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Alkyne Hydroarylations with Chelating Dicarbene Palladium(II) Complex Catalysts: Improved and Unexpected Reactivity Patterns Disclosed Upon Additive Screening[‡]

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Palladium(II) complexes with a ligand set made from a chelating N-heterocyclic dicarbene ligand and two weakly coordinating anions (generally introduced in situ upon addition of 2 equiv. of a suitable silver salt) were found to be very active and selective catalysts for the room-temperature hydroarylation of alkynes at low catalyst loading (0.1 mol-%). Moreover, the screening of various strong acids as reaction promoters revealed that both the strength of the acid and the coordinating ability of its conjugated base influence the catalytic performance. Most remarkably, the use of HBF_4 together with a dicarbene Pd complex catalyst provides a dramatic change in the selectivity of the reaction, with the prevalent formation of a product stemming from the insertion of two molecules of alkyne into the aromatic C–H bond. The results presented herein highlight the fact that the dicarbene ligand, apart from stabilising the catalyst, is also able to enhance catalytic activity and, most notably, to steer the reaction selectivity towards novel products.

Introduction

Aromatic C–H bond functionalisation reactions represent green and economic alternatives to the more classic coupling reactions involving prefunctionalised aromatic substrates, for example, Heck and cross-coupling reactions, which are nowadays widely used for the conversion of aryl halides into more complex organic molecules.[1] Several examples of such reactions have been reported in the recent literature.[2,3] They are based on i) chelate-assisted oxidative addition of the C–H bond to metal centres in a low oxidation state,[4] ii) arene metallation by metal centres, which attack the aromatic ring by electrophilic aromatic substitution or σ-bond metathesis[5] and finally iii) Friedel–Crafts-type reactions promoted by metal centres that upon coordination electrophilically activate organic molecules towards attack at the aromatic ring.[6]

Palladium(II) salts or complexes in a trifluoroacetic acid environment are, for example, known to promote the coupling reaction of arenes with alkynes.[7] In this case, products of the formal *trans*-hydroarylation of the triple bond are formed. The mechanism of this reaction is still debated: some theoretical calculations and experimental evidence suggest a Friedel–Crafts-type alkenylation mechanism (Scheme 1, path a)[8] whereas other data indicate a reaction pathway that occurs by arene metallation (Scheme 1, path b).[7b,9] The reaction is characterised by a high and quite unusual regio- and stereoselectivity: in fact, it is remarkable that the thermodynamically less favoured *cis*-arylalkenes are the major products. Other noble metal centres, such as platinum(II),[10] gold(I) and gold(III),[11] as well as non-noble, electrophilic metal centres (group 3, 4, 13 and 15 elements, lanthanides)[12] have been successfully employed as alternative catalysts, but their efficiency appears to be lower and/or their reaction scope narrower than that of palladium(II).

Very recently we[13] reported palladium(II) complexes with a ligand set made out of a chelating N-heterocyclic dicarbene[14] and two halide ligands, which exhibit in this reaction a superior performance compared with all other previously described catalysts: alkyne hydroarylation can be performed in a few hours at 80 °C with only 0.1 mol-% catalyst and an equimolar amount of arene and alkyne to yield the *trans*-hydroarylation product in high yields and with good selectivity.

The reported reaction protocol is quite general with respect to the alkyne, but limited to electron-rich arenes, although this is a drawback common to all the catalytic systems described in the literature up to now. Furthermore, the reaction conditions involve the use of a relatively high reaction temperature and, most notably, of a great excess of a strong acid. Both these requirements potentially limit the

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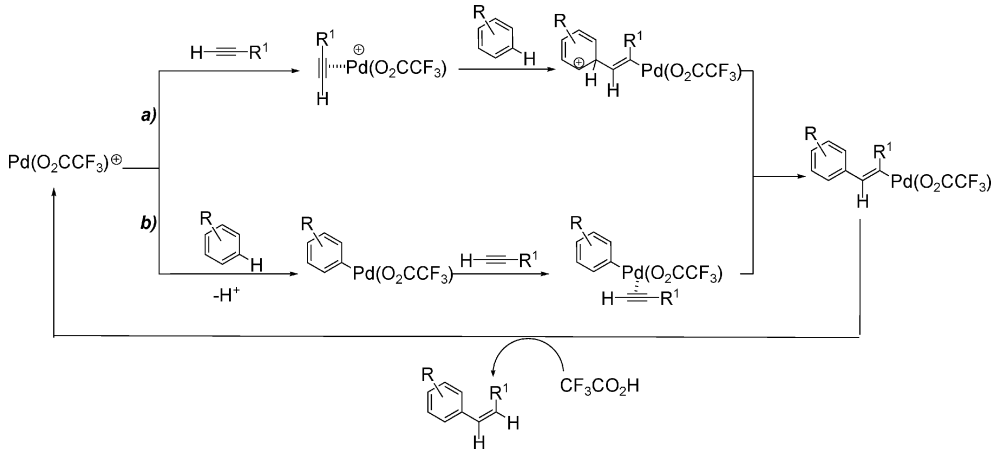


Scheme 1. Proposed reaction mechanisms for the hydroarylation of alkynes: a) Friedel–Crafts-type alkenylation; b) arene metallation.

application of this synthetic method as additional undesired reactions, such as double-bond isomerisation, hydrolysis, alkyne hydration and/or polymerisation, are promoted.[13]

In this contribution, we demonstrate that chelating dicarbene palladium(II) complexes bearing weakly coordinating anionic ligands are more efficient catalysts that can be conveniently employed at room temperature. Furthermore, the use of these catalysts with acids stronger than trifluoroacetic acid allows the amount of acid employed as additive to be significantly reduced. Most remarkably, we show that the nature of the employed acid, and in particular its strength and the coordinating ability of its conjugated base, has a significant effect on the reaction outcome with dicarbene palladium(II) catalysts, producing not only differences in catalytic activity but also dramatic changes in reaction selectivity.

