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A mild and efficient protocol for the conversion of carboxylic acids to olefins by a catalytic decarbonylative elimination reaction

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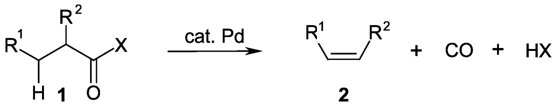
A new method for the conversion of aliphatic carboxylic acids to olefins under unprecedented mild conditions is disclosed, wherein the carboxylic acids are converted *in situ* with pivalic anhydride to the mixed anhydrides, which regioselectively add to a $PdCl_2$–DPE-Phos catalyst. At a temperature of only 110 °C, smooth decarbonylation and β-hydride elimination occur, and the corresponding olefins along with CO, CO_2 and pivalic acid are liberated.

Due to their excellent availability, easy handling, and low price, carboxylic acids are particularly attractive starting materials for organic synthesis. Thus, catalytic reactions in which these substrates are utilized as synthetic equivalents for acyl or aryl halides have attracted considerable interest.[1] Examples are ketone syntheses from carboxylic acids and boronic acids,[2] decarbonylative Heck olefinations of aromatic carboxylic acids,[3] and the direct reduction of carboxylic acids to aldehydes.[4]

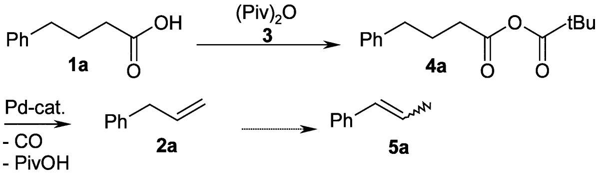
We reasoned that the strategy used in the abovementioned processes should also allow the conversion of carboxylic acids to olefins *via* a catalytic decarbonylative elimination reaction (Scheme 1, X = OH). This reaction promised to be of considerable preparative value since it could provide an easy access to alkenes from the wide variety of available aliphatic carboxylic acids. Furthermore, mechanistic insight gained in this project should be transferable to other catalytic processes involving a decarbonylation step.

While the transformation shown in Scheme 1 is well-established for acid chlorides (X = Cl),[5] only a few examples of the more desirable direct conversion of carboxylic acids have been reported, and they involve rather harsh reaction conditions.[5,6] For example, a temperature of 250 °C is required to convert a fatty acid to an olefin in the presence of excess acetic anhydride as an activating agent and a Pd–PPh_3 complex as the catalyst. In order to stabilize the catalyst at the high temperatures, the ligand has to be added in at least 30-fold excess, and double bond-isomerization of the product can only be avoided if the reaction is performed in a special continuous distillation reaction setup. Clearly, more active and selective catalysts are required to allow a more general application of this reaction in organic synthesis.

In order to identify such catalyst systems, we chose the reaction of phenylbutanoic acid **1a** to 3-phenylpropene **2a** in the presence of pivalic anhydride (**3**) as a model system (Scheme 2).



Scheme 1 Pd-catalyzed decarbonylative elimination reaction.



Scheme 2 Decarbonylative elimination reaction in the presence of Piv_2O.

The mechanism of the desired transformation probably involves a catalytic cycle in which the *in situ* generated mixed anhydride **4a** oxidatively adds to a Pd(0)-species, preferentially yielding the sterically less demanding of the two possible acyl complexes. Decarbonylation of this acyl complex gives rise to an alkyl-Pd-complex, which can liberate the product alkene **2a** *via* β-hydride elimination.[7] At elevated temperatures, the decarbonylation should be the rate-determining step in the overall process, since related reactions involving oxidative additions of mixed anhydrides proceed even at moderate temperatures,[1,2] and β-hydride eliminations are usually considered to occur particularly fast.[8,9]

For our model substrate, a catalytic isomerization of the product **2a** to the internal olefins (*E*)- or (*Z*)-1-phenyl-2-propene (**5a**) can be expected to be a significant side reaction, since it would give rise to a stable benzylic double bond (Scheme 2).

In order to identify suitable reaction conditions for our model reaction, we tested several transition metal complexes under various conditions (Table 1).

As expected, no conversion was observed at a temperature of only 110 °C using a $PdCl_2$–PPh_3 catalyst in a non-polar solvent (Entry 1). However, small amounts of product were formed in the presence of the highly polar solvent 1,3-dimethyltetrahydro-2(1*H*)-pyrimidinone (DMPU, Entry 2). Encouraged by this observation, we used this solvent for testing various palladium catalysts (Entries 3–17).

