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Short Communication

The First *Heck* Reactions with 1-Chloroalk-1-ynes: Syntheses of Enynes with Isolated and Conjugated π-Systems

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Summary. The *Heck* reaction between 1-chloro-2-phenylacetylene and cycloalkenes or cycloalkadienes affords phenylethynyl substituted cycloalkenes as regular *Heck* products as well as 1,3-diphenylprop-2-ynylidene and (cycloalkenyl)phenylmethylidene substituted bicyclic compounds as tandem products by reaction of ClC$\equiv$CPh and the cycloalkene in a ratio of 1:2 and 2:1, respectively.

Keywords. *Heck* reaction; 1-Chloroalk-1-ynes; Cycloalkenes; Cycloalkadienes; Enynes.

Die ersten *Heck*-Reaktionen mit 1-Chloralk-1-inen: Synthesen von Eninen mit isolierten und konjugierten π-Systemen (Kurze Mitt.)

Zusammenfassung. Die *Heck*-Reaktion zwischen 1-Chlor-2-phenylacetylen und Cycloalkenen oder Cycloalkadienen ergibt phenylethinylsubstituierte Cycloalkene als normale *Heck*-Produkte sowie 1,3-diphenylprop-2-inyliden- und (cycloalkenyl)phenylmethyliden-substituierte Bicyclen als Tandemprodukte der Reaktion von ClC$\equiv$CPh und Cycloalkenen im Molverhältnis von 1:2 bzw. 2:1.

Introduction

The palladium catalyzed vinylation of organic halides R*X* (*Heck* reaction) both with conventional catalyst systems (*e.g.* $Pd(OAc)_2/P(o\text{-tol})_3/NEt_3$) and under hydroorganylation conditions with *Larock* catalyst systems [1] (*e.g.* $Pd(OAc)_2/(NEt_3Bz)Cl/NaO_2CH$) is one of the most important C–C bond formation reactions in synthetic organic chemistry. As R*X*, mainly aryl, heterocyclic, vinyl, and benzyl iodides are used [2].

It has been reported that BrC$\equiv$CPh does not afford *Heck* products but 1,4-diphenylbutadiine as homodimer [3]. IC$\equiv$C*R* reacts with vinylogous carbonyl

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compounds to give enynoates and enynones *R*C≡C–CH=CH–C(O)*R*′ (*R*′ = OMe, Me) [4]. Apart from this, 1-halolalk-1-ynes have not been used successfully in *Heck* reactions [5]. Here we report the reaction of 1-chloroalk-1-ynes with cycloalkenes and cycloalkadienes employing *Larock* catalyst systems.

Results and Discussion

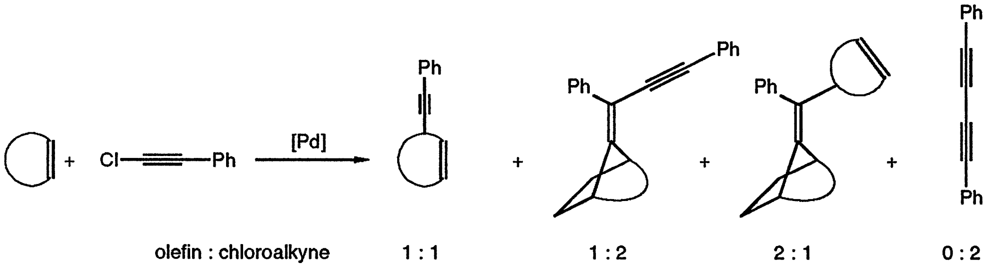
Reactions of *X*C≡CPh (*X* = I, Br, Cl) [6] with cyclohexene in the presence of a typical *Larock* catalyst system ($Pd(OAc)_2/(NEt_3Bz)Cl/NaO_2CH$ = 1:20:60 in *DMF*; 5 mol% Pd referred to *X*C≡CPh) show that the yield of *Heck* products is highest using the chloroalkyne, whereas the iodoalkyne does not react to *Heck* products at all (Table 1). In all three cases, the haloalkynes react to give oligomers as the main products. In the case of BrC≡CPh, oligomers up to a polymerization degree of 16 were identified by means of MALDI-MS measurements. As blank experiments prove (Table 1), these oligomerization reactions are not even in part palladium catalyzed. The formation of 1,4-diphenylbutadiyne is only a minor side reaction and was not observed when using the chloroalkyne.