Results and Discussion

In our previous work[13b] we showed that dicarbene complexes with coordination sets differing only in the halide ligands (e.g., complexes **3**–**5**, Figure 1) exhibited an almost identical catalytic performance within the margin of experimental error. Consequently, it appeared reasonable to assume that under the adopted reaction conditions [1 equiv. alkyne, 1 equiv. arene, 0.001 equiv. catalyst, 5 mL CF_3COOH/1,2-dichloroethane (4:1), approximate reagent concentration 2.1 M, 80 °C, 5 h] a double M–X/CF_3COO–H exchange occurs, as predicted on the basis of DFT calculations by Strassner et al.[15]

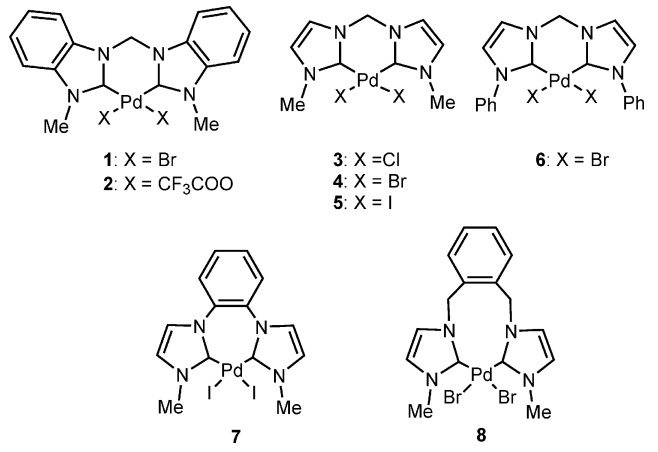
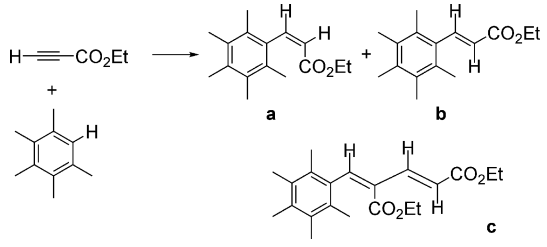


Figure 1. Complexes **1**–**8**.

Effect of the Addition of a Silver Salt

To confirm that the real catalytically active species contains two trifluoroacetate ligands in the coordination sphere we performed a standard hydroarylation reaction between pentamethylbenzene and ethyl propiolate using complex **1** (Figure 1, Scheme 2) in the presence of 2 equiv. with respect to the catalyst of silver trifluoroacetate.



Scheme 2. Hydroarylation reaction between pentamethylbenzene and ethyl propiolate.

The conversion curve (Figure 2, open circles) clearly shows that the reaction proceeds slightly more rapidly than in the absence of the silver salt (Figure 2, filled circles). We repeated the same reaction at room temperature and gratifyingly after 23 h we obtained a good conversion (74%; Figure 2, open squares); for comparison, analogous reactions performed at room temperature with complexes containing bromide or iodide ligands and in the absence of silver salts afforded only a few percent yield after 24 h.[13]

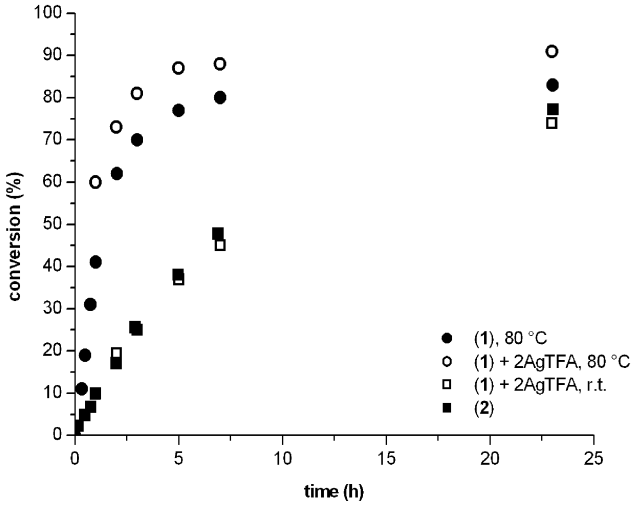


Figure 2. Conversion vs. time diagram for the reaction of pentamethylbenzene and ethyl propiolate catalysed by complexes **1** and **2** at room temperature and 80 °C, with or without added silver trifluoroacetate.

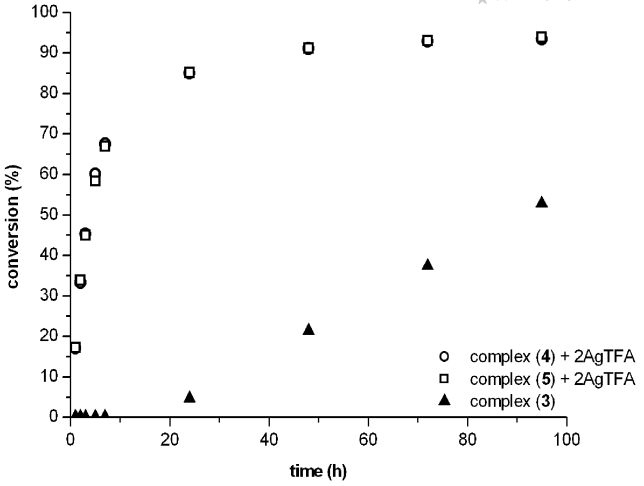


Figure 3. Conversion vs. time diagram for the reaction of pentamethylbenzene and ethyl propiolate catalysed by complexes **3**–**5** at room temperature, with or without added silver trifluoroacetate.

The reaction yield achieved at room temperature after 24 h was comparable to that observed at 80 °C in the absence of added silver salt (83%), although the initial rate was lower. Moreover, by performing the reaction at room temperature, we could avoid the occurrence of side reactions like hydrolysis of the ester function and *Z*/*E* isomerisation of the olefin, thereby increasing the selectivity towards the desired *Z* product (96 vs. 77% at 80 °C).

