard;; [b]isolated yield: 60 %

However, at the higher KI loading (0.2 equiv), 99 % selectivity to **22** at full conversion could be obtained in 16 h at 110 °C (Table 5, entry **5**) with little drop off in performance at 95 °C (Table 5, entry **4**). These excellent results allow for an efficient route to esteramides from the naturally derived methyl 10-undecenoate. Nevertheless, the isolation of the product was difficult. Indeed, two chromatography columns followed by a recristallysation were necessary to obtain a product with sufficient purity. Therefore, a GC yield of 99% led to a 60% isolated yield only (Table 5, entry 5).

Synthesis of *N*–heterocyles

During the course of solvent screening when investigating the aminocarbonylation of 1-octene, we noticed that reactions in tetrahydrofuran ,THF, produced 1–phenylpyrrolidine (Figure 6, **26**). 1-octene was not required for these reactions so further studies were carried out in its absence. A low yield of **26** was obtained after 6 h but higher conversion (53 %, albeit with lower selectivity, See ESI Figure S6) was achieved after 22 h (Table 6, entries **1** and **2**). Small amounts of *N*-phenylformamide(3 % after 6 h) and an unknown of higher retention time (7 % after 6 h) were also produced, but *N*-phenylformamide was also obtained in small quantities as the only product when carrying out similar reactions in toluene. No reaction occurred in the absence of either DTBPMB (Table 6, entry **3**) or CO (Table 6, entry **4**), suggesting that the active species in the catalytic cycle contains both of them. The conversion of THF to pyrrolidines requires the breaking of 2 C–O bonds and the forming of 2 C–N bonds.

Walkup and Searles reported the synthesis of such compounds from a variety of cyclic ethers with primary aromatic amines in 20 % yield using an activated alumina catalyst at 270–350 °C.[37] Higher activity was found using titania at 250–300 °C.[38] As far as we are aware the palladium catalysed reaction we are describing is the first example of the synthesis of *N*-phenylpyrrolidine by the reaction of THF with aniline under mild liquid phase conditions. The reaction proved to be quite general for five membered rings, the best conversions being obtained with γ–butyrolactone (giving *N*–phenylpyrrolidone, Figure 6, **27**; Table 6, entry **6**) and succinic anhydride (giving *N*–phenylsuccinimide, Figure 6, **28**; Table 6, entry **8**), although methanol was added to solubilise the anhydride and this gave the ring opened products, dimethyl 1,4–butandioate and $PhNC(O)(CH_2)_2CO_2Me$ together with a trace of monomethyl 1,4–butanedioate. Furan gave very low conversion to **29** (Figure 6, Table 6, entry **5**). Tetrahydropyran (THP, six membered ring, Table 6, entry **7**) was unreactive, as was 1,4-dioxane (traces of *N*-phenylformamide observed) as were amines other than aniline (Table 6, entries **9**-**12**).

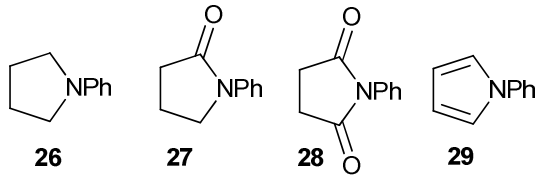

Fig. 6 Products obtained from THF (**26**), γ-butyrolactone (**27**), succinic anhydride (**28**) or furan (**29**, trace only) under aminocarbonylation conditions with aniline (**2**) as the nucleophile

Table 6 Reaction of amines with cyclic ethers

Entry[a]	Substrate	Solvent	time / h	Selectivity / %
1	aniline	THF	6	21 (**26**)
2	aniline	THF	22	60 (**26**)
3[b]	aniline	THF	6	0 (**26**)
4[c]	aniline	THF	6	0 (**26**)
5	aniline	Furan	6	3 (**29**))
6	aniline	1,4–butyrolactone	6	100 (**27**)
7	aniline	THP	3	< 1
8	aniline	succinic anhydride / MeOH	3	27[d], 53[e], 20 [f]
9[g]	*o*-aminomethylbenzoate	THF	3	0
10	octylamine	THF	6	0
11	cyclohexylamine	THF	6	0
12	propylamine	THF	6	0