In general, the reactions of cycloalkenes with 1-chloro-2-phenylacetylene in the presence of the above mentioned catalyst system proceed to give the regular *Heck* products (reaction of 1 mol of cycloalkene with 1 mol of ClC≡CPh; 1:1 product). Furthermore, tandem reactions occur yielding 1,3-diphenylprop-2-ynylidene and (cycloalkenyl)phenylmethylidene substituted bicyclic compounds by reaction of 1 mol cycloalkene with 2 mol ClC≡CPh (1:2 product) and 2 mol cycloalkene with 1 mol ClC≡CPh (2:1 product), respectively (Scheme 1, Table 2).

Table 1. *Heck* reaction of *X*C≡CPh with cyclohexene and stability of *X*C≡CPh in *DMF*

	X	*Heck* reaction (with Pd cat.)			Decomp. reaction (without Pd cat.)	
		U (%)[a]	*n*(*Heck* prod.)[b]	$n(Ph_2C_4)$[b]	*U*(%)[c]	$n(Ph_2C_4)$[b]
1	I	100	<1	1	89	6
2	Br	100	12	3	51	3
3	Cl	86	24	0	15	0

[a] Degree of conversion of *X*C≡CPh in the *Heck* reaction (catalyst system: see text) with cyclohexene (*c*(cyclohexene):*c*(*X*C≡CPh) = 15:1, 48 h, *T* = 25°C; [b] mol%; [c] degree of conversion of *X*C≡CPh yielding oligomers in *DMF* (*t* = 48 h, *T* = 25°C)



Scheme 1

Table 2. Product distribution in the *Heck* reaction of cycloalkenes and cycloalkadienes with ClC≡CPh (catalyst system: see text; $T = 25°C$)

	Olefin	$c_{ol} : c_{ClC\equiv CPh}$	t (d)	U_{gc} (%)[a]	Product distribution (%)[b]			
					1:1	1:2	2:1	0:2
1	cyclohexene	15:1	2	24	10[c]	75	7	–
2	cycloheptene	15:1	4	69	24	8	60	–
3	cycloheptene	1:1	4	33	14	66	14	–
4	*cis*-cyclooctene	50:1	4	53	56	–	38	–
5	1,4-cyclohexadiene	50:1	4	84	90	–	–	6
6	1,3-cycloheptadiene	30:1	4	44	86	4	7	1
7	*cis*,*cis*-1,5-cyclooctadiene	50:1	4	72	93	3	–	3
8	4-vinylcyclohexene[d]	15:1	2	34	85	–	–	–
9	*p*-methylstyrene	15:1	1	24	27	–	67	2

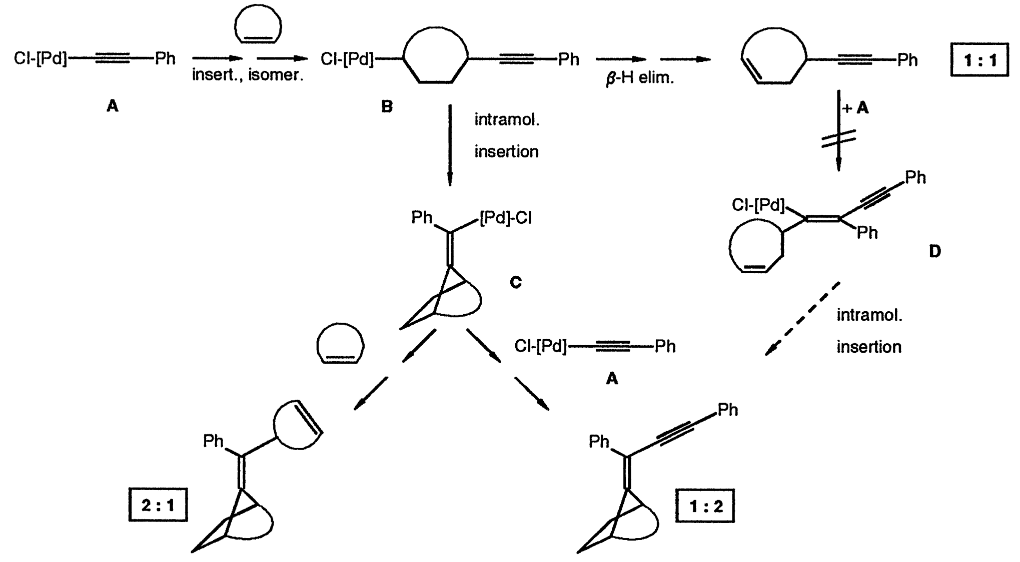
[a] Degree of conversion of ClC≡CPh to low-molecular products; [b] differences to 100% arise from unidentified products; [c] the main isomer is 4-(phenylethynyl)cyclohexene; analogously, 4-substituted cyclohexenes were found to be the main products in the *Heck* arylation of cyclohexene [9]; [d] catalyst system: $Pd(OAc)_2/P(o\text{-tol})_3/NaOAc = 1{:}2{:}60$, solvent: *DMF*, $T = 100°C$

Due to hydroorganylation conditions, hydrogenation of triple and/or double bonds was also observed.