As a further confirmation of our hypothesis, we performed the reaction with preformed complex **2** bearing two coordinated trifluoroacetates (Figure 2, filled squares). As expected, the conversion curve was found to be almost coincident with that of the complex generated in situ by adding silver trifluoroacetate to complex **1**.

At room temperature the Pd–X/Ag–TFA exchange reaction is fast and not influenced by the nature of the coordinated halides, as illustrated by the absence of any induction period and by the practically overlapping conversion curves when complexes **4** and **5** were used as catalysts in the presence of 0.002 equiv. of silver trifluoroacetate (Figure 3, open circles and squares). In contrast, we could observe a long induction period in a test reaction performed with complex **3** bearing chloride ligands in the absence of the silver co-catalyst (Figure 3, filled triangles), which is clearly necessary to generate the bis(trifluoroacetate) catalyst by Pd–X/H–TFA exchange. As stated above, under the same experimental conditions, complexes bearing bromide or iodide ligands, which are expected to be more strongly bonded to the metal[16] and therefore not so easily displaced by trifluoroacetate, are nearly inactive.

From these data it can be concluded that the halide/trifluoroacetate exchange is a crucial step in the formation of the competent catalytic species, which can be conveniently accelerated by using a silver trifluoroacetate co-catalyst.

Catalyst Screening

We then turned our attention to a comparison of the catalytic efficiency at room temperature of a series of palladium complexes with different dicarbene ligands (Figure 1). It has already been observed that the performance of these catalysts at 80 °C was influenced by the type of dicarbene ligand, without, however, clear evidence of the predominance of steric or electronic effects. Therefore we checked the catalytic efficiency of the palladium(II) complexes **1**, **4** and **6**–**8** in the presence of silver trifluoroacetate ([Ag]/[Pd] 2:1), using the standard reaction between pentamethylbenzene and ethyl propiolate. Conversion curves (Figure 4) revealed that all the employed complexes were active at room

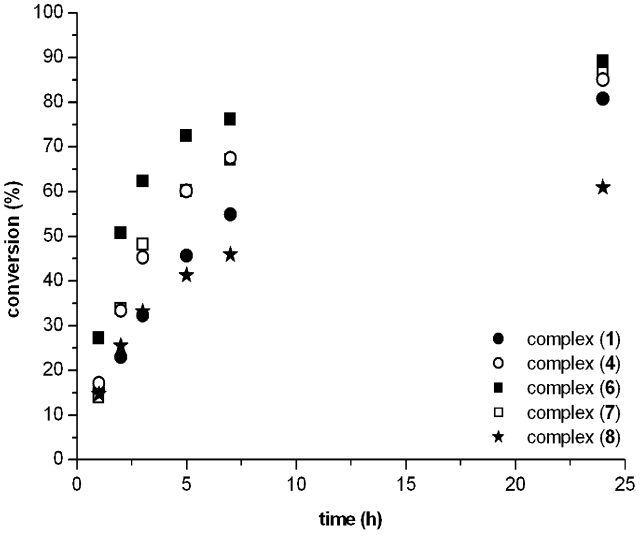


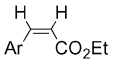
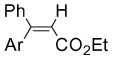
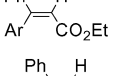
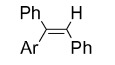
Figure 4. Conversion vs. time diagram for the reaction of pentamethylbenzene and ethyl propiolate catalysed by complexes **1**, **4** and **6**–**8** at room temperature and with added AgTFA.

temperature and that their performances, within the first 5 h, were quite different. The order of decreasing activity (**6** > **4** ≈ **7** > **1** > **8**) is comparable to that already observed at 80 °C and, in particular, complex **6** with the more hindering NHC ligand showed the highest activity. The conversion after 24 h with the benzimidazolin-2-ylidene complex **1** and the imidazolin-2-ylidene complexes **4**, **6** and **7** were similar and quite satisfactory, whereas that of complex **8** was significantly lower, probably because of catalyst decomposition after the first 7 h of reaction. These results suggest that the steric hindrance imposed by the chelating dicarbene ligand at the metal centre is an important factor in determining the reactivity of the catalyst. Further support for this hypothesis comes from preliminary data of electrochemical studies,[17] which have demonstrated that the reduction potentials of the metal in the employed catalysts, which is a measure of the electron density on the metal, cannot be correlated with their observed catalytic activity.

Arene and Alkyne Screening

By using complex **6**, which turned out to be the most active in the previous screening at room temperature, we set out to evaluate the generality of our catalytic system with respect to both the alkyne and the arene. Two sets of standard reagents were employed under the same reaction conditions without attempting to optimise the reaction yield. The results are reported in Tables 1, 2, and 3.

Table 1. Alkyne screening in hydroarylation reactions with pentamethylbenzene catalysed by complex **6** with added AgTFA.

Entry	Alkyne	Time [h]	Product	Yield[a] (*Z*:*E*)
1	H–≡–CO_2Et	5		72
		24		87
		48		94
2	Ph–≡–CO_2Et	24		7
		48		9
3[b]	Ph–≡–CO_2Et	24		8
		48		17
4	Ph–≡–H	48		52
5	Ph–≡–Ph	24		12
		48		20
6	Ph–≡–Me	5		49 (9:1)

[a] The yield was determined by GC–MS and/or ^{1}H NMR spectroscopy. [b] Reaction performed using complex **4** as catalyst. Reaction conditions: see the Exp. Sect.