In sharp contrast to the observations made for decarbonylative Heck olefinations, the addition of phosphines surprisingly did not inhibit the reaction but strongly facilitated it. The nature of the

Table 1 Optimization of the conditions for the model reaction

No	Ligand	Pd-source	Solvent	**2a** (%)	**5a** (%)
1	PPh_3	$PdCl_2$	toluene	0	0
2	PPh_3	$PdCl_2$	DMPU	27	< 2
3	P(*o*-Tol)$_3$	$PdCl_2$	DMPU	3	6
4	PCy_3	$PdCl_2$	DMPU	0	0
5	P(*p*-MeO-Ph)$_3$	$PdCl_2$	DMPU	0	0
6	P(*p*-Cl-Ph)$_3$	$PdCl_2$	DMPU	28	2
7	P(1-Fur)$_3$	$PdCl_2$	DMPU	6	5
8	DPPF	$PdCl_2$	DMPU	52	< 2
9	BINAP	$PdCl_2$	DMPU	3	0
10	DPE-Phos	$PdCl_2$	DMPU	83	< 2
11[a]	DPE-Phos	$PdCl_2$	DMPU	81	< 2
12	DPE-Phos	$Pd(OAc)_2$	DMPU	67	0
13	DPE-Phos	$PdBr_2$	DMPU	< 2	98
14	DPE-Phos	$(dba)_3Pd_2$	DMPU	60	< 2
15[b]	DPE-Phos	$PdCl_2$	DMPU	57	23
16[c]	DPE-Phos	$PdCl_2$	DMPU	0	0
17[d]	DPE-Phos	$PdCl_2$	DMPU	57	23
18	DPE-Phos	$PdCl_2$	toluene	< 2	0
19	DPE-Phos	$PdCl_2$	$C_6H_4Cl_2$	0	0
20	DPE-Phos	$PdCl_2$	NMP	70	< 2
21	DPE-Phos	$PdCl_2$	DMSO	0	< 2
22	DPE-Phos	$PdCl_2$	diglyme	62	< 2

Conditions: 1.0 mmol 4-phenylbutyric acid, 2.0 mmol pivalic anhydride, 3 mol% Pd-source, 9 mol% ligand, 110 °C, DMPU, 16 h, yields were determined by GC using *n*-tetradecane as an internal standard;[a] with 2 mol% ligand; [b] 1 mmol pivalic anhydride; [c] in the presence of 1 mmol K_2CO_3; [d] in the presence of 1 mmol pyridine

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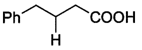
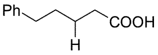
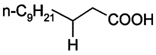
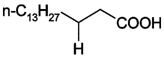
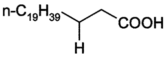
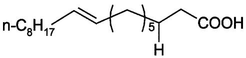
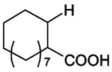
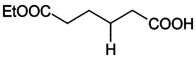
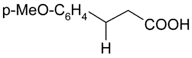
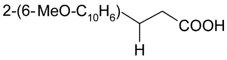
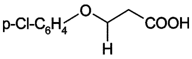
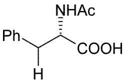
ligand had a strong influence on the reaction outcome (Entries 2–10), while the amount of the ligand had only little effect (Entries 10, 11). Bis(2-diphenylphosphinophenyl) ether (DPE-Phos), a strongly coordinating chelating phosphine, was by far the most effective (Entry 10). This finding is particularly interesting, since the adverse effect of phosphines in the Heck olefinations of carboxylic acid derivatives has been suspected to be due to the phosphines inhibiting the decarbonylation step.[3,10]

The Pd-precursor also had a profound influence on the catalyst performance (Entries 10, 12–14). $PdBr_2$ was more active than $PdCl_2$, but also facilitated the undesirable double bond isomerization of the product. The isomerization step is much slower for the $PdCl_2$–DPE-Phos combination, and can almost completely be avoided by stopping the reaction at a conversion around 80%. Best results were obtained when the activating agent was applied in excess (Entries 10, 15).

A high solvent polarity resulted in best turnovers and highest selectivities. DMPU gave the best results, in NMP and diglyme moderate yields were still obtained, while other solvents were not effective (Entries 18–22). Unlike for similar transformations,[1,3] the addition of water, bases, and other additives did not enhance the yields but facilitated the isomerization (Entries 16, 17).

In order to investigate the scope of the transformation, we applied the best protocol to the synthesis of a variety of olefins (Table 2).† Special emphasis was put on naturally occurring long chain fatty acid substrates. Gratifyingly, the reaction proved to be of reasonably broad scope. Both linear and branched carboxylic acids were successfully converted, and even some functionalized olefins were obtained in satisfactory yields. It is especially worth mentioning that not only olefins, but also vinyl ethers such as **2k** are accessible through this reaction. Unfortunately, the reaction cannot yet be extended to the even more desirable synthesis of enamides from *N*-protected α-amino acids. Thus, only a small amount of **2l** was detected while mainly the corresponding oxazol-5-one was formed.

