

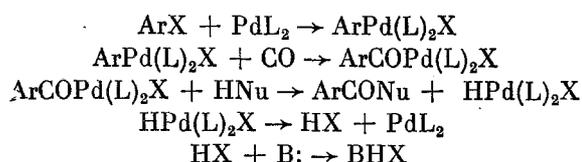
ALKOXYCARBONYLATION AND AMIDATION OF ARYL IODIDES  
 CATALYZED BY PALLADIUM COMPLEXES

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UDC 542.97:547.539.4

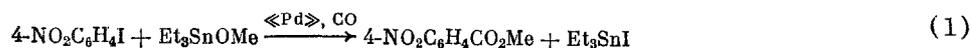
Aryl halides ArX react with alcohols ROH in the presence of CO and Pd complexes to give mixed esters of aromatic carboxylic esters [1-5]. In an analogous manner, amides ArCONH<sub>2</sub> are obtained when amines R<sub>2</sub>NH are used as the nucleophilic reagents in this reaction sequence [6]. Although the mechanism of carbonylation of aryl halides has not been studied in detail, it is generally assumed that the reaction takes place according to Scheme 1 (where L is a ligand; Nu = RO or R<sub>2</sub>N; and B is a base) [7, 8]:

Scheme 1



According to Scheme 1, the role of the base is to neutralize the acid HX which is formed during the course of the reaction sequence. It is known, however, that ArCOPd(L)<sub>2</sub>X does not react with ROH under mild conditions in the absence of base [4], and so it would seem that, at least in the case of Nu = PO, the role of the base is to activate the nucleophilic reagent (HNu + B: ⇌ Nu<sup>-</sup> + BH<sup>+</sup>). The rate of the reaction of HNu with ArCOPd(L)<sub>2</sub>X should thus depend on the nature of the nucleophile as well as on the nature of the base used in the reaction. As can be seen from the literature data [3, 6], these factors also influence the overall rate of the carbonylation of aryl iodides. As a result, in many cases reactions of the acylpalladium complex with the nucleophile is the limiting factor in the overall process; the use of stronger nucleophiles, such as metal alkoxides and amides, should make it possible to carry out the carbonylation of ArX at higher rates and also, possibly, under milder conditions relative to conventional conditions.

In the present paper we report our results concerning the carbonylation of aryl iodides in the presence of various types of metal alkoxides, such as Et<sub>3</sub>SnOMe, Al(OPr)<sub>3</sub>, Mg(OMe)<sub>2</sub>, and NaOMe, as well as in the presence of a tin amide, Me<sub>3</sub>SnNET<sub>2</sub>. In order to determine the optimum conditions for the reaction process, we first investigated the effect of solvent and Pd catalyst on the alkoxy carbonylation of 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>I (I). The tin derivative Et<sub>3</sub>SnOMe (II), which is readily soluble in a wide variety of organic solvents, was used as the nucleophilic reagent. Reaction progress was followed by the disappearance of the starting material (I), and also by the formation of the reaction product, 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>Me (III):



As can be seen from the results in Table 1, alkoxy carbonylation occurs readily even at 20°C and 1 atm CO in the presence of dipolar aprotic solvents; the best results were obtained using HMPA. In solvents of low polarity (THF), or in protic solvents (MeOH), the reaction rate is slow, while in nonpolar solvents such as benzene the reaction does not take place at all. In summary, the carbonylation rate was found to be affected to a large extent by the nature of the solvent, and decreased in the following order: HMPA > DMSO > DMF > MeCN > THF > MeOH > C<sub>6</sub>H<sub>6</sub>. We should note, however, that in the case of dipolar aprotic solvents, there

M. V. Lomonosov Moscow State University. L. Ya. Karpov Institute of Physical Chemistry, Moscow. Translated from *Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya*, No. 7, pp. 1649-1656, July, 1986. Original article submitted February 1, 1985.