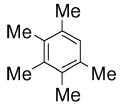
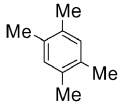
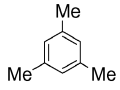
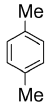
The highest activities and selectivities were observed with electron-poor terminal alkynes, whereas internal alkynes were converted to a minor extent (Table 1). Remarkably, the selectivities for the desired product were in all cases significantly improved in comparison with those obtained at 80 °C because competitive reactions were minimised at room temperature. For example, by using complex **1** at 80 °C, phenylacetylene gave only 20% yield of the desired product after 5 h because of competing alkyne hydration and polymerisation.[13b] On the other hand, with complex **6** at room temperature it was possible to obtain a yield of 52% after 48 h. The results with arylalkynes reported herein should be, however, treated with some caution because it has recently been demonstrated that trifluoroacetic acid alone can catalyse the hydroarylation of these substrates at temperatures close to room temperature.[18]

Table 2. Catalyst screening in the hydroarylation of ethyl phenylpropiolate (or of diphenylacetylene) with pentamethylbenzene, [Pd] = 0.5 mol-%.

Entry	Catalyst	Time [h]	Yield [%][a]
1	**1**	5	13
		24	33
		48	45
2	**4**	5	6
		24	16
		48	29
3[b]	**4**	5	4
		24	12
		48	17
4	**6**	5	1
		24	9
		48	19
5	**8**	5	19
		24	29
		48	30

[a] The yield was determined by GC–MS and/or ^{1}H NMR spectroscopy. [b] Alkyne = diphenylacetylene. Reaction conditions: see the Exp. Sect.

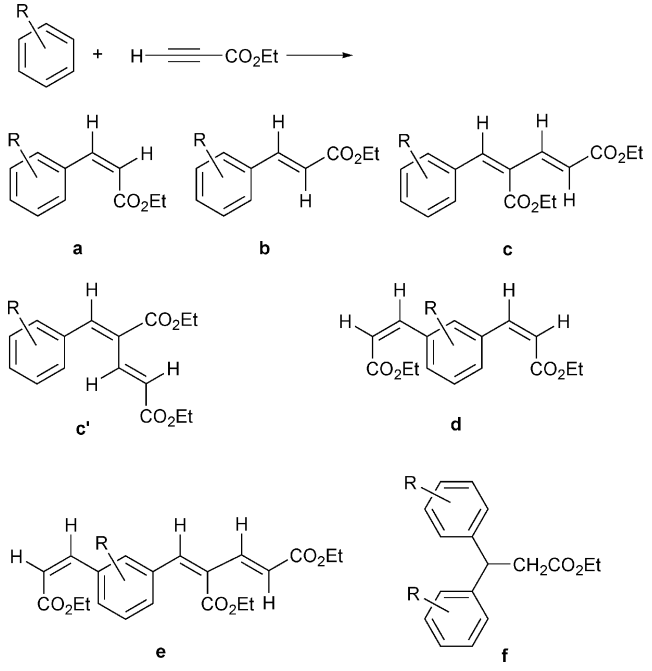
Table 3. Arene screening in the hydroarylation of ethyl propiolate catalysed by complex **6**.

Arene	Time [h]	Conv.[a]	Yield[a] **a**	**c**	**d**
	5	73	72	1	–
	24	88	87	1	–
	48	95	94	1	–
	5	42	40	–	2
	24	68	61	1	6
	48	84	76	1	8
	5	82	82	–	–
	24	90	90	–	–
	48	91	91	–	–
	5	3	3	–	–
	24	12	12	–	–
	48	20	20	–	–

[a] The conversion was based on the arene. The yield was determined by GC–MS and/or ^{1}H NMR spectroscopy. Reaction conditions: see the Exp. Sect.

Quite unexpectedly, by using catalyst **4** in the reaction between pentamethylbenzene and ethyl phenylpropiolate, a higher yield was obtained than with complex **6** (17% yield vs. 9%) (Table 1, entries 3 and 2, respectively), in contrast with the order of reactivity observed in the previous screening. To clarify this aspect we performed some additional tests on this reaction by using other catalysts in 0.5 mol-% amounts instead of the usual 0.1 mol-% because we also wanted to increase the otherwise rather low reaction rate with this alkyne. The results are summarised in Table 2.

The order of reactivity observed after 5 h in the reaction with ethyl phenylpropiolate (**8** > **1** > **4** > **6**) was completely reversed with respect to that obtained with ethyl propiolate and illustrated in Figure 4 (**6** > **4** > **1** > **8**). In both cases, at longer reaction times, complex **8** was found to be deactivated, presumably because of the comparatively low stability of this catalyst under the reaction conditions. These results highlight the importance of the steric properties of the alkyne in determining the efficiency of the catalytic system. A rationalisation of the different behaviour of the complexes with the two alkynes requires knowledge of the reaction mechanism. If we assume a Friedel–Crafts-type mechanism (Scheme 1, path a),[8] which at this stage seems more plausible for our system, then the observed reversal in the order of catalytic efficiency can be explained by considering that an increased steric bulk of the complex enhances the overall catalytic activity (e.g., by favouring protonolysis of the Pd–vinyl intermediate), but negatively affects alkyne coordination to the metal, shifting the equilibrium towards the free alkyne. This last effect is particularly important in the case of hindered internal alkynes such that the required coordination for electrophilic attack to the arene is strongly inhibited.



Scheme 3. Possible products of the alkyne hydroarylation reaction.

The screening of arenes was performed by reacting ethyl propiolate with different methyl-substituted benzenes using our best catalyst **6**. The results reported in Table 3 show that all the substrates were converted irrespective of the number of substituents, although the yield recorded with *p*-xylene was low. The distribution of the products (see Scheme 3) did not change significantly on going from pentamethylbenzene to *p*-xylene; the main product was always the *trans*-hydroarylation product, that is, the *Z* olefin. An exception to this trend is the reaction with 1,2,4,5-tetramethylbenzene, which yields as a major byproduct the double hydroarylation product **d** (Scheme 3). This is probably a consequence of the comparatively low solubility of the starting arene, which is always a shortcoming in this system and favours the reaction of a second molecule of the alkyne with the arene ring.