In the reaction with cyclohexene, the 1:2 product is the major one (Table 2, entry 1), whereas in the reaction with cycloheptene the ratio of products can be influenced by the ratio of cycloheptene to ClC≡CPh (entries 2 and 3). With *cis*-cyclooctene, normal *Heck* reaction predominates (entry 4). Cycloalkadienes were found to react affording phenylethynylcycloalkenes as the principal products (entries 5–7), *i.e.*, regular *Heck* reactions under hydrogenation of one double bond take place. The homodimer 1,4-diphenylbutadiyne (0:2 product) is formed to a small extent only. The reaction of ClC≡CPh with *p*-methyl-styrene (included in Table 2, entry 9, for comparison) affords the 2:1 compound as the main product.

A plausible route for the formation of the tandem products is outlined in Scheme 2. The formation of the 1:1 products *via* **A** and **B** as intermediates is depicted in the first line. Intermediate **B** may also undergo an intramolecular insertion reaction to give **C** which in turn reacts either with cycloalkenes yielding the 2:1 products or with **A** in the sense of a transmetallation and reductive elimination affording the 1:2 products. The transmetallation may have a four-centered transition state [7]. A Pd(IV) intermediate formed by oxidative addition of ClC≡CPh to **C** followed by a reductive elimination may also be discussed [8]. The formation of the 1:2 products *via* a *Heck* reaction of the 1:1 products with **D** as an intermediate and a subsequent intramolecular insertion reaction was rendered unlikely by a separate experiment (4-(phenylethynyl)cyclohexene (Table 3, entry 5) and ClC≡CPh do not react to the corresponding *Heck* products).

The major products were obtained with yields between 14 and 73% (GC) and 6–49% (isolated, not optimized), respectively (Table 3). All substances were completely characterized by one- and two-dimensional ^{1}H and ^{13}C NMR



Scheme 2

Table 3. Syntheses of enynes with isolated and conjugated π-systems (reaction conditions as in Table 2)

	Olefin	Product type		Yield (%) gc/isol (purity (%))
1	cyclohexene	1:2	7-(1,3-diphenylprop-2-ynylidene)-bicyclo[2.2.1]heptane	18/13 (>97)
2	cycloheptene	2:1	8-((cyclohept-4- and 8-((cyclohept-3-enyl)-phenylmethylidene)bicyclo[3.2.1]octane	41/11 (>97)
3	cycloheptene	1:2	8-(1,3-diphenylprop-2-ynylidene)-bicyclo[3.2.1]octane	17/8 (>99)
4	*cis*-cyclooctene	1:1	4- and 5-(phenylethynyl)cyclooctene	24/18 (>90)
5	1,4-cyclohexadiene	1:1	4-(phenylethynyl)cyclohexene[a]	73/36 (>98)
6	1,3-cycloheptadiene	1:1	4-(phenylethynyl)cycloheptene	14/11 (>81)
7	*cis,cis*-1,5-cycloocta-diene	1:1	5-(phenylethynyl)cyclooctene	61/49 (>97)
8	4-vinylcyclohexene	1:1	4-(1-(phenylethynyl)vinyl)cyclohexene	20/6 (>92)

[a] In dry *DMF*; in wet *DMF*, the hydrogenated products (*Z*)-4-(2-phenylethenyl)cyclohexene or 4-(2-phenylethyl)cyclohexene were obtained

experiments. The molecular structure of the bicyclic enyne (Table 3, entry 1) was also authenticated by X-ray diffraction analysis (Fig. 1).