TABLE 1. Solvent Effect on the Carbonylation Reaction of 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>I in the Presence of 1.5 Equiv. Et<sub>3</sub>SnOMe and 2 mole% PhPd(PPh<sub>3</sub>)<sub>2</sub>I (1 atm CO, 20°C, C<sub>0</sub> 0.20 mole/liter)

Solvent	ε *	DN <sub>SbCl<sub>5</sub></sub> *	Reaction time, h	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> Me, %	Conversion of 4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> I, percent
C <sub>6</sub> H <sub>6</sub>	2,3†	—	5	0	—
MeOH	32,6†	—	5	4	4
THF	7,6	20,0	5	7	12
MeCN	38,0	14,1	5	22	22
DMF	36,1	26,6	5	81	—
Same	36,1	26,6	7	84	94
DMSO	45,0	29,8	3	88	100
HMPA	30,0	38,8	1	94	100

\*According to [9], unless stated otherwise.

†According to [10].

TABLE 2. Effect of Catalyst Nature on the Alkoxy carbonylation Reaction of 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>I in the Presence of 1.5 Equiv. Et<sub>3</sub>SnOMe and 2 mole % Catalyst in HMPA (1 atm CO, 20°C, C<sub>0</sub> = 0.20 mole/liter)

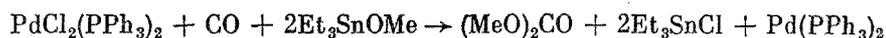
Catalyst	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> Me, %	Unreacted 4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> I, pct.
PdCl <sub>2</sub> (MeCN) <sub>2</sub>	66	17
PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	86	3
PhPd(PPh <sub>3</sub> ) <sub>2</sub> I	94	0
Pd(PPh <sub>3</sub> ) <sub>4</sub>	95	0
PhPd(PPh <sub>3</sub> ) <sub>2</sub> I - 4PPh <sub>3</sub>	68	18
PdCl <sub>2</sub> (AsPh <sub>3</sub> ) <sub>2</sub>	73	0
PdCl <sub>2</sub> (MeCN) <sub>2</sub> - 2P(OEt) <sub>3</sub>	60	40
PdCl <sub>2</sub> (dppf) *	48	26
PdCl <sub>2</sub> (dppe) †	16	67
PdCl <sub>2</sub> (PEt <sub>3</sub> ) <sub>2</sub>	41	52

\*dppf - 1,1'-bis(diphenylphosphino)ferrocene.

†dppe - 1,2-bis(diphenylphosphino)ethane.

does not appear to be a correlation between the rate of the reaction and the solvent polarity (ε). Instead, the rate of the reaction in these cases increases as the donor ability of the solvent, as measured by the Guttmann donor number DN<sub>SbCl<sub>5</sub></sub>, is raised (cf. Table 1). Specific solvation of the Sn atom in dipolar aprotic solvents, and especially in HMPA, leads to polarization of the Sn-O bond and, consequently, to increased reactivity of (II) with respect to the intermediate acyl Pd complex (see Scheme 1). As a result, the overall (total) rate of reaction (1) is increased. The results discussed above are consistent with the assumptions stated earlier concerning the limiting step in the alkoxy carbonylation of ArX.

Experiments concerning the influence of the nature of the Pd catalyst, and also of the Pd/L ratio, on the rate of reaction (1) in HMPA (Table 2) revealed that carbonylation was complete within 1 h at 20°C and 1 atm CO in the presence of 2 mole% PhPd(PPh<sub>3</sub>)<sub>2</sub>I (IV) or Pd(PPh<sub>3</sub>)<sub>4</sub> (V). The product (III) was formed in nearly quantitative yields under these conditions. In the case of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (VI) as catalyst, conversion of (I) was 97% after 1 h, and the yield of (III) was 86%. The small decrease in the rate of the reaction associated with the change from (IV) to (VI) is probably due to the necessity of preliminary formation of a catalytically active Pd(0) species in the latter case [7]:



A large excess of PPh<sub>3</sub> was found to retard reaction (1). Thus, in the presence of (IV)-4PPh<sub>3</sub>, the amount of unreacted (I) was 18% after 1 h, and the yield of (III) was 68%. This effect can be attributed to decreases in the rates of both the oxidative addition step [5, 11] as well as the subsequent carbonylation step of the aryl Pd complex [7] (cf. Scheme 1). Carbonylation of ArPd(PPh<sub>3</sub>)<sub>2</sub>X occurred more easily as AsPh<sub>3</sub> was substituted for PPh<sub>3</sub> [7]. In our case, however, the use of PdCl<sub>2</sub>(Ph<sub>3</sub>As)<sub>2</sub> rather than (IV) or (V) did not increase the rate of reaction (1), and led instead to a decrease in the selectivity of the reaction.

TABLE 3. Alkoxy-carbonylation and Amidation of Organic Halides RX in the Presence of 2 mole % PhPd(PPh<sub>3</sub>)<sub>2</sub>I in HMPA (1 atm CO, 20°C)

Nucleophilic reagent	RX	C <sub>0</sub> , mole/liter	Time, h	Reaction product	Yield, pct.
MeOH	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> I	0,4	5	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> Me	0
Same	Same	0,4	5	Same	11 <sup>b</sup>
Et <sub>3</sub> SnOMe	»	0,4	1	»	100
Same	4-NCC <sub>6</sub> H <sub>4</sub> I	0,8	9	4-NCC <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> Me	88
»	4-MeOCOC <sub>6</sub> H <sub>4</sub> I	0,8	24	4-MeOCOC <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> Me	95
Al(OPr) <sub>3</sub>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> I	0,4	5	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> Pr	0
Mg(OMe) <sub>2</sub>	Same	0,4	5	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> Me	9 <sup>c</sup>
NaOMe	»	0,4	10 min	Same	0 <sup>d</sup>
Same <sup>e</sup>	»	0,4	3	»	75
»	4-MeOCOC <sub>6</sub> H <sub>4</sub> I	0,8	2	4-MeOCOC <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> Me	51 <sup>f</sup>
» <sup>π</sup>	Same	0,8	24	Same	75
»	PhI	0,8	7	PhCO <sub>2</sub> Me	97
»	α-C <sub>10</sub> H <sub>7</sub> I	0,8	4	α-C <sub>10</sub> H <sub>7</sub> CO <sub>2</sub> Me	90
»	E-PhCH=CHBr	0,8	6	E-PhCH=CHCO <sub>2</sub> Me	78
HNEt <sub>2</sub>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> I	0,4	5	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CONEt <sub>2</sub>	23 <sup>g</sup>
Me <sub>3</sub> SnNEt <sub>2</sub>	Same	0,4	0,5	Same	82
Same	PhI	0,4	3	PhCONEt <sub>2</sub>	90

<sup>a</sup>In the presence of 1.5 equiv. K<sub>2</sub>CO<sub>3</sub>.

<sup>b</sup>83% 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>I remains.

<sup>c</sup>80% 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>I remains.

<sup>d</sup>4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>OMe is formed in 92% yield.

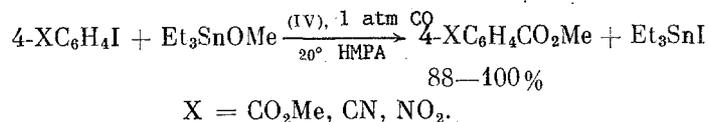
<sup>e</sup>The reaction was carried out in MeOH instead of HMPA.

<sup>f</sup>4-MeOCOC<sub>6</sub>H<sub>4</sub>OMe was also formed, in 29% yield.

<sup>g</sup>57% 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>I remains.