[a] Conditions: aniline (11 mmol), $PdCl_2$ (32 mg, 0.2 mmol), DTBPMB (98 mg, 0.25 mmol), solvent (10 ml), p_{CO} = 30 bar, 100 °C. Conversions, determined by GC FID and calculated[36] response factors, are based on aniline consumed; [b] No DTBPMB was added; [c] No CO; [d] **28**; [e] $PhNC(O)(CH_2)_2CO_2Me$; [f] $(CH_2CO_2Me)_2$ (uncalibarted GC areas.; [g] aniline 7 mmol.

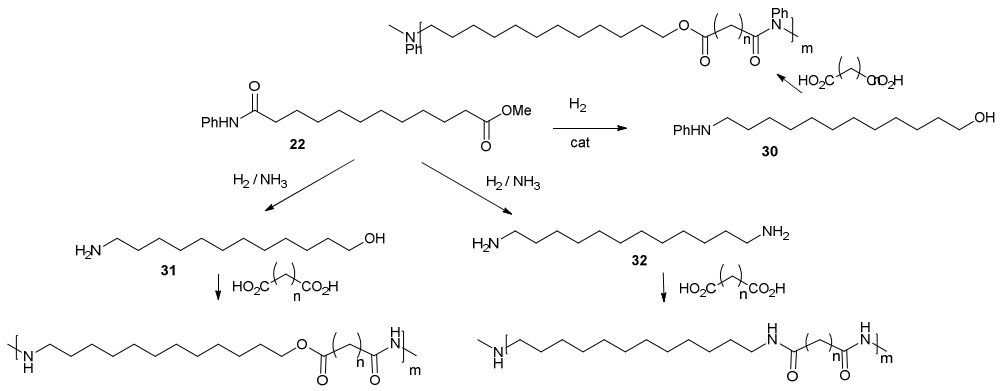

Fig. 7 Possible conversion of **22** to useful monomers for polyamides or polester amides

Conclusion

We conclude that linear amides can be produced with high selectivity from the aminocarbonylation of long chain alkenes or unsaturated esters. In the case of esters, the double bond is preferentially at the end of the chain, as in the castor-oil derived methyl 10-undecenoate. Aniline is the preferred amine, and diethyl ether the preferred solvent. Significant advantages in terms of catalyst activity and stability are obtained if the reactions are carried out in the presence of 2–naphthol and sodium or potassium iodide. If the double bond is buried in the chain, as in ethyl 3-hexenoate, isomerisation is too slow to compete with reaction of the ester group with the amine, whilst if it is conjugated with the ester, as in methyl acrylate, Michael addition of the amine across the double bond dominates. If a five membered oxygen containing heterocycle is used as the solvent and unusual O for NPh exchange occurs to give, in the case of THF, *N*–phenylpyrrolidine.

The production of useful monomers from methyl 10-undecenoate (**21**) would require reduction to an amino alcohol or a diamine, as shown in Figure 7. Simple reduction of **22**, possibly using one of our amide hydrogenation catalysts,[8, 9] would give 12-hydroxydodeceylphenylamine, **30,** which might polymerise with diacids, but a more attractive possibility would be to use **22** to form amino alcohol **31** or diamine **32**. It is evident that under our optimised conditions for the formation of **22**, transamidation of the ester function does not occur, so it is possible that ammonia might only transamidate with the aniline derived part of the molecule. Attempts to hydrogenate **22** in the presence or absence of ammonia are among our next targets.