Effect of Acid and Conjugated Base

Another important parameter to be investigated was the role played by the acid on the reaction outcome. Up to now the standard acid employed in alkyne hydroarylation reactions was trifluoroacetic acid, which has to be added in very large amounts (arene/acid molar ratio of ca. 1:4) to promote reasonable catalytic activity. We have investigated the effect of changes in the nature and amount of added acid, varying both its strength and the coordinating properties of the conjugated base with the aim of decreasing the amount of acid while preserving catalytic activity. In a series of experiments, we used complex **1** in various strong acids HX, namely HTFA (pK_a = –0.25), HBF_4 (pK_a = –4.9) or HOTf (pK_a = –14), adding to the system 2 equiv. of the corresponding silver salt AgX with respect to **1**. Moreover, we reduced the quantity of the acid to an equimolar amount with respect to the arene. The conversion curves in Figure 5 show that the catalytic efficiency increased using stronger acids: for example, after 23 h, the arene conversion obtained with triflic acid was 65%, compared with 25% in trifluoroacetic acid. Quite unexpectedly though, the reaction was fastest in HBF_4, which is a significantly weaker acid than triflic acid; furthermore, with HBF_4, the conversion of the arene stopped abruptly at 50%. Analysis of the reaction products led to the unexpected conclusion that this was due to the prevalent formation of the double insertion product **c** (Scheme 3), which consumed two molecules of alkyne for each arene. Repeating the reaction with an arene/alkyne molar ratio of 1:2 resulted in 86% conversion with 86% selectivity towards product **c**. Remarkably, when simple $Pd(OAc)_2$ was employed as the catalyst under the same reaction conditions, a much lower catalytic activity was observed and it failed to show this peculiar selectivity, providing the conventional *trans*-hydroarylation product in 57% yield after 24 h.

Comparison of the selectivities for the three systems at 23 h (Figure 6) showed that the main product in trifluoroacetic acid was the *Z* olefin (selectivity 89%), whereas in tetrafluoroboric acid the double insertion product was pre-

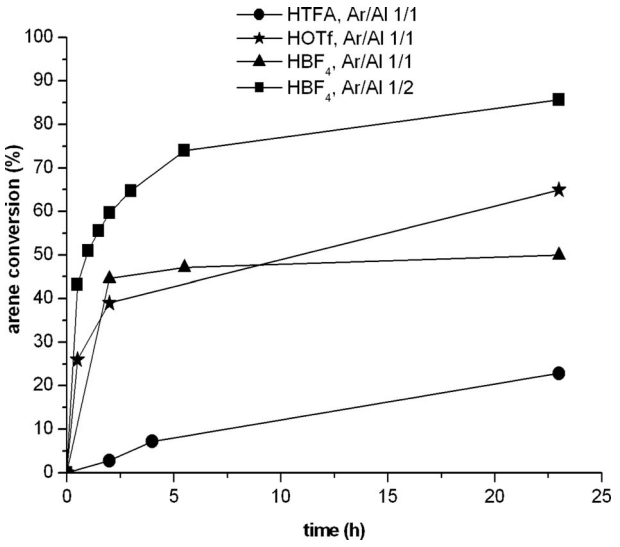


Figure 5. Arene conversion vs. time diagram for the reaction of pentamethylbenzene and ethyl propiolate catalysed by complex **1** in the presence of different HX acids and of the corresponding AgX salt; Ar/Al indicates the arene/alkyne molar ratio.

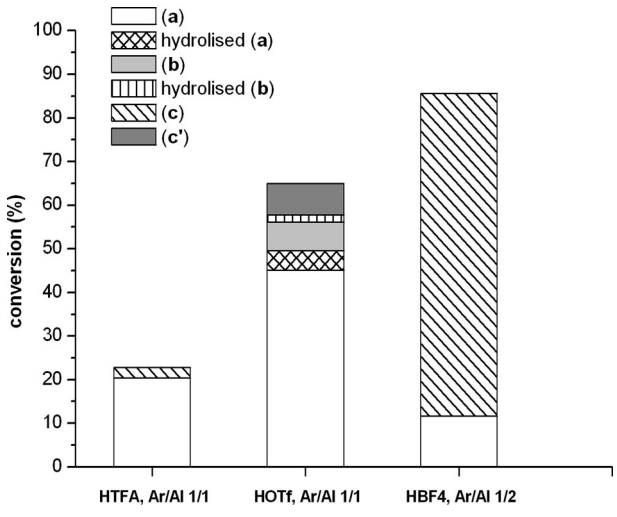


Figure 6. Selectivity at 23 h for the reaction of pentamethylbenzene and ethyl propiolate catalysed by complex **1** in the presence of different acids; Ar/Al indicates the arene/alkyne molar ratio.

dominant, as mentioned above (selectivity 86%). The catalytic system in triflic acid was not very selective (70% selectivity towards the *Z* olefin), the major byproducts being the *E* olefin, hydrolysed olefins and a double insertion product **c**′ (Scheme 3) with *Z*,*E* configuration instead of the usual *E*,*E* (isomer **c**). We have verified that the formation of these byproducts is triggered by the strong acidic environment: for example, pure product **c** dissolved in a mixture HOTf/1,2-dichloroethane isomerises to **c**′ within a few hours. Moreover, triflic acid was also found to promote the hydroarylation reaction to some extent in the absence of Pd complex catalysts.[19] A conversion of 14% with 64% selectivity for the *Z* product was recorded after 24 h. In contrast, neither tetrafluoroboric acid nor trifluoroacetic acid promoted the formation of hydroarylation products with ethyl propiolate in the absence of a Pd catalyst.

We also ran an experiment using oleum 20% as acid and silver tetrafluoroborate as co-catalyst. The activity of this system was superior to that of trifluoroacetic acid, but inferior to that of tetrafluoroboric and triflic acid. Furthermore, complex product mixtures were formed, including several hydrolysis and isomerisation products, so tests with this acid were not pursued further.