Although complexes of Pd with PET<sub>3</sub> exhibit very large activity toward oxidative addition reactions [12], PdCl<sub>2</sub>(PEt<sub>3</sub>)<sub>2</sub> was found to be less effective than either (IV) or (V) toward alkoxy-carbonylation: the reaction gave 41% (III) at 52% conversion of (I) (reaction time 1 h). The highly donating PET<sub>3</sub> ligand significantly decreases the reactivity of ArCOPd(L)<sub>2</sub>X relative to HNu. Previous work [5] has also established that complexes of Pd with PET<sub>3</sub> could not be used as catalysts in the alkoxy-carbonylation of RX. Experiments using PdCl<sub>2</sub>(MeCN)<sub>2</sub>-2P(OEt)<sub>3</sub>, PdCl<sub>2</sub>, and PdCl<sub>2</sub>(dppe) also were accompanied by decreases in the reaction rate, and, in the cases of complexes containing bidentate ligands, by decreased selectivity for the desired reaction (1). Since HMPA should be capable of acting as a weak ligand and also of stabilizing the intermediate Pd complex in solution, it should be possible to use PdCl<sub>2</sub>(MeCN)<sub>2</sub> as a catalyst in reaction (1) without the addition of phosphine ligands; this was found to give 66% of (III) at 83% conversion of (I) (reaction time 1 h).

On the basis of these experimental results, the following conditions are recommended as the optimum conditions for the alkoxy-carbonylation of aryl iodides: HMPA as reaction solvent with triphenylphosphine Pd complex catalysts containing a PPh<sub>3</sub>/Pd ratio of 2-4. As can be seen from the data summarized in Table 3, (II) reacts with 4-XC<sub>6</sub>H<sub>4</sub>I (X = CO<sub>2</sub>Me, CN, NO<sub>2</sub>) in HMPA in the presence of 2 mole% (IV) at 20°C and 1 atm CO pressure to give 4-XC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>Me products in yields of 88-100%:

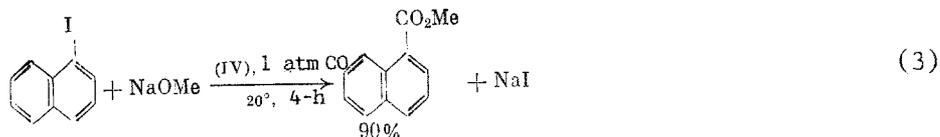


(2)

The reactivity of aryl iodides increases as the electron-accepting (withdrawing) power of the substituent X in the benzene ring increases: NO<sub>2</sub> > CN > CO<sub>2</sub>Me. We note, however, that carbonylation of (I) did not occur under the standard conditions stated herein when (II) was replaced by MeOH. In the presence of K<sub>2</sub>CO<sub>3</sub>, which has been used often as a base in related reactions [5], (I) did react with CO in the presence of MeOH, although the rate of the reaction was quite slow. After 5 h the conversion of (I) was 17%, and the yield of (III) only 11%.

In contrast to (II), Al(OPr)<sub>3</sub> did not react at all with (I) and CO at 20°C, and in the presence of the sparingly soluble derivative HMPAMg(OMe)<sub>2</sub> carbonylation was extremely slow: after 5 h the yield of (III) was 9% (see Table 3).

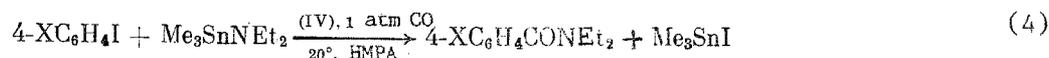
When NaOMe was used as the reactant, reaction of (I) with CO in HMPA was complete after 10 min, although (III) was not formed. Under these conditions the only reaction product was 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>OMe in 92% yield. Nucleophilic replacement of the iodide ion in (I) by an OMe group occurs just as readily in the absence of a Pd catalyst. When the less active substrate 4-MeOCOC<sub>6</sub>H<sub>4</sub>I was used, the reaction gave, in addition to 29% of the substitution product 4-MeOCOC<sub>6</sub>H<sub>4</sub>OMe, 51% of the carbonylation product 4-MeOCOC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>Me. When the MeOH solvent was replaced by the dipolar aprotic solvent HMPA, nucleophilic substitution was completely suppressed, and 4-XC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>Me was obtained in excellent yields under these conditions (X = NO<sub>2</sub>, CO<sub>2</sub>Me) (cf. Table 3). Alkoxy-carbonylation of unactivated aryl iodides could not be achieved when (II) was used as the nucleophilic reagent, due to the low reaction rate. The high reactivity of NaOMe in HMPA allowed us to circumvent this problem. Thus, carbonylation of PhI in the presence of NaOMe was complete within 7 h and PhCO<sub>2</sub>Me was obtained in 97% yield. In an analogous manner, α-C<sub>10</sub>H<sub>7</sub>CO<sub>2</sub>Me was obtained in excellent yield from α-C<sub>10</sub>H<sub>7</sub>I:



We should note that under the conditions described in [2], reaction of α-C<sub>10</sub>H<sub>7</sub>Br\* with BuOH/Bu<sub>3</sub>N (1 atm CO, 100°C) was nonselective and did not proceed to completion even after 80 h; 46% α-C<sub>10</sub>H<sub>7</sub>CO<sub>2</sub>Bu was obtained (at 81% conversion).

The feasibility of using NaOMe as the nucleophilic reagent in alkoxy-carbonylation reactions of vinyl halides was demonstrated in the case of E-PhCH=CHBr. The reaction was found to take place with retention of configuration of the starting bromide (6 h, 78% E-PhCH=CHCO<sub>2</sub>Me).

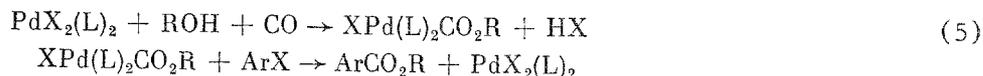
Carbonylation of 4-XC<sub>6</sub>H<sub>4</sub>I (X=H, NO<sub>2</sub>) in the presence of Me<sub>3</sub>SnNEt<sub>2</sub> (VII) led to the formation of carboxylic acid amide derivatives (see Table 3):



In contrast to the results obtained in [6], amidation of (I) under the conditions employed herein was not accompanied by competing reduction of the NO<sub>2</sub> group. Amidation of (I) was found to occur at higher reaction rates than the corresponding alkoxy-carbonylation reactions. For example, (VII) was 2.7 times more active than (II) toward the carbonylation of (I) (using the method of competing concurrent reactions). It should be noted, however, that the use of HNEt<sub>2</sub> in place of (VII) led to a significant decrease in the rate of reaction (4), and also decreased the selectivity of the reaction process. Thus, carbonylation of (I) in the presence of HNEt<sub>2</sub> was only 43% complete after 5 h, and the yield of 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CONEt<sub>2</sub> was 23%.

We have demonstrated that both Sn and Na alkoxides, as well as Sn amide derivatives, can be used successfully as the nucleophilic reagents in carbonylation reactions of ArI. The use of these powerful nucleophiles meant that the alkoxy-carbonylation and amidation of ArI could be carried out at fast rates even at 20°C and 1 atm CO pressure.

As has been noted previously, detailed studies of the mechanism of Pd complex-catalyzed carbonylation of ArX in the presence of alcohols or amides have not been made. A carbo-methoxy Pd complex has been postulated as an intermediate product in these reactions [1, 3]:

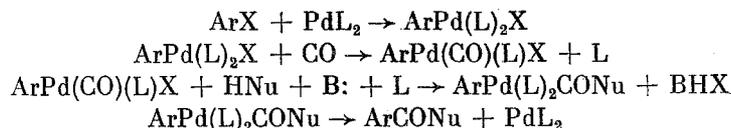


It is known, however, that XPd(L)<sub>2</sub>CO<sub>2</sub>R reacts with organic halides only under much harsher conditions [4, 13] than those employed for the catalytic reactions. On the basis of the known reactivities of Pd complexes (oxidative addition [11], insertion of CO into C-Pd bonds [7]), as well as upon consideration of some kinetic data [13], a mechanism was proposed for these reactions which involved formation of an acylpalladium halide complex followed by subsequent reaction of this complex with a nucleophile (See Scheme 1). The data available till now, however, do not preclude the possibility of an alternative