Table 2 Synthesis of olefins from carboxylic acids

Carboxylic acid	Product	Yield (%)
	**2a**	66
	**2b**	80
	**2c**	78
	**2d**	64
	**2e**	59
	**2f**	69
	**2g**	81[a]
	**2h**	23[b]
	**2i**	65
	**2j**	77
	**2k**	56
	**2l**	5[c]

Conditions: 1.0 mmol carboxylic acid, 2.0 mmol pivalic anhydride, 3 mol% $PdCl_2$, 9 mol% DPE-Phos, 110 °C, DMPU, 16 h, isolated yields.[a] 4:1 mixture of the (*E*)- and (*Z*)-isomers. [b] The low yield is due to the high volatility of the compound. [c] Main product: (*S*)-4-benzyl-2-methyl-4*H*-oxazol-5-one.

In summary, an efficient protocol for the synthesis of olefins and enol ethers directly from easily available carboxylic acids has been developed. In the presence of pivalic anhydride and a palladium–DPE-Phos catalyst, facile decarbonylation of carboxylic acids was achieved at a temperature as low as 110 °C. Under these conditions, double bond isomerization of the products is very slow and can thus easily be avoided. The fact that the reaction can now be performed at moderate temperatures without the need for special distillation techniques makes it much more attractive for applications in organic synthesis.

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Notes and references

† **Synthesis of (*E*)-heptadeca-1,8-diene (2f)**: A dried flask was charged with elaidic acid **1f** (282 mg, 1.00 mmol), pivalic anhydride (**3**) (186 mg, 2.00 mmol), dry palladium chloride (5.3 mg, 0.03 mmol), and DPE-Phos (48 mg, 0.09 mmol). Dry DMPU (4 mL) was added by syringe and the reaction was stirred overnight at 110 °C. After the reaction was almost complete (TLC), ethyl acetate was added and the organic layer was washed consecutively with ammonium chloride solution, water and brine. The product was filtered through a small plug of silica using hexane as eluent. After concentrating to dryness, **2f** (164 mg, 69%) was obtained as a colorless oil. ^{1}H-NMR (300.1 MHz, $CDCl_3$): δ = 5.92–5.71 (m, 1H), 5.49–5.32 (m, 2H), 5.06–4.88 (m, 2H), 3.13–1.85 (m, 6H), 1.48–1.31 (m, 18H), 0.87 (t, ^3J = 8 Hz, 3H) ppm; ^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 139.5, 130.8, 130.6, 114.5, 34.1, 33.0, 32.9, 32.3, 30.0, 29.9, 29.9, 29.7, 29.5, 29.2, 29.0, 23.0, 14.5 ppm; MS (EI, 70 eV): *m/z* (%) = 236 (3, $[M]^+$), 207 (7), 194 (8), 123 (14), 110 (65), 96 (100), 81 (73), 68 (90), 55 (75), 41 (59), 29 (30); HRMS (EI) calcd. for $C_{17}H_{32}$ $[M]^+$: 236.250142, found: 236.250142.

1 A. Zapf, *Angew. Chem., Int. Ed.*, 2003, **42**, 5394.
2 R. Kakino, S. Yasumi, I. Shimizu and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, 2002, **75**, 137; L. J. Gooßen and K. Ghosh, *Angew. Chem., Int. Ed.*, 2001, **40**, 3458; L. J. Gooßen and K. Ghosh, *Chem. Commun.*, 2001, 2084.
3 L. J. Gooßen, J. Paetzold and L. Winkel, *Synlett*, 2002, 1721; L. J. Gooßen and J. Paetzold, *Angew. Chem., Int. Ed.*, 2002, **41**, 1237.
4 K. Nagayama, F. Kawataka, M. Sakamoto, I. Shimizu and A. Yamamoto, *Chem. Lett.*, 1995, 367; L. J. Gooßen and K. Ghosh, *Chem. Commun.*, 2002, 836.
5 J. Tsuji and K. Ohno, *Synthesis*, 1969, 157.
6 J. A. Miller, J. A. Nelson and M. P. Byrne, *J. Org. Chem.*, 1993, **58**, 18.
7 W. Boland and L. Jaenicke, *Liebigs Ann. Chem.*, 1981, 92.
8 J. Tsuji and K. Ohno, *J. Am. Chem. Soc.*, 1968, **90**, 94; J. A. Miller and J. A. Nelson, *Organometallics*, 1991, **10**, 2958.
9 H. Nagashima, K. Sato and J. Tsuji, *Tetrahedron Lett.*, 1982, **23**, 3085; H. Nagashima, K. Sato and J. Tsuji, *Tetrahedron*, 1985, **41**, 5645; G. S. Jones and W. J. Scott, *J. Am. Chem. Soc.*, 1992, **114**, 1491.
10 M. S. Stephan, A. J. J. M. Teunissen, G. K. M. Verzijl and J. G. de Vries, *Angew. Chem., Int. Ed.*, 1998, **37**, 662; A. F. Shmidt and V. V. Smirnov, *Kinet. Catal.*, 2000, **41**, 743.