

A Novel Synthesis of Alkyl Chloroformate in the Gas Phase by Palladium-Catalyzed Reaction Using XCl (X=H or NO), CO, and Alkyl Nitrite

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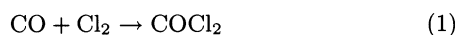
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A novel synthesis of chloroformate was developed by palladium-catalyzed reaction of XCl (X=H or NO), CO, and alkyl nitrite in the gas phase. When PdCl₂/γ-Al₂O₃ or PdCl₂/SiO₂ was used as a catalyst, chloroformate was produced in good yield and with high selectivity. The reaction temperature had a strong influence on the formation rate of chloroformate, and its selectivity drastically depended on the nitrite/chloride ratio. When the nitrite/chloride ratio was less than 2, the selectivity of chloroformate was almost 100%. Dependence of the formation rate on the concentrations of CO and methyl nitrite was also examined.

Organic synthesis using the carbonylation reaction is receiving much attention and is used in many industrial processes. Especially, palladium-catalyzed reactions using alkyl nitrite, not only as a substrate but as a reoxidation reagent of palladium, have been widely explored and a variety of organic compounds are now produced by Ube Industries such as dimethyl carbonate,^{1–3} dibutyl oxalate,⁴ and 3,3-dimethoxypropionitrile,⁵ a key intermediate of vitamin B₁ synthesis.⁶

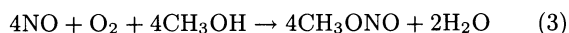
Chloroformates are now produced by the reaction between alcohols and phosgene, which is formed by the reaction Cl₂ with CO over an active charcoal catalyst, according to Eqs. 1 and 2.⁷



Because of the extremely high toxicity of phosgene, however, it is not a good method to produce chloroformate on an industrial scale. Furthermore, it is difficult to remove HCl completely from the product.

It has been reported that the reaction of PdCl₂ and LiCl with CO in ethanol gave ethyl chloroformate and two by-products.⁸ Synthesis of perfluoroalkyl chloroformates by direct carbonylation of perfluoroalkyl hypochlorites has also been reported.⁹ Recently, Giannoccaro have reported chloroformate synthesis by palladium bis(methoxycarbonyl) complex and CuCl₂.¹⁰ But these methods could not be applied to the catalytic synthesis of the usual alkyl chloroformates.

Quite recently, we have reported the novel synthesis of alkyl chloroformates by a palladium-catalyzed reaction using Cl₂, CO, and alkyl nitrite.¹¹ During our research it was found that HCl and NOCl can be used in place of Cl₂. We report here a novel synthesis of alkyl chloroformates in the gas phase by a palladium-catalyzed reaction using XCl (X=H or NO), CO, and alkyl nitrite. This method is safe because it does not require highly toxic materials like phosgene. Moreover, the NO produced can be used to reproduce methyl nitrite by the reaction with methanol and oxygen according to Eq. 3.



Experimental

1. Materials. Methyl nitrite was prepared from controlled amounts of NO and O₂ by passing through methanol. Hydrogen chloride was purchased from Nippon Sanso Co., Ltd. as 1% or 10% standard gas (N₂ as the balance). Other gases are also purchased and used without further purification. One wt% PdCl₂/γ-Al₂O₃ catalyst was purchased from N. E. Chemcat. One wt% PdCl₂/SiO₂ catalyst was prepared using aqueous H₂PdCl₄ solution and silica gel purchased from Fuji Davison Co., Ltd.

2. Apparatus and Procedures. The apparatus for the experiment is shown in Fig. 1. A reaction tube (13 mmφ) was filled with a required amount of catalyst, and fixed vertically. Then hot silicone oil was pumped through the jacket around the reaction tube to keep the catalyst at the required temperature. From the top of the reaction tube, reactant gas, which has been passed through a cold trap kept under 5 °C, was introduced at the required flow rate. After it passed through the catalyst at atmospheric pressure, the

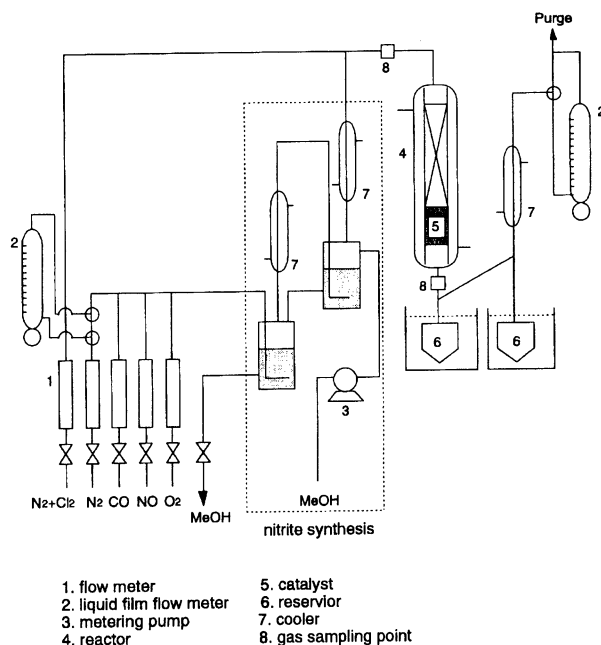


Fig. 1. Apparatus for the experiments.

