

# Regioselective cyclotrimerization of phenylacetylenes to 1,2,4-triarylbenzenes catalyzed by iridium–diphosphine complexes

Erica Farnetti<sup>\*</sup>, Nazario Marsich

*Dipartimento di Scienze Chimiche, Università di Trieste, Via L. Giorgieri 1, Trieste I-34127, Italy*

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## Abstract

The organoiridium derivatives  $\text{HIr}(\text{cod})(\text{P-P})$  ( $\text{cod} = 1,5\text{-cyclooctadiene}$ ;  $\text{P-P} = \text{dppm}$  (bis(diphenylphosphino)methane),  $\text{dppe}$  (1,2-bis(diphenylphosphino)ethane),  $\text{dppp}$  (1,3-bis(diphenylphosphino)propane),  $\text{dppb}$  (1,4-bis(diphenylphosphino)butane)) catalyze the regioselective cyclotrimerization of phenylacetylene as well as of its derivatives  $p\text{-CH}_3\text{OC}_6\text{H}_4\text{C}\equiv\text{CH}$  and  $p\text{-CF}_3\text{C}_6\text{H}_4\text{C}\equiv\text{CH}$ . The catalytic activity of the precursors as well as the selectivity towards formation of the 1,2,4-triarylbenzenes (up to 100%) are influenced by the diphosphine, and both increase by decreasing the size of the phosphine–iridium chelate ring. © 2003 Elsevier B.V. All rights reserved.

**Keywords:** Iridium; Diphosphines; Homogeneous catalysis; Alkynes; Cyclotrimerization

## 1. Introduction

A great deal of attention has recently been paid to the transition-metal catalyzed cyclotrimerization of alkynes, which is a very useful method for the preparation of substituted aromatic compounds [1]. The reaction can be promoted by various metals, the most recent examples including titanium [2], molybdenum [3], cobalt [4], rhodium [5], iridium [6] and platinum [7]. One of the major limitations of this reaction is the low regioselectivity, as a mixture of the possible isomers is usually obtained.

In the course of our studies on polymerization of acetylenes catalyzed by organoiridium derivatives, we recently reported [8] that the compounds  $\text{HIr}(\text{cod})(\text{PR}_3)_2$  ( $\text{PR}_3 = \text{PPh}_3$ ,  $\text{P}(p\text{-MeOC}_6\text{H}_4)_3$ ,  $\text{P}(o\text{-MeOC}_6\text{H}_4)_2$ ,  $\text{PCyPh}_2$ ) promote the polymerization of phenylacetylene: in these reactions only the *trans*-polyene is formed, and in some cases small amounts of oligomers are also detected.

We now find that the analogue compounds where a bidentate phosphine has replaced two  $\text{PR}_3$  ligands,

namely  $\text{HIr}(\text{cod})(\text{P-P})$  ( $\text{cod} = 1,5\text{-cyclooctadiene}$ ;  $\text{P-P} = \text{dppm}$  (bis(diphenylphosphino)methane),  $\text{dppe}$  (1,2-bis(diphenylphosphino)ethane),  $\text{dppp}$  (1,3-bis(diphenylphosphino)propane),  $\text{dppb}$  (1,4-bis(diphenylphosphino)butane)), are also active catalysts for C–C bond formation of phenylacetylenes, but in this case cyclotrimerization takes place instead of polymerization (Scheme 1). Herein we describe preliminary results in alkyne cyclotrimerization catalyzed by the above reported iridium–diphosphine compounds, which promote clean and fast reactions with uncommonly high regioselectivity.

## 2. Experimental

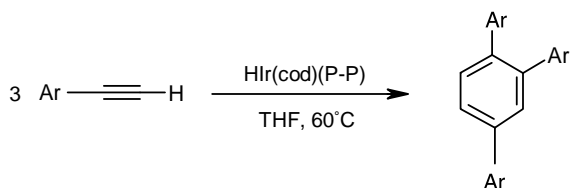
All the reactions and manipulations were routinely performed under an argon atmosphere using standard Schlenk tube techniques.

$\text{HIr}(\text{cod})(\text{dppm})$ ,  $\text{HIr}(\text{cod})(\text{dppe})$ ,  $\text{HIr}(\text{cod})(\text{dppp})$  and  $\text{HIr}(\text{cod})(\text{dppb})$  were synthesized according to the procedure described by Oro and co-workers [9] for  $\text{HIr}(\text{cod})(\text{dppe})$ .

$^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR spectra were recorded on a JEOL EX400 spectrometer operating at 399.77, 100.54 and 161.82 MHz, respectively. Infrared spectra were

<sup>\*</sup> Corresponding author. Tel.: +39-040-5583938; fax: +39-040-5583903.

E-mail address: [farnetti@univ.trieste.it](mailto:farnetti@univ.trieste.it) (E. Farnetti).



recorded in Nujol mull on a Perkin–Elmer System 2000 FT-IR spectrometer.

