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Heck reaction of aryl halides with linear or cyclic alkenes catalysed by a tetraphosphine/palladium catalyst

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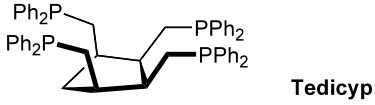
Abstract—*cis,cis,cis*-1,2,3,4-Tetrakis(diphenylphosphinomethyl)cyclopentane/$[PdCl(C_3H_5)]_2$ system catalyses efficiently the Heck reaction of aryl halides with linear alkenes such as pent-1-ene, oct-1-ene or dec-1-ene. Selectivities up to 70% in favour of *E*-1-arylalk-1-ene isomers can be obtained. In the presence of cyclic alkenes the selectivities of the reactions strongly depends on the ring size. Addition to cyclohexene or cycloheptene led mainly to 1-arylcycloalk-3-ene derivatives. On the other hand, addition to cyclooctene led to 1-arylcycloalk-1-ene adducts. © 2003 Elsevier Science Ltd. All rights reserved.

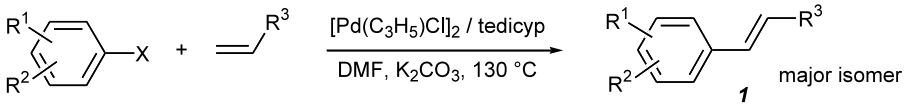
Palladium-catalysed Heck vinylation reaction is one of the most powerful method for the formation of C–C bonds.[1] The efficiency of several catalysts for the reaction of aryl halides with acrylates has been studied in detail. On the other hand, the reaction in the presence of simple linear or cyclic alkenes such as oct-1-ene or cyclooctene has attracted less attention.[2,3] A few ligands have been successfully employed for the reaction in the presence of such substrates. The most popular one is triphenylphosphine, but the catalysts formed by association of this ligands with palladium complexes is generally not very efficient in terms of ratio substrate/catalyst[2a,3a–d] and 1–10% of this catalyst must often be used. For a few years, some more robust and more efficient catalysts such as palladacycles[4] have been tested with these substrates. For example, Beller et al. have reported that the palladacycle $[Pd(o\text{-tol})(OAc)]_2$ is very efficient for the reaction of 4-bromoacetophenone with cyclopentene or cyclohexene.[3f] In the monophosphine ligand series, interesting results have been reported recently by Fu et al. They described that the ligand $P(t\text{-Bu})_3$ is an efficient catalyst for the reaction of 4-chloroacetophenone with hex-1-ene even at room temperature.[2d] If monophosphine ligands or palladacycles have been successfully used for the reaction with these alkenes, to the best of our knowledge, the efficiency of tetraphosphine ligands has not been demonstrated.



Tedicyp

Figure 1.

The nature of phosphine ligands on complexes has an important influence on the rate of catalysed reactions. In order to obtain highly stable palladium catalysts, we have prepared the new tetraphosphine ligand,[5] *cis,cis,cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane or tedicyp[6] (Fig. 1) in which four diphenylphosphino groups are stereospecifically bound to the same face of a cyclopentane ring. The presence of these four phosphines close to the metal centre seems to increase the coordination of the ligand to the metal and



Scheme 1.

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therefore increase the stability of the catalyst. We have reported recently the first results obtained in allylic substitution,[6] for Suzuki cross-coupling[7] and for Heck reaction using tedicyp as the ligand.[8] Herein, we wish to report on the Heck reaction in the presence of aryl halides with non functionalised linear or cyclic alkenes using tedicyp as the ligand.

For this study, based on our previous results,[8] DMF was chosen as the solvent and potassium carbonate as the base. The reactions were performed at 130°C under argon in the presence of a ratio 1/2 of $[Pd(C_3H_5)Cl]_2$/tedicyp as catalyst.

