Mechanism of oxidative carbonylation of phenylacetylene and methylacetylene. Generation and experimental discrimination of hypotheses

L. G. Bruk,[a] S. N. Gorodskii,[a] A. V. Zeigarnik,[a] R. E. Valdés-Perez,[b] and O. N. Temkin[a]*

[a]M. V. Lomonosov Moscow State Academy of Fine Chemical Technology, 86 prosp. Vernadskogo, 117571 Moscow, Russian Federation. Fax: +7 (095) 434 8711. E-mail: bruk@azeigarnik.msk.ru
[b]Computer Science Department, Carnegie Mellon University, Pittsburgh, PA 15213, USA. Fax: +1 (412) 268 5575. E-mail: valdes@cs.cmu.edu

Formal and informal methods for advancing hypotheses on mechanisms were used in a study of the oxidative carbonylation of phenylacetylene to methyl phenylpropiolate catalyzed by the $PdCl_2$—CuCl—$CuCl_2$ system. The hypotheses remaining after discrimination and consistent with all experimental data include the steps of formation of the Cu^I alkynyl complex, transfer of the phenylethynyl group from Cu^I to Pd^{II}, insertion of carbon monoxide into a Pd—C or Pd—OMe bond of the Pd^{II} σ-alkynyl complex. Comparison of the formal and informal methods for advancing hypotheses confirmed a higher efficiency of the first method.

Key words: phenylacetylene, oxidative carbonylation, reaction mechanisms, catalysts, palladium complexes, alkynylcarboxylic acid ester, methyl phenylpropiolate, kinetic isotope effect.

The study of the mechanism of the oxidative carbonylation of alkynes (1), which is the simplest method for the synthesis of alkynylcarboxylic acid esters, is of theoretical and practical interest.[1]

$$RC{\equiv}CH + CO + MeOH + 2\ NaOAc + 2\ CuCl_2 \xrightarrow[1\ atm,\ 20\ ^\circ C]{PdCl_2} RC{\equiv}CCOOMe + 2\ AcOH + 2\ NaCl + 2\ CuCl \quad (1)$$

Along with the target product, the products of oxidative dimerization (reaction (2)) and oxidative chlorination (reaction (3)) of alkyne and carbon dioxide are formed under the experimental conditions.

$$RC{\equiv}CH + 2\ NaOAc + 2\ CuCl_2 \longrightarrow RC{\equiv}CC{\equiv}CPh + 2\ CuCl + 2\ NaCl + 2\ AcOH \quad (2)$$

$$RC{\equiv}CH + NaOAc + 2\ CuCl_2 \longrightarrow RC{\equiv}CCl + 2\ CuCl + NaCl + AcOH \quad (3)$$

R = Ph, Me, Me_2COH

Most of our study was performed with phenylacetylene.

Previously,[2] based on the published data, we advanced five hypotheses on the mechanism of reaction (1). Further study showed that four of them are inconsistent with the experimental data. Considering the strategy of advancing and discriminating (selecting) hypotheses on mechanisms using a computer at the stage of their advancement,[3,4] it was of interest to compare the efficiency of the informal and formal (computational) methods for the search for hypotheses. The ChemNet[4,5] and MECHEM[6,7] programs were used in the formalized approach.

To clarify the logic of both procedures, in this work after the Experimental section, we summarized the main experimental facts and the results of selection of the hypotheses advanced by the informal method on the basis of the published data.[2]

Experimental

Experiments were carried out in a constant-temperature glass (at 20 °C) reactor with vigorous stirring of the liquid and gas phases in a closed system. The volume of the absorbed gas (CO) was measured by the volumetric method. The composition of the reaction solution was determined by GLC. The content of products of carbonylation ($PhC{\equiv}CCOOMe$) and oxidative chlorination ($PhC{\equiv}CCl$) of phenylacetylene was determined on a column (1 m × 3 mm) packed with Porapak P (a thermal-conductivity detector; helium as carrier gas; temperature of separation, 210 °C). The composition of the gas phase was determined by gas adsorption chromatography on a column (3 m × 3 mm) packed with active carbon AG-3 (fraction 0.25—0.50 mm, temperature of separation 140 °C).

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 5, pp. 882—889, May, 1999.

1066-5285/99/4805-0873 $22.00

All reagents except for those mentioned below were reagent grade or analytical-purity grade and used without additional purification. Phenylacetylene (reagent grade) was distilled *in vacuo* before use. Carbon monoxide was obtained by the decomposition of formic acid in concentrated H_2SO_4. Copper dichloride $CuCl_2 \cdot 2H_2O$ was dried at 120 °C to constant weight before use. Copper(I) chloride was recrystallized from hot water, washed with acetone, and dried at 80 °C in a nitrogen atmosphere. Methanol contained water (0.2 mol L^{-1}). Deuterated methanol contained at most 99% MeOD.

The kinetic isotope effect (KIE) was studied at 19 °C and a CO pressure of 1 atm in a methanol solution at the following concentrations of the catalyst and other components, C/mol L^{-1}: CuCl, 0.3; $PdCl_2$, $1.4 \cdot 10^{-3}$; $CuCl_2$, 0.2; LiCl, 3; Et_3N, 0.5; and AcOH, 0.35. The AcONa—Et_3N buffer mixture was used to maintain the constant pH. KIE was calculated as a ratio of the initial rates of formation of methyl phenylpropiolate (in nondeuterated and deuterated methanol) determined from the change in the product concentration over 15 min after the beginning of the reaction. KIE and kinetic studies were carried out under the same conditions.[2]

Results and Discussion

Informal advancement of hypotheses

Based on the analysis of the published data, five hypothetical mechanisms of reaction (1) (Scheme 1, *M1*—*M5*) were proposed.