Chemical yields of the catalytic mixtures were determined by GC on a Hewlett Packard 6890 instrument equipped with a HP-1 column, using naphthalene as internal standard.

### 2.1. Experimental procedure for the catalytic reactions

A typical procedure is described in the following: A solution of HIr(cod)(P-P) (0.017 mmol) and of the GC standard naphthalene (100 mg) in 5.0 ml of THF (or other solvent of choice) was heated to the desired reaction temperature under inert atmosphere. Then, 173 mg of phenylacetylene (1.7 mmol,  $[\text{sub}]/[\text{Ir}] = 100$ ) was added. Samples were withdrawn from the reaction mixture at time intervals and composition of the mixture was followed with time by GC. The final reaction mixture was concentrated to dryness and analyzed by  $^1\text{H}$  and  $^{13}\text{C}$  NMR. In all the reactions reported, neither polyphenylacetylenes nor linear oligomers were detected.

## 3. Results and discussion

The results obtained in the cyclotrimerization of phenylacetylene catalyzed by HIr(cod)(P-P) are summarized in Table 1. When HIr(cod)(dppe) [9] was treated in tetrahydrofuran (THF) at 60 °C with 100 equivalents of the monomer, the pale yellow solution turned dark orange immediately. After 1 h the resulting brown solution according to GC analysis contained less than 30% of the monomer and after 6 h the conversion was 98%.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the crude products [10] revealed that only 1,2,4-triphenylbenzene was

formed, together with traces of the other isomer 1,3,5-triphenylbenzene, whereas polymerization and linear oligomerization products (enynes [11] and linear trimers [12]) were not present in the final mixture. The reaction was repeated employing the analogue compounds with dppp and dppb, respectively: again 1,2,4-triphenylbenzene was the main product, but both the conversion and the regioselectivity were lower than with the dppe derivative. In contrast, the reaction promoted by HIr(cod)(dppm) [13] was very fast, as phenylacetylene was completely consumed after 15 min, and 1,2,4-triphenylbenzene was now the only reaction product, apart from a hardly detectable amount of the symmetric isomer. The latter catalytic reaction was repeated at 40 and 20 °C in order to observe the effect of temperature on both catalytic activity and selectivity: the expected decrease in activity was observed, yet with a conversion above 80% in 8 h at 20 °C. On the other hand, the lower temperatures had a slightly negative effect on the regioselectivity, which decreased to 96% at 20 °C. Other solvents were also tested for the catalytic reactions: good results were obtained with toluene and methanol, even if the iridium derivative is poorly soluble in the latter, thus giving lower conversion; at variance, chloroform and dichloromethane could not be employed, because the iridium precursors undergo partial decomposition in these solvents.

In order to study the substrate dependent influence on the regioselectivity, as well as the generality of the reaction, cyclotrimerization of the substituted phenylacetylenes  $p\text{-MeOC}_6\text{H}_4\text{C}\equiv\text{CH}$  and  $p\text{-CF}_3\text{C}_6\text{H}_4\text{C}\equiv\text{CH}$  catalyzed by HIr(cod)(dppm) was investigated. The reactions performed at 60 °C with the substituted monomers were very fast, and comparable with that of unsubstituted phenylacetylene (see Table 2, runs 1–3); all these reactions yield the 1,2,4-trisubstituted benzene with excellent regioselectivity. The effect of the substituent on the alkyne aryl ring could be better appreciated at a lower reaction temperature: at 40 °C, substrate consumption became faster when changing from  $p\text{-CF}_3\text{C}_6\text{H}_4\text{C}\equiv\text{CH}$  to  $\text{C}_6\text{H}_5\text{C}\equiv\text{CH}$  to  $p\text{-MeOC}_6\text{H}_4\text{C}\equiv\text{CH}$  (see Table 2 runs 4–6). Therefore, cyclotrimerization appears to be accelerated when more electron-rich acetylenes are employed; on the contrary,

Table 1  
Cyclotrimerization of phenylacetylene catalyzed by HIr(cod)(P-P)

P-P	<i>T</i> (°C)	Time (h)	Conv. (%)	1,2,4-Ph <sub>3</sub> C <sub>6</sub> H <sub>3</sub> (%)	1,3,5-Ph <sub>3</sub> C <sub>6</sub> H <sub>3</sub> (%)
Dppb	60	6	31	28	3
Dppp	60	6	47	45	2
Dppe	60	6	98	97	1
Dppm	60	0.25	100	99	1
Dppm	40	1.5	98	95	3
Dppm	20	8	81	78	3

**Experimental conditions:**  $[\text{Ir}] = 3.4 \times 10^{-3} \text{ mol l}^{-1}$ ;  $[\text{sub}] = 0.34 \text{ mol l}^{-1}$ ;  $[\text{sub}]/[\text{Ir}] = 100$ ; solvent THF. dppb = 1,4-bis(diphenylphosphino)butane; dppp = 1,3-bis(diphenylphosphino)propane; dppe = 1,2-bis(diphenylphosphino)ethane; dppm = bis(diphenylphosphino)methane.

