Pergamon

Tetrahedron Letters 42 (2001) 6923–6924

TETRAHEDRON
LETTERS

A novel and efficient synthesis of maleic anhydrides by palladium-catalyzed dicarbonylation of terminal acetylenes in H_2O/dioxane

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Received 25 April 2001; revised 24 July 2001; accepted 3 August 2001

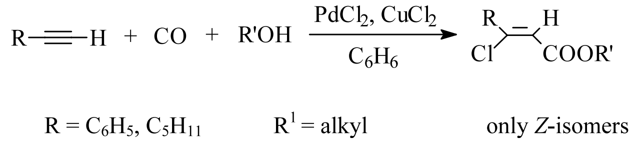
Abstract—Maleic anhydrides can be obtained in high yields by the $PdCl_2$-catalyzed dicarbonylation of terminal acetylenes in H_2O/dioxane. It is not necessary to add reoxidants to the reaction, but reoxidants can affect the yield and the rate. We also found that the rate decreased and only traces of maleic anhydrides were formed in the presence of KCl or LiCl. © 2001 Elsevier Science Ltd. All rights reserved.

In 1999, we showed that (*Z*)-3-chloroacrylate esters could be synthesized in the corresponding alcohol/benzene mixture at room temperature under CO (1 atm) in the presence of $PdCl_2$ and $CuCl_2$ (Scheme 1).[1] In this reaction, the solvent plays an important role in influencing the chemoselectivity and stereoselectivity. We now report that different kinds of product could be obtained from the palladium-catalyzed carbonylation reaction by changing the solvent. This finding is expected to have a broad impact on studies of Pd(II)-catalyzed carbonylation reactions leading to new methodology.

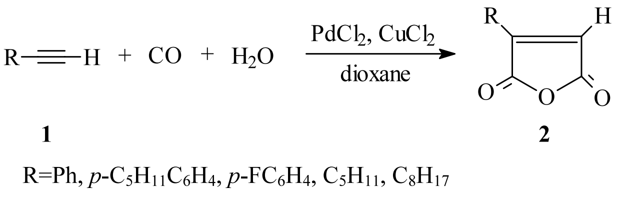
We report that another catalytic carbonylation reaction takes place using $PdCl_2$ and $CuCl_2$ as the catalyst system when dioxane is used as the solvent. Maleic anhydrides can be obtained in high yields (Scheme 2).

A typical procedure is as follows: alkyne **1** (1 mmol), $PdCl_2$ (0.056 mmol), and $CuCl_2$ (2 mmol) were added to dioxane (10 mL containing 0.3% of H_2O). The mixture was stirred under an atmospheric pressure of CO at room temperature for the required time. After filtration, the dioxane was removed by rotary evaporation to give the crude product that was then purified using preparative TLC on silica gel (light petroleum–diethyl ether). Our results are summarized in Tables 1 and 2.

Table 1 reports the results of the palladium-catalyzed dicarbonylation of phenylacetylene under a variety of conditions. In MeOH/dioxane, phenylmaleic anhydride was primarily obtained (80%) in the presence of $PdCl_2$ and $CuCl_2$ (entry 1). This result suggested that the water in the dioxane competes with the MeOH.[2] To verify these results, two other experiments were carried out: one in dioxane (AR, containing 0.3% of H_2O) and the other in H_2O/dioxane (1/5, 10 mL). Only phenylmaleic anhydride was isolated from both reactions (entries 2 and 3). We also examined different solvents (entries 1–7). The best solvent was found to be H_2O/dioxane since the excess H_2O did not affect the reaction. No maleic anhydride was produced when other solvents such as H_2O, THF, H_2O/THF, or H_2O/C_6H_6, were used.



Scheme 1.



Scheme 2.