Scheme 1

M1:

$$PdCl_2 + CO + MeOH \underset{HCl}{\rightleftharpoons} ClPdCOOMe \xrightarrow{PhC\equiv CH} ClPd{-}(Ph)C{=}CHCOOMe \longrightarrow HPdCl + PhC{\equiv}CCOOMe;$$

M2:

$$CO + 2\,MeOH \xrightarrow[-2\,H^+]{[Pd]} (MeO)_2CO \xrightarrow[-MeOH]{PhC\equiv CH} PhC{\equiv}CCOOMe;$$

M3:

$$CO + MeOH \xrightarrow{[Pd],\,CuCl_2} ClCOOMe \xrightarrow[-CuCl]{CuC\equiv CPh} PhC{\equiv}CCOOMe;$$

M4:

$$PhC{\equiv}CH + CuCl \underset{HCl}{\rightleftharpoons} PhC{\equiv}CCu \xrightarrow[-3\,CuCl]{2\,CuCl_2} PhC{\equiv}CCl,$$

$$PhC{\equiv}CCl + CO + MeOH \xrightarrow{[Pd]} PhC{\equiv}CCOOMe + HCl;$$

M5:

$$PhC{\equiv}CH + CuCl \xrightarrow[-HCl]{} CuC{\equiv}CPh \underset{CuCl}{\overset{PdCl_2}{\rightleftharpoons}}$$

$$\longrightarrow ClPdC{\equiv}CPh \xrightarrow{CO} ClPdCOC{\equiv}CPh \xrightarrow{MeOH}$$

$$\longrightarrow PhC{\equiv}CCOOMe + HCl + Pd^0.$$

The first mechanism (*M1*) was proposed in 1972.[8] Mechanism *M2* is associated with the synthesis of ester of alkynylcarboxylic acid from alkyne and dialkyl carbonate.[9,10] Mechanisms *M3* and *M4* were formulated by analogy to other processes. For example, *M3* is similar to the mechanism of formation of ketones from the σ-organometallic Hg^{II} and Cu^{I} compounds and acyl chlorides (reactions (4) and (5)),[11,12] and *M4* is similar to the mechanism of carbonylation of bromo- and iodoalkynes.[13]

$$RHgCl + R'COCl \longrightarrow RCOR' + HgCl_2 \qquad (4)$$

$$RC{\equiv}CCu + R'COCl \longrightarrow RC{\equiv}COR' + CuCl \qquad (5)$$

The formation of intermediates in mechanisms *M1*—*M4* ($(MeO)_2CO$, ClCOOMe,[14] RC≡CCu, and RC≡CCl [15]) is possible in alcohol solutions of $PdCl_2$, CuCl, and $CuCl_2$. Some steps of mechanism *M5* are known[15,16] for the Pd^{II} complexes and alkynyl compounds of Cu^{I}, Ag^{I}, and Hg^{II}. The oxidative carbonylation of alcohols occurs *via* intermediate palladium alkoxycarbonyl complexes (XPdCOOR).[14] Therefore, the first two hypotheses can be related to the schemes of the "alcoholate"- or "alkoxycarbonyl"-type mechanisms. Cu^{I} and Pd^{II} σ-alkynyl complexes play a key role in schemes *M4* and *M5*. We categorize these as "alkynyl"-type mechanisms. Variant *M3* has the features of both types.

The characteristic feature of reaction (1) is the induction period on the "concentration—time" plots for methyl phenylpropiolate, dimethyldiacetylene, and chloroalkyne and on the "rate of CO absorption—time" curves (Fig. 1, curve *3*). In selecting hypotheses, we used the results of studying the induction period and quasi-steady-state kinetic data.

The alkynyl-type mechanisms agree well with the induction period because they assume the participation

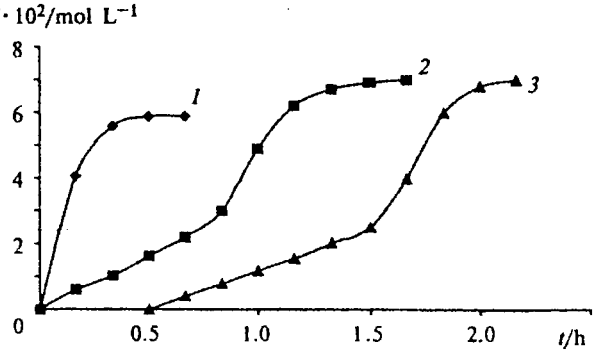


Fig. 1. Dynamics of accumulation of PhC≡CCOOMe during the oxidative carbonylation of PhC≡CH with addition of CuCl to the initial solution and without it in the $PdCl_2$—$CuCl_2$—NaOAc system ($[PdCl_2]_0 = 5.6 \cdot 10^{-3}$ mol L^{-1}; $[CuCl_2]_0 = 0.2$ mol L^{-1}; $[NaOAc]_0 = 0.2$ mol L^{-1}; 19 °C; 1 atm CO; volume of the methanol solution 10 mL); $[CuCl]_0$/mol L^{-1} = 0 (*1*); 0.04 (*2*); and 0.20 (*3*).