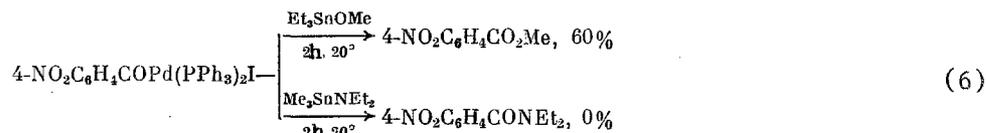
\*Under the conditions described in [2], RI was more than twice as active as RBr.

mechanistic pathway (Scheme 2) [2, 6]:

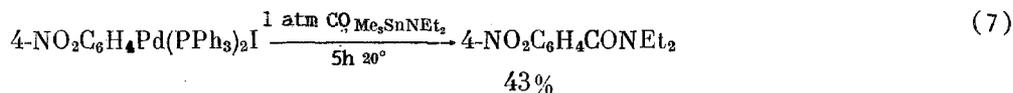
Scheme 2



We have carried out stoichiometric reactions of both 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Pd(PPh<sub>3</sub>)<sub>2</sub>I (VIII) and the acyl complex 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>COPd(PPh<sub>3</sub>)<sub>2</sub>I (IX). Carbonylation of (VIII) at 20°C and 1 atm CO resulted in the formation of a solution of (IX) in HMPA, which was reacted further with (II) after CO had been replaced by argon. After 2 h the starting complex (IX) had disappeared completely, and (III) was obtained in 60% yield. It is interesting that in an analogous reaction of (IX) with (VII) the amide 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CONEt<sub>2</sub> was not formed at all [instead, TLC revealed that after 2 h the starting complex (IX) was converted to a series of unidentified products]:

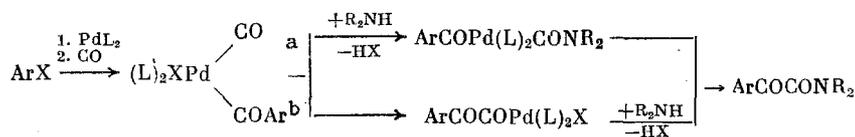


According to [4], acyl Pd complexes react readily with alcohols in the presence of bases; as in our experiments, these reactions lead to the formation of carboxylic acid ester derivatives. Reaction of RCOPd(L)<sub>2</sub>X with amines has not been studied to any appreciable extent. It has been noted, however, that reaction of PhCOPd(PPh<sub>3</sub>)<sub>2</sub>Cl with HNEt<sub>2</sub> led to the formation of PhCONEt<sub>2</sub> in trace amounts [14]. In contrast, reactions of RPd(L)<sub>2</sub>X derivatives with HNR<sub>2</sub> under a CO atmosphere are known to give excellent yields of carbonylation products (RCONEt<sub>2</sub> and RCOCONEt<sub>2</sub>). We have also observed the formation of an amide when the stoichiometric reaction is carried out:



These results taken together are consistent with an amidation mechanism which involves intermediate formation of a carbamoyl Pd complex rather than an acyl complex (see Scheme 2). We should note that formation of a carbamoyl Pd complex as a result of amine attack on a CO molecule coordinated to Pd has recently been demonstrated in a study of the mechanism of double carbonylation of organic halides [14] (Scheme 3). The authors found the ArCOCONR<sub>2</sub> was formed exclusively via pathway a. Analogous double carbonylation reactions of ArX to give ArCOCO<sub>2</sub>R under conditions of Pd catalysts are not known. It is possible that pathway a is not a viable reaction when ROH is used as the nucleophile. It is not possible, however, to exclude the possibility of nucleophilic

Scheme 3



attack of an alcohol on a Pd-coordinated CO molecule during alkoxycarbonylation of ArX (see Scheme 2). The results obtained by stoichiometric reactions do demonstrate, however, that ArCO<sub>2</sub>R can be formed readily according to Scheme 1. By the same token, the available results do not invalidate the possibility of alkoxycarbonylation occurring via intermediate formation of a carboalkoxy Pd complex (carboalkoxy Pd complexes are known to be important intermediates in a variety of carbonylation reactions involving olefins and acetylenes).