First, we studied the reactivity of dec-1-ene, oct-1-ene and pent-1-ene with several aryl halides in the presence of 1–0.01% catalyst (Scheme 1, Table 1). In all cases mixtures of isomers were obtained. The formation of up to 15 isomers has been observed but selectivities of 34–70% in favour of *E*-1-arylalk-1-ene adducts have been obtained with some substrates. The selectivity depends on the aryl halide and on the alkene. Better selectivities are observed with aryl bromides than with iodobenzene (Table 1, entries 1–20). Furthermore, the presence of electron-withdrawing substituents on the aryl bromides increases the selectivity in favour of *E*-1-arylalk-1-ene. On the other hand, with an electron

Table 1. Heck reactions with linear alkenes catalysed by tedicyp–palladium complex (Scheme 1)[9]

Entry	Aryl halide	Alkene	Ratio substrate/catalyst	Selectivity in favour of isomer ***1*** (%) (Scheme 1)[a]	Yield (%)[b]
1	Iodobenzene	Dec-1-ene	10000	43	88 (90)
2	4-Bromoanisole	Dec-1-ene	100	51	58 (65)
3	4-Bromoacetophenone	Dec-1-ene	10000	61	84 (94)
4	4-Bromobenzophenone	Dec-1-ene	2000	64	95 (100)
5	4-Bromobenzophenone	Dec-1-ene	10000	64	(80)
6	4-Bromobenzaldehyde	Dec-1-ene	10000	66	91 (100)
7	4-Trifluoromethylbromobenzene	Dec-1-ene	10000	59	88 (95)
8	4-Bromobenzonitrile	Dec-1-ene	10000	52	88 (92)
9	3,5-Bistrifluoromethylbromobenzene	Dec-1-ene	10000	70	82 (88)
10	2-Bromotoluene	Dec-1-ene	1000	36	70
11	2-Bromothiophene	Dec-1-ene	1000	34	82 (92)
12	3-Bromopyridine	Dec-1-ene	1000	50	88 (100)
13	3-Bromoquinoline	Dec-1-ene	10000	62	85 (90)
14	Iodobenzene	Oct-1-ene	1000	59	92 (100)
15	Iodobenzene	Oct-1-ene	10000	60	(43)
16	4-Bromoanisole	Oct-1-ene	1000	62	90 (100)
17	4-Bromoacetophenone	Oct-1-ene	1000	68	90 (100)
18	Iodobenzene	Pent-1-ene	1000	58	76 (100)[c]
19	4-Bromoanisole	Pent-1-ene	250	66	55[c]
20	4-Bromoacetophenone	Pent-1-ene	1000	70	87 (100)[c]
21	Iodobenzene	3,3-Dimethylbut-1-ene	250	>97	82 (100)[c]
22	4-Bromoacetophenone	3,3-Dimethylbut-1-ene	250	>97	77[c]
23	4-Bromobenzophenone	3,3-Dimethylbut-1-ene	250	>97	79[c]
24	4-Trifluoromethylbromobenzene	3,3-Dimethylbut-1-ene	250	>97	77[c]
25	Iodobenzene	Allylbenzene	1000	5/4/91[d]	80
26	Bromobenzene	Allylbenzene	250	4/3/93[d]	89 (95)
27	2-Bromotoluene	Allylbenzene	250	66/34[e]	88
28	9-Bromoanthracene	Allylbenzene	100	82/18[f]	91
29	2,6-Dimethylbromobenzene	Allylbenzene	250	85/15[g]	82 (97)

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/tedicyp 1/2 see Ref. 6, ArX (1 equiv.), alkene (2 equiv.), K_2CO_3 (2 equiv.), DMF, 130°C, 20 h, under argon, isolated yields (mixture of isomers).

[a] Selectivities determined by GC and NMR.

[b] Yields in parentheses correspond to GC or NMR yields.

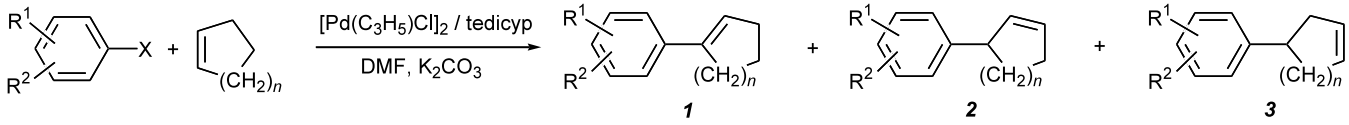
[c] Reaction performed in an autoclave.

[d] Ratio of the isomers 2,3-diphenylprop-1-ene/*Z*-1,3-diphenylprop-1-ene/*E*-1,3-diphenylprop-1-ene.

[e] Ratio of the isomers *E*-1-phenyl-3-(2-methylphenyl)prop-1-ene/*E*-3-phenyl-1-(2-methylphenyl)prop-1-ene.

[f] Ratio of the isomers *E*-1-phenyl-3-(9-anthryl)prop-1-ene/*E*-3-phenyl-1-(9-anthryl)prop-1-ene.