of an intermediate Cu^I alkynyl complex, and Cu^I is absent from the starting catalytic solution. At the same time, in the case of the alkoxycarbonyl-type mechanisms, the induction period should not appear. These ideas were confirmed in the experiments with CuCl added to the initial solution, where the induction period either decreased or was absent, depending on the initial CuCl concentration (see Fig. 1). The results of studying the carbonylation of Cu^I, Hg^{II}, and Ag^I phenylethynyl compounds to form the same product under the conditions of reaction (1) with close quantitative parameters (rate, selectivity to alkyne) also agree well with the alkynyl-type mechanisms.[2]

Based on the data obtained, we excluded the hypothetical mechanisms *M1* and *M2*. In the case of *M3*, the induction period could be observed for the formation of the carbonylation product, but not for the rate of carbon monoxide absorption. In addition, chlorocarbonate (and dimethyl carbonate) was not observed in the contact solution during experiments. Therefore, mechanism *M3* was also excluded from consideration.

For the selection of hypothetical schemes *M4* and *M5*, we studied the kinetics of the process by the method of a one-factor experiment. The chosen conditions allowed us to maintain constant compositions of the Cu^I, Cu^{II}, and Pd^{II} complexes and concentration of the chloride ion ([LiCl] ≫ [CuCl] + [$CuCl_2$]). The [CuCl], [$CuCl_2$], and [$PdCl_2$] values were proportional to the corresponding initial concentrations $[CuCl]_0$, $[CuCl_2]_0$, and $[PdCl_2]_0$ (T = 20 °C, p = 1 atm).

The analysis of the hypothetical conjugation nodes of the sequences of the steps of the formation of chloroalkyne and alkynylcarboxylic acid ester (for *M4*, the successive scheme; for *M5*, the parallel scheme with the conjugation node on the Cu^I σ-phenylethynyl complex) allowed us to design a purposeful kinetic experiment with variable $[PdCl_2]_0$, $[CuCl]_0$, and $[CuCl_2]_0$ concentrations.[2]

All experimental dependences agree qualitatively and quantitatively with mechanism *M5* and conflict with *M4*. Rate laws (Eqs. (12) and (13)) that describe experimental dependences within the experimental error were derived from the detailed scheme *M5* (Eqs. (6)—(11)) taking into account the mechanism of chloroalkyne formation[17] and assuming that step (6) is at quasi-equilibrium, steady-state concentrations of intermediates I^1, I^2, and I^3, and insignificant contribution of intermediates to the material balance with respect to [CuCl], [$CuCl_2$], and [$PdCl_2$]:

$$PhC{\equiv}CH + CuCl \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{I^1}{PhC{\equiv}CCu} + H^+, \quad (6)$$

$$I^1 + CuCl_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} I^2, \quad (7)$$

$$I^2 + CuCl_2 \xrightarrow{k_3} PhC{\equiv}CCl + 3\ CuCl, \quad (8)$$

$$I^1 + PdCl_2 \xrightarrow{k_4} I^3 + CuCl, \quad (9)$$

$$I^3 + CO + MeOH \xrightarrow{k_5} PhC{\equiv}CCOOMe + Pd, \quad (10)$$

$$Pd + 2\ CuCl_2 \xrightarrow{k_6} PdCl_2 + 2\ CuCl, \quad (11)$$

$$r^0_{PhC\equiv CCOOMe} = \frac{k_I[PhC{\equiv}CH]_0[CuCl]_0[PdCl_2]_0}{[H^+] + k_{II}[CuCl_2]_0^2 + k_{III}[PdCl_2]_0}, \quad (12)$$

$$r^0_{PhC\equiv CCl} = \frac{k_{IV}[PhC{\equiv}CH]_0[CuCl]_0[CuCl_2]_0^2}{[H^+] + k_{II}[CuCl_2]_0^2 + k_{III}[PdCl_2]_0}, \quad (13)$$

where $k_I = k_4K_1$, $k_{II} = k_3K_2/k_{-1}$, $k_{III} = k_4/k_{-1}$, $k_{IV} = k_3K_1K_2$; r^0 is the initial rate of formation of the corresponding product.

Computational advancement of hypotheses and their discrimination

After the informal advancement of the hypotheses about the mechanism and selection described above, we repeated the procedure of advancement, but using the ChemNet[4] and MECHEM[6,7] programs, to compare the results and find hypotheses that are missing without formalized methods.

In this work, we applied the earlier suggested method[5] for the combined use of ChemNet and MECHEM as described below. The essence of the variant is the following. Given a set of the types of steps input by us in the general form (transforms) and constraints on the size of the molecules, the number of different types, and the oxidation states of a metal in the catalytically active complexes and intermediates, ChemNet generated the reaction network (all reactions and intermediates possible in this system under specified constraints). In this case, the purpose of the MECHEM program reduced to identifying the simplest mechanisms of formation of the target product (methyl phenylpropiolate) from the reaction network obtained by ChemNet.

The list of transforms used in the ChemNet program is given in Scheme 2. Starting species and constraints are listed below.