Considering the peculiar reaction selectivity obtained with tetrafluoroboric acid, we set out to further investigate this system. First, we ran a reaction with an arene/alkyne molar ratio of 1:3 to verify if the formation of the double insertion product **c** took place after the *trans*-hydroarylation reaction and to evaluate the selectivity of the system towards multiple insertions. The selectivity towards product **c** (86% after 24 h) was the same as that obtained with an arene/alkyne molar ratio of 1:2. Moreover, we did not observe a decrease in the amount of *trans*-hydroarylation product **a** in favour of product **c**. This indicates that the synthesis of **c** is not sequential to the formation of **a**. Consequently, it is reasonable to assume that **c** is formed directly by insertion of a second alkyne molecule into the Pd–vinyl intermediate (Scheme 1), as already proposed by Fujiwara and co-workers.[7b]

In a subsequent experiment the quantity of tetrafluoroboric acid was reduced to an arene/acid molar ratio of 1:0.1; the system was still very active in the hydroarylation of alkynes, reaching 59% conversion after 25 h compared with 86% with an equimolar amount of acid (Figure 7). Moreover, the selectivity of the system was not affected by the use of a reduced amount of acid as it remained constant at 86% in product **c**. Interestingly, the same reaction run with the bis-trifluoroacetato complex **2** in HBF_4 (Figure 7, full squares) was very slow (14% conversion after 25 h) and also the selectivity of the system towards the double insertion product reached only 67% (compared with 86% with complex **1** and $AgBF_4$).

These data confirm that the presence of a strong acid is necessary for the success of the reaction; the high activity observed with acids stronger than the standard trifluoroacetic acid is attributable to the faster protonolysis of the Pd–vinyl intermediate, which is generally proposed as the rate-determining step of the catalytic cycle, particularly in the case of the Friedel–Crafts-type mechanism (Scheme 1).[8a] However, no simple direct correlation is observed between the strength of the acid and the efficiency of the catalytic process. We interpret this by considering that the coordinating ability of the conjugated base ($CF_3COO^- > CF_3SO_3^- > BF_4^-$) also influences the catalytic activity: a weaker acid like HBF_4 ($pK_a = -4.9$) performs better than a stronger acid like HOTf ($pK_a = -14$) because its conjugated base BF_4^- compared with $CF_3SO_3^-$ leaves two coordination sites on the metal centre almost free and capable of accommodating the reagents. Similarly, the presence of more strongly coordinating trifluoroacetate ligands on the starting complex strongly decreases the catalytic activity in tetrafluoroboric acid. The same considera-

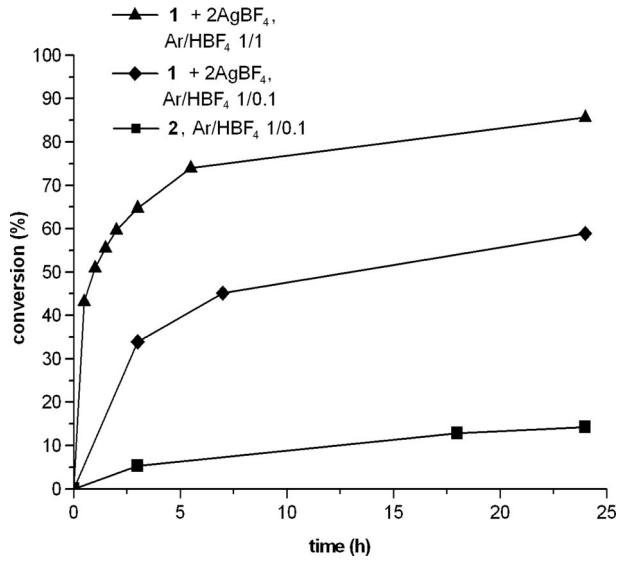


Figure 7. Arene conversion vs. time diagram for the reaction of pentamethylbenzene and ethyl propiolate catalysed by complexes **1** and **2** in HBF_4; [arene]/[alkyne] = 1:2.

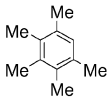
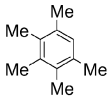
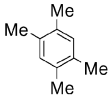
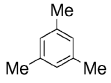
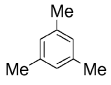
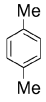
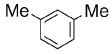
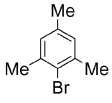
tions could be invoked to explain the dramatic change in the reaction selectivity observed with HBF_4 as in this case the metal centre should better coordinate a second molecule of alkyne thereby preferentially affording the double insertion product **c**. However, the selectivity maintained by using simple $Pd(OAc)_2$ in HBF_4 makes it apparent that this explanation is not fully satisfactory. Furthermore, very recently Oyamada and Kitamura showed that some bidentate phosphane ligands, most notably diphenylphosphanylethane (dppe), were able to steer the reaction selectivity towards product **c**, even when using trifluoroacetic acid as a cosolvent.[20] Therefore, the high preference for the formation of the double insertion product **c** appears at present to be a peculiarity of selected palladium(II) complex catalysts. We are currently investigating whether ligand features determine this selectivity change.

Substrate Screening in HBF_4

The generality of the preferred reaction pathway with tetrafluoroboric acid leading to the double insertion product has been evaluated with respect to both the alkyne and the arene (Tables 4 and 5). Complex **1** (0.1 mol-%) in the presence of $AgBF_4$ (0.2 mol-%) was used under standard reaction conditions (arene/alkyne molar ratio of 1:1, arene/HBF_4 molar ratio of 1:1, 1,2-dichloroethane, room temperature).

The results reported in Table 4 demonstrate that the effect of the addition of $HBF_4/AgBF_4$ on the selectivity of the reaction is general: the double insertion product **c** was the major product with all the arene substrates employed. The recorded yield in **c** after 24 h depends on the nature of the arene and follows the already observed trends for Pd-catalysed hydroarylation reactions,[7,13] that is, it decreases for less methyl-substituted arenes or upon introduction of

Table 4. Arene screening in the hydroarylation of ethyl propiolate catalysed by complex **1** in HBF_4.