[g] Ratio of the isomers *E*-1-phenyl-3-(2,6-dimethylphenyl)prop-1-ene/*E*-3-phenyl-1-(2,6-dimethylphenyl)prop-1-ene.



Scheme 2.

rich heteroaryl bromide: 2-bromothiophene or in the presence of the sterically hindered 2-bromotoluene, low selectivities of 34 and 36% are obtained (Table 1, entries 10 and 11). The length of the alkyl chain on the alkene has also an influence on the selectivity. Higher selectivities in favour of *E*-1-arylalkene isomers are obtained with pent-1-ene than with dec-1-ene. An isomerisation of dec-1-ene is observed during the reaction. Heck reaction with this mixture of isomers probably led to several adducts with internal C=C bond and internal aryl substituent. However, even when the reaction is performed in the presence of a larger excess of alkene (10 equiv.) a similar mixture of isomers is obtained. The temperature has also a minor influence on the selectivity. The addition of 4-bromoacetophenone to dec-1-ene at 130 and 100°C led to *E*-1-(4-acetylphenyl)dec-1-ene in 61% selectivity.

The reaction of aryl halides with sterically hindered 3,3-dimethylbut-1-ene led to the corresponding adducts with a very high selectivity in favour of *E*-1-aryl-3,3-dimethylbut-1-ene in good yields (Table 1, entries 21–24). Reaction of sterically hindered aryl halides with allyl benzene led mainly to *E*-1-phenyl-3-arylprop-1-ene derivatives (Table 1, entries 27–29). As expected, a higher selectivity is observed with 2,6-dimethylbromobenzene than with 2-bromotoluene.

Several reactions were also performed with cycloalkenes: cyclopentene, cyclohexene, cycloheptene, cyclooctene and cyclododecene (Scheme 2, Table 2). In all cases, in the presence of 0.01–1% catalyst, the addition products are obtained in good yields; however, mixtures of isomers are obtained. The selectivity strongly depends on the ring size. With cyclooctene the

Table 2. Heck reactions with cycloalkenes catalysed by tedicyp-palladium complex (Scheme 2)[9]

Entry	Aryl halide	Cycloalkene	Temp. (°C)	Ratio substrate/catalyst	Selectivity in isomer ***1*** or ratio of isomers ***1***/***2***/***3*** (%) (Scheme 2)[a]	Yield (%)[b]
1	4-Bromoacetophenone	Cyclopentene	130[c]	1000	75/8/17	87 (100)
2	4-Bromoacetophenone	Cyclopentene	130[c]	10000	90/2/8	(100)
3	4-Bromoanisole	Cyclopentene	130[c]	250	19/70/11	92 (100)
4	4-Bromoacetophenone	Cyclohexene	80	100	3/5/92	(50)
5	4-Bromoacetophenone	Cyclohexene	130[c]	100	3/5/92	81 (100)
6	4-Bromoacetophenone	Cyclohexene	130[c]	1000	2/5/93	(100)
7	Iodobenzene	Cycloheptene	100	250	2/14/84	90
8	Iodobenzene	Cycloheptene	100	1000	2/15/83	(55)
9	4-Bromoacetophenone	Cycloheptene	100	250	5/11/84	90 (100)
10	4-Bromoacetophenone	Cycloheptene	100	1000	5/12/83	(72)
11	4-Trifluoromethylbromobenzene	Cycloheptene	100	250	6/11/83	88 (100)
12	4-Trifluoromethylbromobenzene	Cycloheptene	100	1000	6/12/82	(52)
13	4-Bromoanisole	Cycloheptene	100	100	1/21/78	95
14	4-Bromoanisole	Cycloheptene	100	250	1/22/77	(60)
15	Iodobenzene	Cyclooctene	130	1000	***1***: 87%	83 (100)
16	Iodobenzene	Cyclooctene	130	10000	***1***: 85%	(66)
17	4-Bromobenzophenone	Cyclooctene	130	1000	***1*** >90%	95 (100)
18	4-Bromobenzophenone	Cyclooctene	130	10000	***1*** >90%	(40)
19	4-Bromoacetophenone	Cyclooctene	130	2000	***1*** >90%	85 (100)
20	4-Bromobenzaldehyde	Cyclooctene	130	10000	***1***: 87%	82 (100)
21	4-Trifluoromethylbromobenzene	Cyclooctene	130	1000	***1*** >90%	96
22	4-Trifluoromethylbromobenzene	Cyclooctene	130	10000	***1*** >90%	(25)
23	4-Bromobenzonitrile	Cyclooctene	130	250	***1*** >90%	89 (100)
24	4-Nitrobromobenzene	Cyclooctene	130	250	***1*** >90%	92 (100)
25	3,5-Bistrifluoromethylbromobenzene	Cyclooctene	130	1000	***1*** >90%	58
26	4-Bromoanisole	Cyclooctene	130	1000	***1***: 85%	83 (98)
27	2-Iodothiophene	Cyclooctene	130	250	***1*** >90%	91 (100)
28	2-Iodothiophene	Cyclooctene	130	1000	***1*** >90%	(77)
29	3-Bromopyridine	Cyclooctene	130	250	***1*** >90%	90 (100)
30	3-Bromopyridine	Cyclooctene	130	1000	***1*** >90%	73
31	3-Bromoquinoline	Cyclooctene	130	1000	***1*** >90%	69
32	2-Bromotoluene	Cyclododecene	130	1000	Mixture[d]	71
33	Iodobenzene	Cyclododecene	130	1000	Mixture[e]	80
34	4-Bromoacetophenone	Cyclododecene	130	1000	Mixture[e]	70
35	4-Bromoanisole	Cyclododecene	130	250	Mixture[e]	80