1. For reaction (1) written in the form of the equation

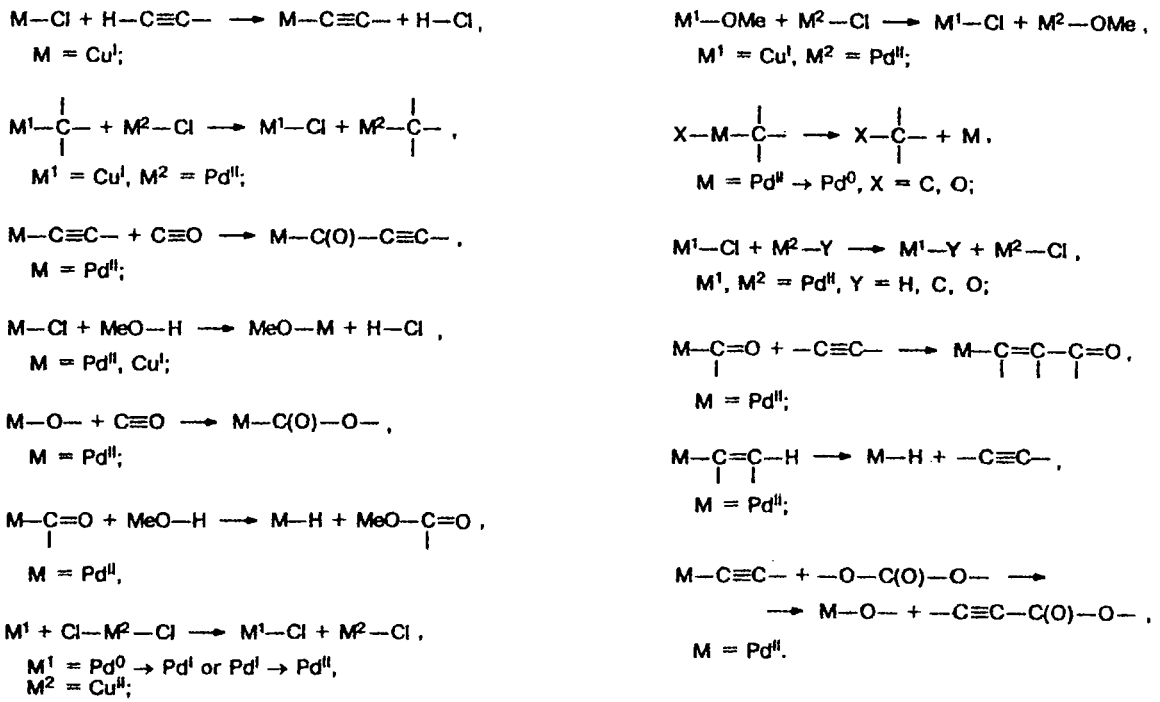
$$PhC{\equiv}CH + CO + MeOH + 2\ CuCl_2 \longrightarrow PhC{\equiv}CCOOMe + 2\ HCl + 2\ CuCl, \quad (14)$$

the reactants and components of the system PhC≡CH, CO, MeOH, $CuCl_2$, CuCl, and $PdCl_2$ were the starting species.

2. The maximum number of atoms in the molecule obtained was 20 (Me and Ph were considered as inseparable pseudo-atoms).

3. Each molecule should contain at most three carbon atoms (the carbon atoms in the Me and Ph groups

Scheme 2



were ignored), at most three oxygen atoms, and one phenyl group.

4. The acceptable oxidation states of copper are I and II, and for palladium, they are 0, I, and II.

5. The highest coordination numbers for copper and palladium were set at two.

Using the ChemNet program with these constraints, we obtained 233 elementary steps and 34 species (within 2 min on a Pentium 75-based PC). These elementary steps were then input into the MECHEM program, and the stoichiometry of reaction (14) was specified. As a result, 41 mechanisms were generated (Tables 1—3).

Table 1. Seven-step mechanisms (six intermediates)

Step	Mechanism							
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*
$CuCl_2 + Pd \longrightarrow CuCl + PdCl$	1	1	1	1	1	1	1	1
$CuCl_2 + PdCl \longrightarrow PdCl_2 + CuCl$	1	1	1	1	1	1	1	1
$PhCCH + CuCl \longrightarrow HCl + CuCCPh$	1	1	1		1	1	1	1
$PdCl_2 + MeOH \longrightarrow HCl + MeOPdCl$	1	1	1	1				
$PdCl_2 + CuCCPh \longrightarrow CuCl + ClPdCCPh$					1	1	1	1
$MeOOCPdCCPh \longrightarrow PhCCCOOMe + Pd$	1	1				1		
$MeOPdCOCCPh \longrightarrow PhCCCOOMe + Pd$			1		1			1
$CO + MeOPdCl \longrightarrow ClPd{-}COOMe$	1			1				
$MeOPdCl + CuCCPh \longrightarrow CuCl + MeOPdCCPh$		1	1					
$CO + MeOPdCCPh \longrightarrow MeOOCPdCCPh$		1				1		
$CO + MeOPdCCPh \longrightarrow MeOPdCOCCPh$			1		1			
$HPdCl \longrightarrow HCl + Pd$				1			1	
$MeOH + ClPdCCPh \longrightarrow HCl + MeOPdCCPh$					1	1		
$CO + ClPdCCPh \longrightarrow ClPdCOCCPh$							1	1
$CuCCPh + ClPdCOOMe \longrightarrow CuCl + MeOOCPdCCPh$	1							
$PhCCH + ClPdCOOMe \longrightarrow ClPd{-}CPh{=}CH{-}COOMe$				1				
$ClPd{-}CPh{=}CH{-}COOMe \longrightarrow PhCCCOOMe + HPdCl$				1				
$MeOH + ClPdCOCCPh \longrightarrow PhCCCOOMe + HPdCl$							1	
$MeOH + ClPdCOCCPh \longrightarrow HCl + MeOPdCOCCPh$								1