It was shown for the first time that 1-chloro-2-phenylacetylene is a useful starting material for *Heck* reactions with cycloolefins and cyclodienes yielding not only the regular *Heck* products but also bicylic unsaturated hydrocarbons. In

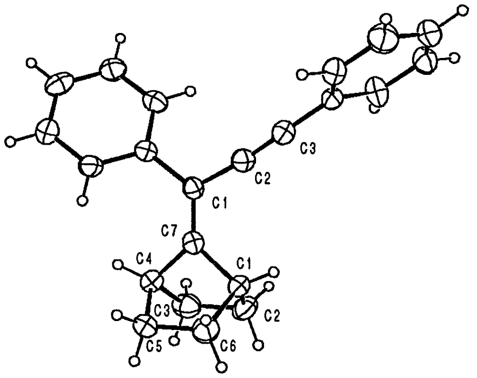


Fig. 1. Molecular structure of 7-(1,3-diphenylprop-2-ynylidene)bicyclo[2.2.1]heptane

further investigations it was demonstrated that other 1-chloroalk-1-ynes (ClC≡C*R*, *R* = *n*-butyl, *n*-octyl, cyclohexyl) react analogously.

Experimental

Typical procedure

The olefin (15.0 mmol), 1-chloro-2-phenylacetylene (136 mg, 1.0 mmol), and the catalyst ($Pd(OAc)_2$, 11 mg, 0.05 mmol; $(NEt_3Bz)Cl$, 228 mg, 1.0 mmol; NaO_2CH, 204 mg, 3.0 mmol) were stirred in *DMF* (2 ml) under argon in the dark at 25°C for 2–4 d. After addition of water (20 ml) the precipitate was filtered and washed with ether. From the combined organic phase (dried over Na_2SO_4), the solvents were removed *in vacuo*. The residue was analyzed by gas chromatography using biphenyl as internal standard.

For preparative purposes the reactions were performed as described above but on a fivefold scale. The residue obtained after removal of solvents was purified by means of preparative centrifugally accelerated thin-layer chromatography (Chromatotron, Harrison Research) on silica gel using *n*-hexane as eluent (1–3 runs).

7-(1,3-diphenylprop-2-ynylidene)bicyclo[2.2.1]heptane (as a representative)

Colorless crystals; m.p.: 80–81°C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.41$–1.59 (m, 4H, $H2_{endo}$, $H3_{endo}$, $H5_{endo}$, $H6_{endo}$), 1.68–1.82 (m, 2H, $H3_{exo}$, $H5_{exo}$), 1.82–1.94 (m, 2H, $H2_{exo}$, $H6_{exo}$), 2.83 (t, 1H, $^{3}J_{H,H} = 4.2$ Hz, H4), 3.03 (t, 1H, $^{3}J_{H,H} = 4.4$ Hz, H1), 7.24–7.34 (m, 4H, H_p of 1-Ph, 3-Ph, $2\times H_o$ of 3-Ph), 7.34–7.40 (m, 2H, $2\times H_o$ of 1-Ph), 7.44–7.52 (m, 4H, $2\times H_m$ of 1-Ph and 3-Ph) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): bicyclo[2.2.1]heptane: $\delta = 28.30$ (C2 + C6), 29.02 (C3 + C5), 37.00 (C4, $^{1}J_{C,H} = 146.6$ Hz), 40.05 (Cl, $^{1}J_{C,H} = 145.6$ Hz), 161.29 (C7) ppm; 1,3-diphenylprop-2-ynylidene: $\delta = 88.55$ (C3, $^{3}J_{C_i,H_m} = 5.0$ Hz), 89.54 (C2), 108.55 (C1), 124.03 (C_i of 3-Ph, $^{3}J_{C_i,H_m} = 8.0$ Hz), 126.81/127.63 (C_p of 1-Ph and 3-Ph), 128.02 ($2\times C_o$ of 1-Ph), 128.17 ($2\times C_o$ of 3-Ph), 128.47/131.40 (C_m of 1-Ph and 3-Ph), 139.07 (C_i of 1-Ph, $^{3}J_{C_i,H_m} = 8.0$ Hz) ppm; the numbering follows Fig. 1; MS (70 eV): *m*/*z* (%) = 285 (22) [M+1], 284 (100) [M^{+}], 283 (22) [M−1]; IR (KBr): $\nu(C{\equiv}C) = 2202\ cm^{-1}$; X-ray structure analysis (STOE IPDS): space group: $P2_1/a$; unit cell parameters: $a = 17.427(3)$ Å, $b = 10.015(3)$ Å, $c = 19.293(4)$ Å, $\beta = 100.44(2)°$, $Z = 8$; θ-range: $\theta = 2.30$–$23.99°$; refl. (coll.): 22591; data/parameters: 5179/397; final *R* indices: $R_1 = 0.0672$ [$I > 2\sigma(I)$], $wR_2 = 0.1829$ (all data).

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