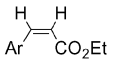
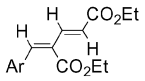
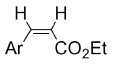
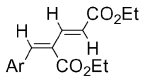
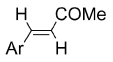
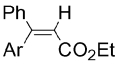
Entry	Arene	Time [h]	Conv.[a]	Yield[a] a	c	d	e	f
1		5	47 (88)	6	41	–	–	–
		24	50 (93)	7	43	–		–
2[b]		5	74 (71)	6	68	–	–	–
		24	86 (80)	12	74	–	–	–
3		5	25 (52)	–	23	–	2	–
		24	42 (88)	2	34	–	6	–
4		5	40 (84)	<1	36	<1	4	–
		24	48 (99)	2	38	3	5	–
5[b]		5	60 (130)	2	46 (6[c])	–	4	–
		24	76 (172)	5	55 (9[c])	–	7	–
6		24	4 (7)	1	3	–	–	–
		48	8 (12)	4	4	–	–	–
7		24	22 (27)	2	6 (4)[d]	–	–	5
		48	29 (34)	3	8 (4)[d]	–	–	7
8		24	4 (7)	1	3	–	–	–
		48	13 (22)	4	9	–	–	–

[a] The conversion was based on the arene. The conversion based on the alkyne is presented in parentheses. The yield was determined by GC–MS and/or ^1H NMR spectroscopy. [b] Reaction performed by using an arene/alkyne molar ratio of 1:2. [c] Additional yield in the product resulting from double insertion at both the 2- and 6-positions. [d] Yields of the double insertion product at the 2-position or, in parentheses, at the 5-position. Reaction conditions: see the Exp. Sect.

an electron-withdrawing group into the arene, as in 2-bromo-1,3,5-trimethylbenzene (Table 4, entry 8). The alkyne/arene molar ratio was found to influence the product distribution (Table 4, entries 4 and 5); the main product was always the double insertion product, but at a lower arene/alkyne ratio the double *trans*-hydroarylation product **d** was not present.

The position of the methyl substituents on the ring also played an important role in determining the reactivity of the substrates; for example, *p*-xylene showed a lower reactivity than *m*-xylene (Table 2, entries 6 and 7) and this can be attributed to the activation of both the 2- and 5-positions of the ring in the latter case. Moreover, with *m*-xylene a 2:1 arene/alkyne adduct has been isolated, which is pre-

Table 5. Alkyne screening in hydroarylations with pentamethylbenzene catalysed by complex **1** in HBF_4.

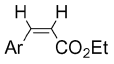
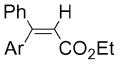
Entry	Alkyne	Time [h]	Product	Yield[a] (*Z*:*E*)
1	H–≡–CO_2Et	5		6
				41
2[b]	H–≡–CO_2Et	5		6
				68
3	H–≡–COMe	5		43
4	Ph–≡–H	5		59
5	Ph–≡–CO_2Et	24		23 (20:3)
6	Ph–≡–Ph	5		12 (12:0)
		24		33 (1:10)
		48		42 (0:42)
7	Ph–≡–Me	5		40

[a] The yield was determined by GC–MS and/or ^1H NMR spectroscopy. [b] The reaction was performed by using an arene/alkyne molar ratio of 1:2. Reaction conditions: see the Exp. Sect.

sumably formed by a hydroarylation reaction of olefin **a**. Altogether, the conversions are remarkably good and comparable to those observed in trifluoroacetic acid, despite the smaller quantity of acid used.

Concerning the behaviour of this catalytic system in the reaction of pentamethylbenzene with differently substituted alkynes (Table 5), terminal alkynes were found once more to be more reactive than internal ones. The selectivity of the system strongly depends on the nature of the alkyne. Terminal alkynes conjugated with electron-withdrawing groups, like ethyl propiolate, predominantly give the double insertion product **c**. A double insertion product is also produced as a minor product with 3-butyn-2-one; in this case, the Pd–vinyl intermediate undergoes rapid isomerisation to yield the *cis*-hydroarylation product. In this case, however, different stereoisomers of the double insertion product can form so that additional work is needed for their identification and quantification. Finally, no double insertion product was observed with terminal or internal arylalkynes. Possibly, in this case the coordination of a second molecule of alkyne to the Pd–vinyl intermediate is unfavoured for steric reasons, thus preventing the formation of product **c**. Note also that in the case of arylalkynes the hydroarylation reaction was promoted to a certain degree by HBF_4 alone (Table 6), which clearly complicates the evaluation of the catalytic performance of the Pd complex. The acid also promotes isomerisation processes, particularly marked in the case of diphenylacetylene (Table 5, entry 6): at 5 h the only observed product is the *Z* olefin, whereas at 48 h it is the *E* isomer.

Table 6. Alkyne screening in hydroarylations with pentamethylbenzene in HBF_4 without metal catalyst.

Entry	Alkyne	Time [h]	Product	Yield[a] (*Z*:*E*)
1	H–≡–CO_2Et	24		0
2	Ph–≡–H	24		32
3	Ph–≡–CO_2Et	24		15
4	Ph–≡–Ph	24		30 (8:22)

[a] The yield was determined by GC–MS and/or ^1H NMR spectroscopy. Reaction conditions: see the Exp. Sect.