Note. Here and in Tables 2 and 3, the entries correspond to the stoichiometric numbers of steps (Horiuti numbers) of the specific mechanism. The absence of an entry implies the absence of the step in the given mechanism.

Table 2. Eight-step mechanisms (seven intermediates)

Step	Mechanism												
	9	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*	*19*	*20*	*21*
$CuCl_2 + Pd \longrightarrow CuCl + PdCl$	1	1	1	1	1	1	1	1	1	1	1	1	1
$CuCl_2 + PdCl \longrightarrow PdCl_2 + CuCl$	1	1	1	1	1	1	1	1	1	1	1	1	1
$PhCCH + CuCl \longrightarrow HCl + CuCCPh$	1	1	1	1	1	1		1	1	1	1	1	1
$PdCl_2 + CuCCPh \longrightarrow CuCl + ClPdCCPh$				1	1	1		1		1	1	1	1
$CuCl + MeOH \longrightarrow HCl + CuOMe$	1	1	1	1	1	1	1						
$MeOOCPdCCPh \longrightarrow PhCCCOOMe + Pd$	1	1				1		1	1			1	
$MeOPdCOCCPh \longrightarrow PhCCCOOMe + Pd$			1	1	1					1	1		1
$PdCl_2 + MeOH \longrightarrow HCl + MeOPdCl$								1	1	1	1	1	
$PdCl_2 + CuOMe \longrightarrow CuCl + MeOPdCl$	1	1	1				1						
$CO + MeOPdCl \longrightarrow ClPd{-}COOMe$	1						1	1	1				
$CO + MeOPdCCPh \longrightarrow MeOOCPdCCPh$		1				1						1	
$CO + MeOPdCCPh \longrightarrow MeOPdCOCCPh$			1		1						1		
$CO + ClPdCCPh \longrightarrow ClPdCOCCPh$				1						1			1
$CuCCPh + MeOPdCl \longrightarrow CuCl + MeOPdCCPh$		1	1										
$CuOMe + ClPdCCPh \longrightarrow CuCl + MeOPdCCPh$					1	1							
$MeOPdCl + ClPdCCPh \longrightarrow PdCl_2 + MeOPdCCPh$											1	1	
$CuCCPh + ClPdCOOMe \longrightarrow CuCl + MeOOCPdCCPh$	1												
$CuOMe + ClPdCOCCPh \longrightarrow CuCl + MeOPdCOCCPh$				1									
$PhCCH + ClPdCOOMe \longrightarrow ClPd{-}CPh{=}CH{-}COOMe$							1						
$ClPd{-}CPh{=}CH{-}COOMe \longrightarrow PhCCCOOMe + HPdCl$							1						
$HPdCl \longrightarrow HCl + Pd$							1						
$ClPdCOOMe + ClPdCCPh \longrightarrow PdCl_2 + MeOOCPdCCPh$								1					
$MeOPdCl + CuCCPh \longrightarrow CuCl + MeOPdCCPh$									1				
$ClPdCOOMe + MeOPdCCPh \longrightarrow$ $\longrightarrow MeOPdCl + MeOOCPdCCPh$									1				
$MeOPdCl + ClPd{-}CO{-}CCPh \longrightarrow$ $\longrightarrow PdCl_2 + MeOPdCOCCPh$										1			
$MeOH + ClPdCCPh \longrightarrow HCl + MeOPdCCPh$													1
$MeOPdCCPh + ClPdCOCCPh \longrightarrow$ $\longrightarrow ClPdCCPh + MeOPdCOCCPh$													1

The mechanisms obtained by ChemNet and MECHEM are the sets of steps satisfying the constraints. The purpose of a researcher in the analysis of each mechanism is to take into account the possibility of the reversibility of reactions, the presence of quasi-equilibrium and rate-limiting steps, and other factors that can affect the kinetics of the process.

Some of the hypotheses advanced by the formal method have been suggested previously: mechanism *M1*, the mechanism with the intermediate formation of dimethyl carbonate, and numerous variants of the phenylethynyl mechanism. No variant of mechanisms with the intermediate formation of chlorocarbonate and chloroacetylene was considered because we did not input the corresponding transforms into ChemNet. The previously obtained experimental data excluded the possibility of these mechanisms.

Many mixed, intermediate variants of the mechanisms are a characteristic feature of the formalized advancement of hypotheses. This case is very characteristic.