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Experimental

All reactions were performed using standard Schlenk techniques. All solvents were degassed with nitrogen. Unless otherwise stated, solvents were used as supplied and were not previously dried. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded at 298 K on a Bruker 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR spectrometer, using the residual solvent peak to reference the spectra to tetramethylsilane at δ = 0 ppm. Elemental analyses were performed by the Elemental Analysis Service of the London Metropolitan University. Gas chromatograms were recorded on a Hewlett Packard 6890 series GC system equipped with an Agilent J&W HP-1 general purpose column (fused silica capillary) with an HP 5973 Mass selective detector for qualitative (MS) and FID detector for quantitative analysis. A Hewlett-Packard Chemstation allowed for the computerized integration of peak areas. Method: flow rate 1 ml min^{-1} (He carrier gas), split ratio 100 : 1, starting temperature 50 °C (4 min) ramp rate 20 °C min^{-1} to 130 °C (2 min), ramp rate 20 °C min^{-1} to 220 °C (15.5 min). [$PdCl_2$] (Lancaster), 1–naphthol (May & Baker LTC), 2–naphthol, phenol, [$Pd_2(dba)_3$], [$Pd(dba)_2$], sodium iodide, potassium iodide, aniline, 1–hexene, 1–octene, 2–octene, 4–octene, 2–methyl–1–pentene, 2–methyl–2–pentene, 3–methyl–1–pentene, methyl acrylate, ethyl 3–hexenoate (Sigma Aldrich), 1,2–*bis*(di*tert*butylphosphinomethyl) benzene (Lucite International), methyl 10–undecenoate (Tokyo Chemical Industry) and methane sulfonic acid (Alfa Aesar) were used as supplied. Solvents were obtained from a solvent purification system.

General procedure for the aminocarbonylation of alkenes

Under air, [$PdCl_2$] (32 mg, 0.2 mmol) was introduced into a Hastelloy autoclave, which was sealed and purged with nitrogen. 1,2–*bis*(di*tert*butylphosphinomethyl)benzene was dissolved in diethyl ether (10 mL) in a degassed Schlenk tube. Alkene (6 mmol) and aniline (1 mL, 11 mmol) were added to the solution, which was transferred into the autoclave *via* cannula. The autoclave was pressurised with CO (20 bar) and heated to 100 °C for 3 to 6 h, cooled, vented and the content was analysed by GC–FID using measured response factors (quantitative) and GC-MS (identification of products).

Aminocarbonylation of 1–octene in the presence of a promoter

Under air, 2–napthol (1.4, 9.5 mmol) and NaI (9.5 mg, 0.064 mmol) were introduced into a Hastelloy autoclave, which was sealed and purged with nitrogen. 1,2–*bis*(di*tert*butylphosphinomethyl)benzene (25 mg, 0.0637 mmol) and [$Pd(OAc)_2$] (5.6 mg, 0.025 mmol) were dissolved in toluene (10 mL) in a degassed Schlenk flask. 1–Octene (2 mL, 12.7

mmol), methane sulfonic acid (10 μL, 0.15 mmol) and aniline (1.2 mL, 12.74 mmoles) were added to the solution, which was transferred into the autoclave *via* cannula. The autoclave was pressurised with CO (20 bar) and heated to 140 °C for 1 h, cooled, vented and the content was analysed by GC–FID using calculated response factors and an internal standard and GC-MS.

General procedure for the aminocarbonylation of unsaturated esters

Under air, [$Pd_2(dba)_3$] (114 mg, 0.125 mmol), 1,2–*bis*(di*tert*butylphosphinomethyl)benzene (251 mg, 0.064 mmol), 2–naphthol (1.4 g, 9.5 mmol) and KI (10 mg, 0.064 mmol) were introduced into a Hastelloy autoclave, which was sealed and purged with nitrogen. Solvent (10 mL), unsaturated ester (12.7 mmol) and aniline (1.16 mL, 12.7 mmol) were degassed for 10 minutes with nitrogen in a Schlenk flask and introduced into the autoclave by cannula. Methane sulfonic acid (10 μL, 0.15 mmol) was added separately to the autoclave by cannula. The autoclave was purged three times with CO and the pressure was set between 30 and 50 bar. The autoclave was heated to between 70 and 140 °C for 16 h. After cooling, venting and opening, a sample was taken for GC–FID using calculated[36] response factors and an internal standard and GC-MS.