## EXPERIMENTAL

GLC analysis were performed on a Tsvet-110 chromatograph equipped with a flame-ionization detector and using a 1.5-m column filled with 3% SE-30 on n-Super Chromaton. Silufol UV-254 plates were used for TLC analyses (with UV irradiation). The UV spectra were recorded on a Hitachi-124 spectrophotometer using methanol solutions. The IR spectra were obtained on a Perkin-Elmer 580 spectrophotometer.

PhI,  $\alpha$ -ClOH<sub>7</sub>I, E-PhCH=CHBr, PPh<sub>3</sub>, and P(OEt)<sub>3</sub> were of reagent grade quality and were purified by distillation or recrystallization, as appropriate. The other organic halides, Pd complexes, and Sn derivatives used in this study were prepared according to known methods. NaOMe and Mg(OMe)<sub>2</sub> were prepared by dissolving metallic Na and Mg, respectively, in absolute methanol, and were employed in the form of 0.5 M solutions in MeOH. Al(OPr)<sub>3</sub> was obtained by dissolving metallic Al in absolute propanol and was used as a 0.5 M solution in propanol. HMPA was purified by twofold distillation from CaH<sub>2</sub> under vacuum. DMF was stirred over KOH and distilled from BaO under vacuum. DMSO was treated for 1 day with NaOH and then distilled from NaOH under vacuum. Acetonitrile was refluxed over P<sub>2</sub>O<sub>5</sub> and distilled, and the distillate was refluxed over CaH<sub>2</sub> and distilled again. Absolute C<sub>6</sub>H<sub>6</sub>, MeOH, and THF were purified according to standard procedures.

The yields of carbonylation reaction products as well as conversions of the organic halide starting materials were determined by TLC analysis and UV spectrophotometric detection versus standard compounds, or by GLC analysis relative to an internal standard. Products were identified by TLC or GLC by comparison with authentic samples prepared independently.

Studies of the Effect of the Solvent and Pd-Catalyst on the Carbonylation of (I) in the Presence of (II). A flask which was equipped with a magnetic stirrer and filled with CO was charged with 0.25 mmole (I), 0.375 mmole (II), and 1.25 ml of solvent. The mixture was stirred, and  $0.5 \cdot 10^{-2}$  mole of Pd catalyst was added [in the case of catalyst (IV)-4PPh<sub>3</sub> or PdCl<sub>2</sub>(MeCN)<sub>2</sub>-2P(OEt)<sub>3</sub>, the mixture was first treated with  $2 \cdot 10^{-2}$  mmole PPh<sub>3</sub> or  $1 \cdot 10^{-2}$  mmole P(OEt)<sub>3</sub>, respectively, followed by  $0.5 \cdot 10^{-2}$  mmole of Pd complex]. The reaction mixture was then stirred at 20°C under 1 atm CO pressure.

Alkoxy carbonylation or Amidation of Organic Halides RX, Catalyzed by (IV). A flask, fitted with magnetic stirrer and filled with CO, was charged with 0.75 mmole of the appropriate nucleophilic reagent (when Na, Mg, or Al alkoxides were used as the nucleophiles, 1.5 ml of 0.5 M solutions of these reagents in the corresponding alcohols were transferred under vacuum to the flask), followed by 0.5 mmole RX and 1.25 or 2.5 ml of HMPA [in several cases MeOH was used in place of HMPA as solvent (see Table 3)]. (IV) ( $1 \cdot 10^{-2}$  mmole) was added and the reaction mixture was stirred at 20°C and 1 atm CO pressure.