Conclusions

We have been able to significantly improve our original system for the hydroarylation of alkynes with chelating dicarbene palladium(II) catalysts by the appropriate choice of additives such as a strong acid and a silver salt. By using a catalyst with weakly coordinating anionic ligands, generated in situ upon addition of 2 equiv. of the corresponding silver salt, the reaction can be performed at room temperature, thus minimising side reactions, like hydration and polymerisation of the alkyne and hydrolysis of the ester function. The use of acids stronger than trifluoroacetic acid, like HBF_4 or HOTf, allows a significant reduction in the quantity of the acid used while maintaining the catalytic activity. Most notably, use of the dicarbene Pd catalyst **1** in HBF_4 with 2 equiv. of $AgBF_4$ produced a highly active catalytic system able to direct the selectivity of the reaction towards the formation of the double insertion product. The applicability of this reaction protocol is quite general with respect to electron-rich arenes.

It is important to note that in the light of the findings presented herein, the role of the chelating dicarbene ligand is not limited to the stabilisation of the metal in its +II oxidation state: the ligand is also able to promote catalytic activity and to control the reaction selectivity. Given the

nature of these ligands, this is further confirmation that the combination of a strongly coordinating and electron-donating ligand, together with the presence of positive charge on the metal, may yield complexes that in spite of the nature of the ligand exhibit excellent performance as electrophilic catalysts.[21]

Work currently in progress aims at expanding the scope of the reaction to different classes of aromatic systems, at finding novel applications for electrophilic metal carbene complexes as well as at developing still less-impacting reaction media.

Experimental Section

General Remarks: All manipulations were carried out using standard Schlenk techniques under argon or dinitrogen. The reagents were purchased by Aldrich as high-purity products and generally used as received. Complexes **1**,[13b] **3**,[22] **4**,[23] **5**,[24] **6**,[25] **7**[26] and **8**,[27] were prepared according to literature procedures. All solvents were used as received as technical grade solvents. NMR spectra were recorded with a Bruker Avance 300 spectrometer (300.1 MHz for ^{1}H and 75.5 for ^{13}C). Chemical shifts (δ) are reported in units of ppm relative to the residual solvent signals. Elemental analyses were carried out by the microanalytical laboratory of our department with a Fisons EA 1108 CHNS-O apparatus.

Synthesis of (1,1′-Dimethyl-3,3′-methylenedibenzimidazolin-2,2′-ylidene)palladium(II) Bis(trifluoroacetate) (2): A suspension of complex **1** (0.20 g, 0.25 mmol) and AgTFA (0.11 g, 0.50 mmol) in acetonitrile (15 mL) was heated at 60 °C for 4 h and then filtered through Celite to remove silver salts. The solvent was removed under vacuum and the off-white residue was washed with diethyl ether (2 × 5 mL), filtered and dried under vacuum (132 mg, yield 76%). $C_{21}H_{16}F_6N_4O_4Pd{\cdot}0.5AgBr$ (702.7): calcd. C 35.90, H 2.30, N 7.97; found C 35.63, H 1.79, N 7.88. ^{1}H NMR ([D$_6$]DMSO, 25 °C): δ = 4.02 (s, 3 H, CH_3), 6.75 and 7.40 (2 d, 1 H, CH_2), 7.40–7.60 (m, 4 H, Ar), 7.76 (d, 1 H, CH=CH), 8.25 (d, 1 H, CH=CH) ppm. ^{13}C{^{1}H} NMR ([D$_6$]DMSO, 25 °C): δ = 34.0 (CH_3), 57.1 (CH_2), 111.3, 111.9, 124.5, 124.6, 132.3, 133.7 (CAr) ppm. Signals arising from carbene carbon atoms and CF_3COO groups were not detected.

General Procedures for the Catalytic Tests

Tests Reported in Tables 1, 2, and 3. Determination of Conversion Curves Reported in Figures 2, 3, and 4: The arene (13.2 mmol, if solid), the palladium(II) complex (1.32 or 6.6 μmol for the tests reported in Table 2) and silver trifluoroacetate (2.64 or 13.2 μmol for the tests reported in Table 2) were placed in a 100 mL round-bottomed flask previously evacuated and filled with argon. Trifluoroacetic acid (4 mL), 1,2-dichloroethane (1 mL) and the arene (if liquid) were then added and the resulting solution was stirred at 25 °C for 5 min. Finally the alkyne (13.2 mmol) was added and the reaction mixture was stirred at 25 °C for the time indicated in the tables. Portions of the solution (0.2 mL) were drawn off from the reaction mixture and analysed by ^{1}H NMR or GC–MS.

Tests Reported in Tables 4 and 5. Determination of the Conversion Curves Reported in Figure 5: The arene (13.2 mmol, if solid), the palladium(II) complex (1.32 μmol) and the silver salt (2.64 μmol, AgTFA when HTFA was used, AgOTf for HOTf, $AgBF_4$ for HBF_4) were placed in a 100 mL round-bottomed flask previously evacuated and filled with argon. The acid (13.2 mmol), 1,2-dichloroethane (the quantity necessary to reach a total volume of 6.3 mL) and the arene (if liquid) were then added and the resulting solution was stirred at 25 °C for 5 min. Finally the alkyne (13.2 mmol) was added and the reaction mixture was stirred at 25 °C for the time indicated in the tables. Portions of the solution (0.2 mL) were drawn off from the reaction mixture and analysed by ^{1}H NMR or GC–MS. The same conditions were used for the tests reported in Table 6, however, without the use of a catalyst and silver salt.

Determination of Conversion Curves Reported in Figure 7: Pentamethylbenzene (13.2 mmol), the palladium(II) complex (1.32 μmol) and $AgBF_4$ (2.64 μmol) were placed in a 100 mL round-bottomed flask previously evacuated and filled with argon. HBF_4 (13.2 mmol or 1.32 mmol) and 1,2-dichloroethane (the quantity necessary to reach a total volume of 6.3 mL) were then added and the resulting solution was stirred at 25 °C for 5 min. Finally, ethyl propiolate (13.2 mmol) was added and the reaction mixture was stirred at 25 °C. Portions of the solution (0.2 mL) were drawn off from the reaction mixture and analysed by ^{1}H NMR or GC–MS.

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