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/tedicyp 1/2 see Ref. 6, ArX (1 equiv.), cycloalkene (2 equiv.), K_2CO_3 (2 equiv.), DMF, 20 h, under argon, isolated yields (mixture of isomers).

[a] Selectivities determined by GC and NMR.

[b] Yields in parentheses correspond to GC or NMR yields.

[c] Reaction performed in an autoclave.

[d] Mixture of 4 isomers.

[e] Mixture of 6–7 isomers.

major isomer obtained is the 1-arylcyclooct-1-ene (Table 2, entries 15–31).

We have investigated the vinylation of several aryl bromides with cyclooctene and in all cases the 1-arylcyclooct-1-ene was obtained in 85–90% selectivity. Heteroaromatic substrates such as 2-iodothiophene, 3-bromopyridine or 3-bromoquinoline in the presence of cyclooctene also led to 1-arylcyclooct-1-enes selectively (Table 2, entries 27–31).

Next, we performed some reactions with cyclohexene and cycloheptene. With these substrates the selective formation of the 4-arylcycloalk-1-ene was observed (Table 2, entries 4–14). A minor influence of the substituents on the aryl halide was observed. Finally, a few reactions have been performed with cyclododecene but in all cases the formation of mixtures of 4–7 isomers were obtained (Table 2, entries 32–35). The behaviour of all these cycloalkenes seems to come mainly from the conformation of the Pd-substrate intermediates rather than from the thermodynamic stability of the products.

In summary, in the presence of the Tedicyp/palladium complex, the Heck vinylation of several aryl halides with linear and cyclic alkenes can be performed with as little as 0.01% catalyst. With linear alkenes, mixtures of isomers are obtained. The selectivity of the addition depends on the aryl halide and on the alkene. In all cases, the major isomer is the 1-arylalkene. The selectivity of the reaction with cyclic alkenes is even more sensitive to the substrates. High selectivities in favour of the 1-arylcyclooct-1-enes can be obtained from the reaction of several aryl halides with cyclooctene. Good selectivities in favour of 4-arylcycloalk-1-enes are obtained with cyclohexene or cycloheptene. These results represent economically attractive and environmentally friendly procedures. Moreover, due to the high price of palladium, the practical advantage of such low catalyst loading reactions can become increasingly important for industrial processes.

Acknowledgements

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9. As a typical experiment, the reaction of 4-bromoacetophenone (1.99 g, 10 mmol), cyclooctene (2.20 g, 20 mmol) and K_2CO_3 (2.76 g, 20 mmol) at 130°C during 20 h in dry DMF (10 mL) in the presence of *cis*,*cis*,*cis*-1,2,3,4-tetrakis (diphenylphosphinomethyl)cyclopentane/[PdCl-$(C_3H_5)]_2$ complex (0.005 mmol) under argon affords the corresponding product after evaporation and filtration on silica gel (ether/pentane: 1/2) in 85% (1.94 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.88 (d, 2H, $J=8.7$ Hz), 7.48 (d, 2H, $J=8.7$ Hz), 6.15 (t, 1H, $J=8.3$ Hz), 2.63 (m, 2H), 2.58 (s, 3H), 2.32 (m, 2H), 1.59 (m, 8H). MS (EI, 70 eV); m/z (%): 228 (100) [M^+].