Some of the newly obtained mechanisms can be discriminated on the basis of the experimental data briefly presented above. Mechanism *4* (see Table 1) and mechanism *15* (see Table 2) correspond to mechanism *M1*, ruled out at the stage of selecting the hypotheses formulated without computer programs. Mechanisms *30* and *34* in Table 3 are related to the intermediate formation of dimethyl carbonate, which was not observed in the contact solution (see above). At the same time, the tables contain many mechanisms that were not considered previously and cannot be discriminated on the basis of the data presented at the beginning of this work. Let us consider mechanism *2* (see Table 1) as an example. One of the most probable variants of this mechanism (including the parallel formation of chloroalkyne) is presented by reactions (15)—(22):

$$PhC{\equiv}CH + CuCl \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} HCl + \underset{I^1}{PhC{\equiv}CCu}, \qquad (15)$$

$$I^1 + CuCl_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} I^2, \qquad (16)$$

$$I^2 + CuCl_2 \xrightarrow{k_3} PhC{\equiv}CCl + 3\ CuCl, \qquad (17)$$

Table 3. Nine-step mechanisms (six intermediates)

Step	Mechanism																			
	22	*23*	*24*	*25*	*26*	*27*	*28*	*29*	*30*	*31*	*32*	*33*	*34*	*35*	*36*	*37*	*38*	*39*	*40*	*41*
PhCCH + CuCl ⟶ CuCCPh + HCl	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
$CuCl_2$ + Pd ⟶ CuCl + PdCl	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
$CuCl_2$ + PdCl ⟶ $PdCl_2$ + CuCl	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
$PdCl_2$ + CuCCPh ⟶ CuCl + ClPdCCPh	1	1		1		1	1	1	1	1		1	1	1	1		1	1	1	1
$PdCl_2$ + MeOH ⟶ HCl + MeOPdCl			1	1	1	1	1	1	1	1	1	1	1	1						
MeOOC–Pd–CCPh ⟶ Pd + PhCCCOOMe	1				1		1			1	1	1		1		1		1		1
MeOPd–CO–CCPh ⟶ Pd + PhCCCOOMe		1	1	1		1		1							1		1		1	
CO + MeOPdCl ⟶ ClPdCOOMe	1										1	1	1	1		1				1
CO + ClPdCCPh ⟶ ClPdCOCCPh		1	1	1				1							1				1	
2 MeOPdCl ⟶ $PdCl_2$ + $Pd(OMe)_2$					1	1	1	1	1	1										
CuCl + MeOH ⟶ HCl + CuOMe															1	1	1	1	1	1
$PdCl_2$ + CuOMe ⟶ CuCl + MeOPdCl																1	1	1	1	1
MeOPdCl + ClPdCCPh ⟶ $PdCl_2$ + MeOPdCCPh				1								1					1	1		
CuCCPh + MeOPdCl ⟶ CuCl + MeOPdCCPh			1								1					1				
CO + $Pd(OMe)_2$ ⟶ MeOPdCOOMe					1				1	1										
MeOH + ClPdCCPh ⟶ HCl + MeOPdCCPh	1	1																		
$PdCl_2$ + MeOPdCCPh ⟶ ClPdCCPh + MeOPdCl	1	1																		
ClPdCCPh + ClPdCOOMe ⟶ $PdCl_2$ + MeOOCPdCCPh	1																			1
$PdCl_2$ + MeOPdCCPh ⟶ MeOPdCl + ClPdCCPh			1								1									
MeOPdCl + ClPdCOCCPh ⟶ $PdCl_2$ + MeOPdCOCCPh			1																1	
ClPdCOCCPh + MeOPdCCPh ⟶ ⟶ ClPdCCPh + MeOPdCOCCPh				1											1					
$Pd(OMe)_2$ + ClPdCCPh ⟶ MeOPdCl + MeOPdCCPh						1	1													
CO + MeOPdCCPh ⟶ MeOPdCOCCPh						1											1			
CO + MeOPdCCPh ⟶ MeOOCPdCCPh							1											1		
MeOPdCOOMe ⟶ Pd + $(MeO)_2CO$									1				1							
ClPdCCPh + $(MeO)_2CO$ ⟶ PhCCCOOMe + MeOPdCl									1				1							
ClPdCCPh + MeOPdCOOMe ⟶ ⟶ MeOPdCl + MeOOCPdCCPh										1				1						
ClPdCOOMe + MeOPdCCPh ⟶ ⟶ MeOPdCl + MeOOCPdCCPh												1				1				
MeOPdCl + ClPdCOOMe ⟶ $PdCl_2$ + MeOPdCOOMe													1	1						
ClPdCOCCPh + MeOPdCl ⟶ ⟶ $PdCl_2$ + MeOPdCOCCPh		1																		
$PdCl_2$ + MeOPdCOOMe ⟶ MeOPdCl + ClPdCOOMe					1															
CuCCPh + ClPdCOOMe ⟶ CuCl + MeOOCPdCCPh					1															
$Pd(OMe)_2$ + ClPdCOCCPh ⟶ ⟶ MeOPdCl + MeOPdCOCCPh								1												
ClPdCOOMe + ClPdCCPh ⟶ $PdCl_2$ + MeOOCPdCCPh											1									
CuOMe + ClPdCCPh ⟶ CuCl + MeOPdCCPh															1					

$$PdCl_2 + MeOH \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} ClPdOMe + HCl, \quad (18)$$

$$I^1 + ClPdOMe \xrightarrow{k_6} CuCl + \underset{I^3}{MeOPdC{\equiv}CPh}, \quad (19)$$

$$I^3 + CO \xrightarrow{k_7} \underset{I^4}{MeOCOPdC{\equiv}CPh}, \quad (20)$$

$$I^4 \longrightarrow PhC{\equiv}CCOOMe + Pd, \quad (21)$$

$$Pd + 2\,CuCl_2 \longrightarrow PdCl_2 + 2\,CuCl. \quad (22)$$

The rate laws for the formation of products of phenylacetylene transformation derived from the mechanism presented above almost coincide with the equations corresponding to mechanism *M5*. Evidently, this mechanism and several analogous mechanisms (see Tables 1—3) cannot be discriminated on the basis of the previously obtained experimental data.