Aminocarbonylation of methyl 10–undecenoate; isolation of methyl 12-oxo-12-(phenylamino)dodecanoate (22)

Under air, [$Pd_2(dba)_3$] (92 mg, 0.1 mmol), 1,2–*bis*(di*tert*butylphosphinomethyl)benzene (395 mg, 1 mmol), 2–naphthol (1.4 g, 9.5 mmol) and KI (32 mg, 0.2 mmol) were introduced into a Hastelloy autoclave, which was sealed and purged with nitrogen. Diethyl ether (10 mL), methyl 10–undecenoate (1.42 mL, 6.35 mmol) and aniline (1.16 mL, 12.7 mmol) were de- gassed for 10 minutes with nitrogen in an ice-cold Schlenk flask and introduced into the autoclave by cannula. Methane sulfonic acid (0.1 mL, 1.5 mmol) was added separately to the autoclave by cannula. The autoclave was purged three times with CO and the pressure was set to 30 bar. The autoclave was heated to 110 °C for 16 h. After cooling, venting and opening, the remaining black mixture was solubilised in dichloromethane and the mixture filtered through paper. A sample was taken for GC analysis (conversion 99 %). The solvent was removed on a rotary evaporator. The remaining solid was passed through a first silica chromatography column (ethyl acetate:hexane / 1:3) and the obtained solid was passed through a second silica chromatography column (ethyl acetate:hexane / 1:9). After evaporation of the appropriate fractions, the solid was recrystallised from ethyl acetate/hexane. Isolated yields: from 49 % to 60 %. Elemental analysis: found C 71.45, H 9.09, N 4.29 %; $C_{19}H_{29}O_3N$ requires C 71.44, H 9.15, N 4.38 %. Melting point 79–80 °C (average of three measurements). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.51 (d, J = 8.1 Hz, 2H, Ph*H*), 7.31 (t, J = 7.8 Hz, 2H, Ph*H*), 7.16 (s, 1H, N*H*), 7.09 (t, J = 7.3 Hz, 1H, Ph*H*), 3.66 (s, 3H, –OCH_3), 2.35 (t, J = 7.6 Hz, 2H, –CH_2CONHPh), 2.30 (t, J = 7.5 Hz, 2H, –CH_2CO$_2$Me), 1.72 (quintet, J = 7.4 Hz, 2H, –CH_2CH$_2$CONHPh), 1.61 (quintet, J = 7.5 Hz, 2H, -CH_2CH$_2$CO$_2$Me), 1.28 (s, 12 H, alkyl chain). ^{13}C NMR (100 MHz; CDCl3): δ = 174.72 (s, –CH$_2$*C*ONH Ph), 171.68 (s, -CH$_2$*C*O$_2$Me), 129.33 (s, –*CPh*), 124.48 (s, –*CPh*), 120.04 (s, –*CPh*), 51.81 (s, –COO*C*H$_3$), 38.19 (s, –*C*H$_2$CONHPh), 34.45 (s, –*C*H$_2$CO$_2$Me), 29.6629.43 (alkyl chain), 25.92 (s, -*C*H$_2$CH$_2$CONHPh), 25.27 (s, –*C*H$_2$CH$_2$CO$_2$Me).

Synthesis of *N*-heterocycles

1,2–*bis*(di*tert*butylphosphinomethyl)benzene (25 mg, 0.98 mmol) and $PdCl_2$ (32 mg, 0.2 mmol) were dissolved in the solvent (10 mL) in a degassed Schlenk flask and aniline (11 mmoles) was added to the solution, which was transferred to the autoclave *via* cannula. The autoclave was pressurised with CO (30 bar), heated to 100 °C for 1 h, cooled, vented and the content was analysed by GC-FID GC–FID using calculated response[36] and GC-MS.