Table 2  
Cyclotrimerization of phenylacetylenes catalyzed by  $\text{HIr}(\text{cod})(\text{dppm})$

Run	Substrate	$T$ ( $^{\circ}\text{C}$ )	Time	Conv. (%)	1,2,4- $\text{Ar}_3\text{C}_6\text{H}_3$ (%)	1,3,5- $\text{Ar}_3\text{C}_6\text{H}_3$ (%)
1	$\text{PhC}\equiv\text{CH}$	60	5 min	90	89	1
2	$p\text{-MeOC}_6\text{H}_4\text{C}\equiv\text{CH}$	60	5 min	100	100	–
3	$p\text{-CF}_3\text{C}_6\text{H}_4\text{C}\equiv\text{CH}$	60	5 min	87	86	1
4	$\text{PhC}\equiv\text{CH}$	40	1.5 h	98	95	3
5	$p\text{-MeOC}_6\text{H}_4\text{C}\equiv\text{CH}$	40	1 h	100	97	3
6	$p\text{-CF}_3\text{C}_6\text{H}_4\text{C}\equiv\text{CH}$	40	2 h	98	97	1

Experimental conditions: see Table 1.

the regioselectivity appears to be dependent on the reaction temperature, but independent on substituents on the alkyne phenyl ring.

Finally, the catalytic activity of  $\text{HIr}(\text{cod})(\text{dppm})$  and  $\text{HIr}(\text{cod})(\text{dppe})$  with the disubstituted acetylene phenylpropyne ( $\text{PhC}\equiv\text{CMe}$ ) was also tested: even if cyclotrimerization of internal alkynes is more difficult to achieve, some examples have recently been reported [3,4a,5a]. However, in our case with both catalyst precursors, after 5 h at 60  $^{\circ}\text{C}$  in THF solution, no reaction occurred.

According to the mechanism proposed for transition metal-catalyzed cyclotrimerization of alkynes (see Scheme 2) [14], the regioselectivity of the reaction is determined by the metallacyclopentadiene intermediate. In the reactions catalyzed by  $\text{HIr}(\text{cod})(\text{dppm})$ , selective formation of the one of the two regioisomers shown in Scheme 2 must be proposed, to account for the selective formation of 1,2,4-triarylbenzene. As in the series of catalysts under discussion the regioselectivity increases by decreasing the chelate ring size, i.e., by decreasing the ligand bite angle and therefore the steric crowding around the metal [15,16], preferred formation of the metallacycle with both aryl substituents adjacent to iridium can be suggested here.

In conclusion, we have reported that highly regioselective cyclotrimerization of phenylacetylene and

substituted derivatives is catalyzed by the organoiridium compounds  $\text{HIr}(\text{cod})(\text{P-P})$  ( $\text{P-P} = \text{dppm}, \text{dppe}, \text{dppp}, \text{dppb}$ ). To the best of our knowledge there are only two examples in the literature of comparable regioselectivity in phenylacetylene cyclotrimerization, i.e., the reaction catalyzed by supported titanium–arene complexes described by Ladipo and coworkers [17] and the palladium-catalyzed cyclotrimerization of  $p\text{-MeC}_6\text{H}_4\text{C}\equiv\text{CH}$  reported by Jiang and Chen [18].

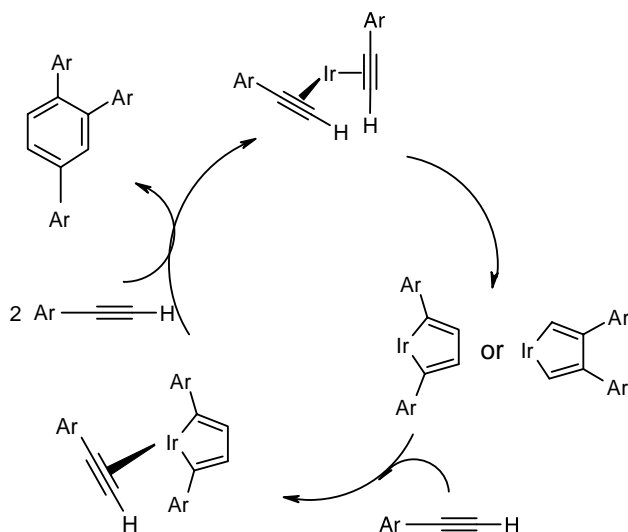
The parameters that determine the formation of only one of the possible isomeric metallacyclic intermediates, and therefore the regioselectivity of the catalytic reaction, are under investigation. For this purpose, we are currently studying the effect on both catalytic activity and selectivity of the phosphine substituents as well as the iridium–phosphine chelate ring size in an extended series of iridium derivatives.

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