The main difference between *M5* and the mechanisms close to mechanism *2* in Table 1 is in the sequence of steps of the transfer of the phenylethynyl group from Cu^I to Pd^{II} and the cleavage of the O—H bond in methanol. Generally speaking, these mechanisms may have different dependences of the rates of formation of the products of phenylacetylene transformation on the methanol concentration, the partial CO pressure, and the concentration of the H^+ ion. However, it is difficult to study these dependences, because this study would require a special solvent which would allow the concentration of methanol to be varied, preserving the properties of the solution. Otherwise ligand should be used that would stabilize the state of the catalyst when varying the partial CO pressure over wide ranges and the acid concentration.

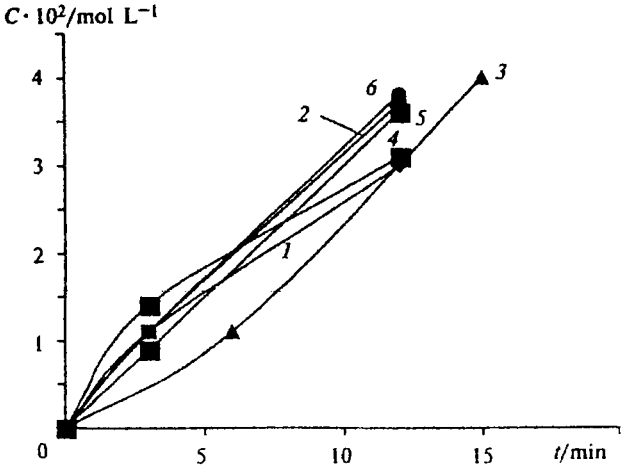


Fig. 2. A plot of methyl phenylpropiolate concentration *vs.* time: *1*—*4*, series of experiments with MeOH; *5*, *6*, series of experiments with MeOD.

Table 4. Kinetic isotope effects of formation of PhC≡CCOOMe for the replacement of MeOH by MeOD

Alcohol	Entry	v_0	v_{aver}	s
		mol L^{-1} h^{-1}		
MeOH	*1*	0.150	0.163	±0.017
	2	0.185		
	3	0.156		
	4	0.160		
MeOD	*5*	0.18	0.185	±0.017
	6	0.19		

Note. Here v_0 is the initial rate, v_{aver} is the average initial rate, and s is the standard deviation; r_H/r_D = 0.88.

Based on the analysis of the newly obtained hypotheses, it is very fruitful for their selection to study the kinetic isotope effect (KIE) when MeOH is replaced by MeOD. For the mechanisms in which the cleavage of a MeO—H bond occurs after the irreversible step of the transfer of the alkynyl group from Cu^I to Pd^{II}, the kinetic isotope effect k_H/k_D should be close to unity (see mechanisms *5*—*8* in Table 1 and mechanism *21* in Table 2). For other mechanisms, this value should be ~3—4 (by analogy to the known kinetic isotope effects of the processes involving H_2O).[18,19]

The results obtained (Table 4) indicate that the difference between the rates of formation of methyl phenylpropiolate when MeOH and MeOD are used is comparable with the experimental error.

Closeness of the KIE value (r_H/r_D ratio) to unity allows us to exclude all mechanisms except *5*—*8* (see Table 1) and *21* (see Table 2) from consideration. The latter mechanism contains a nonlinear step involving two palladium-containing intermediates

$$MeOPdC{\equiv}CPh + ClPdCOC{\equiv}CPh \longrightarrow$$
$$\longrightarrow ClPdC{\equiv}CPh + MeOPdCOC{\equiv}CPh,$$

which seems highly improbable because the concentrations of these intermediates should be very low.

The same intermediate MeOPdCOC≡CPh can be obtained in a simpler way: the reaction of ClPdCOC≡CPh with methanol. In addition, if this or similar steps play an important role in the process, the appearance of critical phenomena[20] or oscillations[21] would be expected. Phenomena of this type were not detected in the system.

Mechanisms *5*—*8* in Table 1 are rather close and differ in three features.

1. The nucleophilic attack on the carbon atom of the carbonyl group is either intermolecular (*7*, *8*) or intramolecular (*5*).

2. Carbon monoxide is inserted into either the Pd—C (*5*, *7*, *8*) or the Pd—OMe bond (*6*).

3. When the σ-organometallic compound dissociates, either the palladium hydride complex (*7*) or Pd^0 (*5*, *6*, *8*) is formed.

The palladium hydride complex, if formed, can directly be oxidized by the Cu^{II} compounds in the reaction

$$HPdCl + 2\ CuCl_2 \longrightarrow PdCl_2 + 2\ CuCl + HCl.$$

Further studies toward discriminating mechanisms *5*—*8* (see Table 1) based on the contrasts between them are necessary to refine the mechanism and choose from the four remaining hypotheses.