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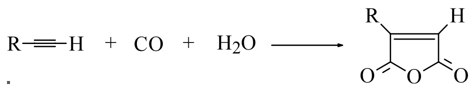
PII: S0040-4039(01)01438-1

Table 1. Synthesis of phenylmaleic anhydride by palladium-catalyzed dicarbonylation of phenylacetylene[a]



Entry	Catalyst	Solvent (10 mL)	Reaction time (h)[b]	Yields (%)[c]
1[d]	$PdCl_2/CuCl_2$	Dioxane	2	80
2	$PdCl_2/CuCl_2$	Dioxane	2	99
3[e]	$PdCl_2/CuCl_2$	H_2O/dioxane	2	98
4	$PdCl_2/CuCl_2$	H_2O	15	Trace
5	$PdCl_2/CuCl_2$	THF	14	–
6[e]	$PdCl_2/CuCl_2$	H_2O/THF	14	–
7[e]	$PdCl_2/CuCl_2$	H_2O/C_6H_6	14	–
8	$PdCl_2$	Dioxane	14	76
9[f]	$PdCl_2$/KCl	Dioxane	15	Trace
10[g]	$PdCl_2$/LiCl	Dioxane	15	10

[a] Reaction conditions: **1** (1 mmol), $PdCl_2$ (0.056 mmol), $CuCl_2$ (2 mmol) and dioxane (AR, 10 mL containing 0.3% of H_2O).

[b] The rate of the reaction was determined by GC analysis using an internal standard.

[c] Isolated yield.

[d] Reaction in MeOH/dioxane (10 mL, 0.6/9.4), methyl (*Z*)-3-chlorophenylacrylate esters/phenylmaleic anhydride: 15/85.

[e] The ratio of H_2O/solvent = 2/10.

[f] KCl (4 mmol).

[g] LiCl (4 mmol), conversion 35%.

Table 2. Palladium-catalyzed dicarbonylation of terminal alkynes[a]

Entry	Alkyne	Reaction time (h)[b]	Yields of **2** (%)[c]
1[d]	PhC≡CH	9	98
2	*p*-$C_5H_{11}C_6H_4C$≡CH	4	94
3	*p*-FC_6H_4C≡CH	4	96
4	$C_5H_{11}C$≡CH	2	84
5	$C_8H_{17}C$≡CH	3	87

[a] Reaction conditions: **1** (1 mmol), $PdCl_2$ (0.056 mmol), $CuCl_2$ (2 mmol), CO (1 atm) and dioxane (containing 0.3% of H_2O, 10 mL) at room temperature.

[b] The rate of the reaction was determined by GC analysis using an internal standard.

[c] Isolated yield.

[d] PhC≡CH (5 mmol), $PdCl_2$ (0.056 mmol), $CuCl_2$ (10 mmol) in dioxane (AR, containing 0.3% of H_2O, 50 mL).

Generally, syntheses of maleic anhydrides by palladium(II)-catalyzed dicarbonylation of terminal acetylenes need reoxidants to complete the catalytic cycle.[3–9] To our surprise, the reaction proceeds smoothly in the absence of reoxidants (for example $CuCl_2$) using $PdCl_2$ as the catalyst. In the presence of $PdCl_2$ alone, although the rate and yield decreased to some extent, phenylacetylene could be completely converted into the anhydride after 14 h and the catalyst was changed into a black solid powder after the reaction had finished (entry 8), X-ray crystallography showed that the black solid powder was Pd black. Less than 10% of maleic anhydride was obtained in the presence of $PdCl_2$ with 4 mmol of KCl or LiCl (entries 9 and 10).

A range of terminal acetylenes was evaluated as substrates for the dicarbonylation reaction (Table 2). The reaction proceeded smoothly and high yields were obtained when 5 mmol of phenylacetylene was added in the presence of $PdCl_2$ (0.056 mmol), $CuCl_2$ (10 mmol), CO (1 atm) and dioxane (AR containing 0.3% of H_2O, 50 mL) at room temperature (entry 1 in Table 2). Other terminal acetylenes were also converted into the corresponding maleic anhydrides smoothly in excellent yields using $PdCl_2$ and $CuCl_2$ as the catalyst (entries 2–5).

It is important to note that the carbonylation reaction can proceed smoothly in the absence of reoxidant, but reoxidant ($CuCl_2$) can enhance the yield and rate. Other reagents such as LiCl and KCl decreased the reaction rate.

In summary, we have shown that a reoxidant is not necessary in the $PdCl_2$-catalyzed dicarbonylation of terminal acetylenes in H_2O/dioxane, but it can affect the yield and the rate of the reaction. We have also developed a mild, general and efficient method for the synthesis of maleic anhydrides using $PdCl_2$ and $CuCl_2$ as the catalyst. Further synthetic applications and studies of the mechanism of the dicarbonylation reaction are underway.

Acknowledgements

We thank the National Natural Science Foundation of China for financial support (Nos. 29772036 and 29872039).

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