Notes and References

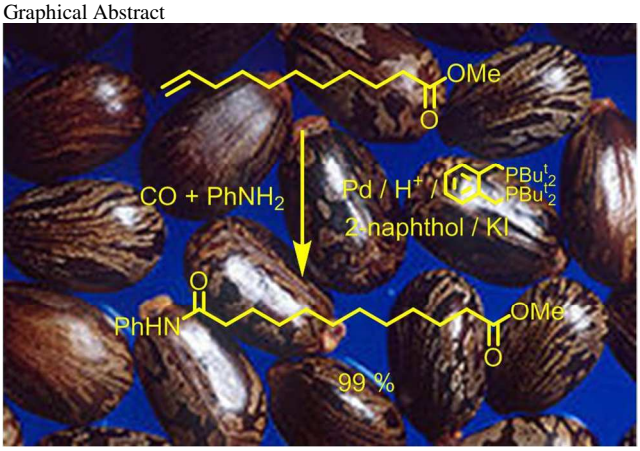
[a] *EaStCHEM, School of Chemistry, University of St Andrews, St Andrews, KY16 9ST, Scotland, UK. Fax: +44 1334 463 808; Tel: +44 1334 463 805;*
E-mail: djc@st-andrews.ac.uk
[b] *Lucite International, Technology Centre, PO Box 90, Wilton, Middlesborough,, TS6 8JE, England, UK. Fax: +44 1642 447 119; Tel: +441642 447 109; E-mail: graham.eastham@lucite.com*

Elecronic Supplementary Information including details of reactions of methyl acrylate, representative GC analyses of selected products and full characterisation of methyl 12-oxo-12-(phenylamino)dodecanoate (**22**) is available.

1. M. R. L. Furst, R. Le Goff, D. Quinzler, S. Mecking, C. H. Botting and D. J. Cole-Hamilton, *Green Chem.*, 2012, **14**, 472.
2. M. R. L. Furst, T. Seidensticker and D. J. Cole-Hamilton, *Green Chem.*, 2013, **15**, 1218
3. C. Jiménez-Rodriguez, G. R. Eastham and D. J. Cole-Hamilton, *Inorg. Chem. Commun.*, 2005, **8**, 878.
4. D. S. Ogunniyi, *Bioresource Technol.*, 2006, **97**, 1086.
5. K. Isobe, T. Azuma, H. Nishikawa and T. Imamura, 1997, US5693605.
6. H. Kelkenberger, W. Riback and N. Engel, 1991, US5009814.
7. G. Oetter, K. Oppenlander, K. Trefensee and M. Zimstein, 2000, US6165971.
8. J. Coetzee, D. L. Dodds, J. Klankermayer, S. Brosinski, W. Leitner, A. M. Z. Slawin and D. J. Cole-Hamilton, *Chem. Eur. J.*, 2013, **19**, 11039.
9. J. Coetzee, H. G. Manyar, C. Hardacre and D. J. Cole-Hamilton, *ChemCatChem*, 2013, 2843.
10. R. Burch, C. Paun, X. M. Cao, P. Crawford, P. Goodrich, C. Hardacre, P. Hu, L. McLaughlin, J. Sa and J. M. Thompson, *J. Catal.*, 2011, **283**, 89.
11. M. Stein and B. Breit, *Angew. Chem. Int. Ed.*, 2013, **52**, 2231.
12. E. Baumann, *Ber. Deutsch. Chem. Ges.*, 1886, **19**, 3218.
13. E. Fischer, *Ber. Deutsch. Chem. Ges.*, 1903, **26**, 2982.
14. M. B. Smith and J. March, in *March's Advanced Organic Chemistry, 6th Edn.*, John Wiley and Sons, Hoboken, 2007.
15. I. Ugi and C. Steinbruckner, *Angew. Chem.*, 1960, **72**, 267.
16. A. W. Chapman, *J. Chem. Soc.*, 1925, 1992.
17. C. Gunanathan, Y. Ben-David and D. Milstein, *Science*, 2007, **317**, 790.
18. K. Okuro, H. Kai and H. Alper, *Tetrahedron-Asymmetry*, 1997, **8**, 2307.
19. C. Coperet, T. Sugihara and E. Negishi, *Tetrahedron Lett.*, 1995, **36**, 1771.
20. S. P. Zhao, S. I. Sassa, H. Inoue, M. Yamazaki, H. Watanabe, T. Mori and Y. Morikawa, *J. Mol. Catal. A-Chem.*, 2000, **159**, 103.
21. C. Jiménez-Rodriguez, G. R. Eastham and D. J. Cole-Hamilton, *Dalton Trans.*, 2005, 1826.