Synthesis of (IX) and Its Reaction with (II) and (VII). (IX) was prepared via carbonylation of (VIII) according to the method outlined in [7], and was used without isolation in all subsequent reactions. A flask, fitted with magnetic stirring and filled with CO, was charged with 0.1 mmole of (VIII) and 0.5 ml of HMPA. The reaction mixture was stirred at 20°C and 1 atm CO. After 5 h,  $\sim 1$  equiv. of CO had been absorbed; TLC analysis revealed the complete disappearance of starting material and the formation of a new Pd complex, whose IR spectrum (the IR spectrum of the reaction mixture was recorded using cuvettes made of BaF<sub>2</sub>) showed an intense band at 1642 cm<sup>-1</sup>, which is characteristic of acyl Pd complexes [7]. The CO atmosphere was replaced by argon and the reaction solution of (IX) in HMPA was treated with 0.15 mmole of (II) or (VII). After 2 h the starting material (IX) had disappeared (TLC). In the case of (II), (III) was formed in 60% yield. When (VII) was used as the nucleophile, 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CONEt<sub>2</sub> was not formed; (IX) was converted to a series of unidentified products.

Carbonylation of (VIII) in the presence of (VII). A flask fitted with magnetic stirrer, was charged with 0.1 mmole of (VIII), 0.15 mmole of (VII), and 0.5 ml HMPA. The reaction mixture was stirred at 20°C and 1 atm CO. After 5 h the starting material (IX) had disappeared and 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CONEt<sub>2</sub> was formed in 43% yield.

## CONCLUSIONS

1. Tin and sodium alkoxides, as well as tin amides, can be used as coreagents in the palladium complex-catalyzed carbonylation of aryl iodides. The use of such powerful nucleophiles as metal alkoxides and amides permits the carbonylation reactions to be carried out under milder conditions and at faster rates than those described in the literature.

2. A mechanism for the alkoxy-carbonylation and amidation of aryl halides has been proposed based on results obtained using stoichiometric reactions of palladium complexes.

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#### CONDENSED PYRIDINES.

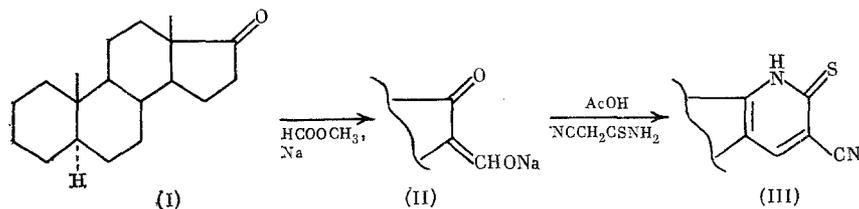
#### COMMUNICATION 5\*. SYNTHESIS AND TRANSFORMATIONS OF 3'-CYANO-5 $\alpha$ -ANDROSTENO[17,16-b]PYRIDINE-2'(1'H)-THIONE

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UDC 542.91:547.83:547.92

The known biological activity of steroids and substituted 3-cyano-2(1H)-pyridinethiones prompted us to combine them into one molecule, and to examine the properties of the compounds obtained. With minor exceptions [2, 3], condensed 3-cyano-2(1H)-pyridinethiones still remain a very little investigated class of compounds, while androsteno[17,16-b]pyridinethiones have not yet been synthesized up to the present time.

With the reaction of the sodium salt of 16-formyl-5 $\alpha$ -androstan-17-one (II) [obtained by formylation of 5 $\alpha$ -androstan-17-one (I) by methyl formate] with cyanoacetamide, we synthesized the first representative of 3-cyano-2(1H)-pyridinethiones condensed with steroids, and namely, 3'-cyano-5 $\alpha$ -androsteno[17,16-b]pyridine-2'(1'H)-thione (III):



The structure of thione (III) was confirmed by spectral data and chemical transformations. Its UV spectrum contains characteristic absorption maxima of the thione fragment, while in the IR spectrum there is an absorption band of stretching vibrations of the

\*For communication 4, see [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from *Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya*, No. 7, pp. 1656-1659, July, 1986. Original article submitted February 12, 1985.