* * *

Thus, the use of the strategy based on advancing and selecting mechanistic hypotheses for the reaction under study makes it possible to design and efficiently perform discriminating experiments aimed at checking the most characteristic features (distinctions) of competing hypotheses. Of course, an experienced researcher knows the main hypotheses on the mechanism of each specific reaction discussed in scientific publications. However, an advantage of the formalized method is finding many mixed, intermediate variants of mechanisms that are not usually considered intuitively. Correspondingly, experiments without the formalized method are designed and their results are interpreted ignoring this large group of hypothetical mechanisms. This substantially affects conclusions. In addition, information on the possible mechanisms grows rapidly, and computer programs can help in storing and processing this information.

The use of libraries of elementary reactions (involving catalysts) and special computer programs allows almost any researcher not only to consider all main hypotheses, but also to find all (with specified constraints) hybrid variants of the main hypotheses. In addition, the formulation of steps (transforms) in the generalized form results in finding new mechanisms that were not considered previously for a given reaction.

The hypotheses remaining after the selection make it possible to focus the scope of our knowledge about the mechanism of the reaction under study and to formulate directions of further studies.

This work was financially supported by the Russian Foundation for Basic Research (Project Nos. 97-03-32324 and-98-03-32108a).

References

1. J. Tsuji, M. Takahashi, and T. Takahashi, *Tetrahedron Lett.*, 1980, **21**, 849.
2. T. T. Zung, L. G. Bruk, and O. N. Temkin, *Izv. Akad. Nauk, Ser. Khim.*, 1993, 1806 [*Russ. Chem. Bull.*, 1993, **42**, 1730 (Engl. Transl.)].
3. O. N. Temkin, L. G. Bruk, and A. V. Zeigarnik, *Kinet. Katal.*, 1993, **34**, 445 [*Kinet. Catal.*, 1993, **34** (Engl. Transl.)].
4. A. V. Zeigarnik, L. G. Bruk, O. N. Temkin, V. A. Likholobov, and L. I. Maer, *Usp. Khim.*, 1996, **65**, 125 [*Russ. Chem. Rev.*, 1996, **65** (Engl. Transl.)].
5. A. V. Zeigarnik, R. E. Valdés-Peréz, O. N. Temkin, L. G. Bruk, and S. I. Shalgunov, *Organometallics*, 1997, **16**, 3114.
6. R. E. Valdés-Peréz and A. V. Zeigarnik, *J. Mol. Catal., A: Chem.*, 1997, **119**, 405.
7. R. E. Valdés-Peréz, *J. Chem. Inf. Comput. Sci.*, 1994, **34**, 976.
8. R. F. Heck, *J. Am. Chem. Soc.*, 1972, **94**, 2721.
9. Eur. Pat. Appl. EP365, 083; *Chem. Abstrs.*, 1990, **113**, 97039.
10. France Pat. No. 2408575, 1978.
11. I. P. Beletskaya and N. A. Bumagin, *Proc. 4th Intern. Sympos. on Homogeneous Catalysis*, Leningrad, 1984, **1**, 215.
12. J. F. Normant and M. Bourgain, *Tetrahedron Lett.*, 1970, **11**, 2659.
13. R. Takeuchi, Y. Tsuji, and M. Fujita, *J. Org. Chem.*, 1989, **54**, 1831.
14. L. N. Zhir-Lebed' and O. N. Temkin, *Kinet. Katal.*, 1984, **25**, 316 [*Kinet. Catal.*, 1984, **25** (Engl. Transl.)].
15. O. N. Temkin, G. K. Shestakov, and Yu. A. Treger, *Atsetilen: Khimiya. Mekhanizmy reaktsii. Tekhnologiya* [*Acetylene: Chemistry. Reaction Mechanisms. Technology*], Khimiya, Moscow, 1991 (in Russian).
16. N. A. Bumagin, I. O. Kalinovskii, A. B. Ponomarev, and I. P. Beletskaya, *Dokl. Akad. Nauk SSSR*, 1982, **265**, 1138 [*Dokl. Chem.*, 1982 (Engl. Transl.)].
17. L. V. Shchel'tsin, S. M. Brailovskii, E. Yu. Murugova, and O. N. Temkin, *Kinet. Katal.*, 1988, **29**, 1044 [*Kinet. Catal.*, 1988, **29** (Engl. Transl.)].
18. V. N. Zudin, V. D. Chinakov, V. M. Nekipelov, V. A. Rogov, V. A. Likholobov, and Yu. I. Yermakov, *J. Mol. Catal.*, 1989, **52**, 27.
19. I. I. Moiseev, M. N. Vargaftik, and Ya. K. Syrkin, *Dokl. Akad. Nauk SSSR*, 1963, **153**, 140 [*Dokl. Chem.*, 1963 (Engl. Transl.)].
20. L. G. Bruk, I. V. Oshanina, A. S. Zakieva, A. P. Kozlova, and O. N. Temkin, *Kinet. Katal.*, 1998, **39**, 183 [*Kinet. Catal.*, 1998, **39** (Engl. Transl.)].
21. A. V. Malashkevich, L. G. Bruk, and O. N. Temkin, *J. Phys. Chem. A*, 1997, **101**, 9825.

Received October 12, 1998