22. C. J. Rodriguez, D. F. Foster, G. R. Eastham and D. J. Cole-Hamilton, *Chem. Commun.*, 2004, 1720.
23. A. J. Rucklidge, G. E. Morris and D. J. Cole-Hamilton, *Chem. Commun.*, 2005, 1176.
24. A. J. Rucklidge, G. E. Morris, A. M. Z. Slawin and D. J. Cole-Hamilton, *Helv. Chim. Acta*, 2006, **89**, 1783.
25. H. Ooka, T. Inoue, S. Itsuno and M. Tanaka, *Chem. Commun.*, 2005, 1173.
26. D. Quinzler and S. Mecking, *Angew. Chem. Int. Ed.*, 2010, **49**, 4306.
27. F. Stempfle, D. Quinzler, I. Heckler and S. Mecking, *Macromolecules*, 2011, **44**, 4159.
28. F. Stempfle, P. Roesle and S. Mecking, *ACS Symp. Ser,*, 2012, **1105**, 151.
29. G. Walther, J. Deutsch, A. Martin, F.-E. Baumann, D. Fridag and A. Köckritz, *ChemSusChem*, 2011, **4**, 1052.
30. M. M. De Castro Loureiro Barreto Rosa, H. M. Gillespie, A. K. Van Helden, P. D. Savage, E. Drent and E. G. McKenna, 2000, US6103927
31. J. R. Martinelli, T. P. Clark, D. A. Watson, R. H. Munday and S. L. Buchwald, *Angew. Chem. Int. Ed.*, 2007, **46**, 8460.
32. G. R. Eastham, R. P. Tooze, M. Kilner, D. F. Foster and D. J. Cole-Hamilton, *J. Chem. Soc., Dalton Trans.*, 2002, 1613.
33. P. Roesle, C. J. Duerr, H. M. Moeller, L. Cavallo, L. Caporaso and S. Mecking, *J. Am. Chem. Soc.*, 2012, **134**, 17696.
34. S. M. A. Donald, S. A. Macgregor, V. Settels, D. J. Cole-Hamilton and G. R. Eastham, *Chem. Commun.*, 2007, 562.
35. Y. Q. Wan, M. Alterman, M. Larhed and A. Hallberg, *J. Org. Chem.*, 2002, **67**, 6232.
36. J. C. Sternberg, D. T. Gallaway and L. Jones, in *Gas Chromatography*, eds. N. Brenner, N. S. Gallaway, J. E. Callen and D. Weiss, Academic Press, New York, 1962, pp. 231.
37. R. E. Walkup and S. Searles, *Tetrahedron*, 1985, **41**, 101.
38. D. C. Hargis and R. L. Shubkin, *Tetrahedron Lett.*, 1990, **31**, 2991.

Graphical Abstract



Title Amplification

Methyl 10-undecenoate from castor oil is aminocarbonylated to α,ω–amidoesters for possible use in polyamide or polyester amide monomer production.