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Table 1. Formation Rate of Methyl Chloroformate by Using HCl^{a)}

Run	Reactant gas concentration (in)					Formation rate MCF ^{b)} mg h ⁻¹	By-products
	CO	MN ^{b)}	NO	MeOH	HCl		
	vol%						
1	8.4	0.0	0.0	19.0	0.5	0	No reaction
2	6.1	6.6	2.3	8.1	0.5	600	DMC ^{b)} 330 mg h ⁻¹
3	3.7	1.9	3.9	6.8	1.0	1225	DMC ^{b)} 7 mg h ⁻¹

a) Reaction conditions 1% PdCl₂/Al₂O₃ 2 cm³, 60 °C, gas flow rate 30000 cm³ h⁻¹.

b) MN: Methyl nitrite, MCF: Methyl chloroformate, DMC: Dimethyl carbonate.

product gas was analyzed by gas chromatography. Typical reaction conditions are as follows.

Pressure: 1 atm; Gas flow rate: 30000 cm³ h⁻¹; Catalyst: 1% PdCl₂/γ-Al₂O₃ or 1% PdCl₂/SiO₂; Catalyst volume: 1–2 cm³; Temperature: 30–130 °C; CO concentration: 4–10 vol%; XCl concentration: 0.5–1 vol%; Nitrite/Cl molar ratio: 2–10; Balance gas: N₂

3. Analysis. Analytical conditions of gas chromatography are as follows.

Methyl Nitrite: Column: Chromosorb 101 (60–80 mesh), 2 m; Column temperature: 50 °C; Carrier gas: He 1.2 kg cm⁻²; Detector: FID.

CO and NO: Column: Chromosorb 101 0.3 m + Molecular sieve 5A 1.7 m; Column temperature: 50 °C; Carrier gas: He 1.6 kg cm⁻²; Detector: TCD.

Dimethyl Carbonate and Methyl Chloroformate: Column: 20% PEG-20M/Chromosorb WAW (80–100 mesh), 3 m; Column temperature: 60 °C; Carrier gas: He 0.4 kg cm⁻²; Detector: FID.

Results and Discussion

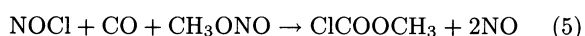
Synthesis of Chloroformate Using HCl. By the reaction of HCl, CO, and methyl nitrite in the presence of palladium catalyst, methyl chloroformate (MCF) was found to be formed in good yield and highly selectively. In this reaction HCl can be converted to methyl chloroformate completely under the best reaction conditions as shown in Table 1 (Run 3, yield 100%, selectively 99.4%). Moreover, the NO produced can be used to reproduce methyl nitrite by the reaction with methanol and oxygen as Eq. 3.

On the other hand, methyl chloroformate was not formed by the reaction between HCl, CO, and methanol (Table 1, Run 1). This result shows that nitrite is indispensable for the formation of chloroformate.

Synthesis of Chloroformate Using NOCl. It is well known that HCl and methyl nitrite reach an equilibrium between NOCl and methanol.¹²⁾



The equilibrium is established instantly to increase the concentration of NOCl at high temperature. For this reason, it can be considered that chloroformate can be formed as the following equation.



When NOCl was used instead of HCl, similar results

were obtained (Table 2, Runs 2 and 3). This supports that consideration. Moreover, the reaction between NOCl, CO and methanol also gave methyl chloroformate (Table 2, Run 1). It seems that methyl nitrite, which is formed from NOCl and methanol, reacts with CO and NOCl.

Verification of Reaction Path. As described above, it was found that methyl chloroformate is formed from HCl, CO, and methyl nitrite in good yield. First, the chlorine balance was measured to verify the reaction path. When HCl was introduced at a rate of 9.8 mmol h⁻¹ to 2 cm³ of the catalyst (1% PdCl₂/γ-Al₂O₃) under the reaction conditions of gas flow rate 30000 cm³ h⁻¹, temperature 60 °C, methyl nitrite 3.3 vol%, CO 4.2 vol%, methanol 7.8 vol%, and NO 1.9 vol%, methyl chloroformate was found to be formed at a rate of 8.8 mmol h⁻¹. We concluded from this result that the molar ratio of chloroformate produced to HCl introduced is 1. Secondly, the mass balance of the reactants and the products was measured. The results are shown in Table 3. Though the mass balance was not very good, chloroformate was formed at about the same amount as the consumed nitrite. From these results, the reaction seems to proceed according to Eqs. 4 and 5.

Temperature Dependence. It was found that the reaction is very much influenced by the reaction temperature. The results are shown in Fig. 2. The formation rate of chloroformate is highest around 60 °C, and decreases as the temperature becomes higher. Chloroformate decomposes to chloromethane and CO₂ at high temperatures on Al₂O₃ (Eq. 6)

Table 2. Formation Rate of Chloroformate by Using NOCl^{a)}

Run	Reactant gas flow rate (in)			Product flow rate MCF ^{b)} mmol h ⁻¹
	CO	MN ^{b)}	NOCl	
	mmol h ⁻¹			
1	41.8	5.1 ^{c)}	21.3	4.4
2	40.2	30.3 ^{d)}	2.0	1.7
3	48.8	24.4 ^{d)}	7.6	7.5

a) Reaction conditions 1% PdCl₂/Al₂O₃ 2 cm³, 60 °C, gas flow rate 30000 cm³ h⁻¹, MeOH 7–12 vol%.

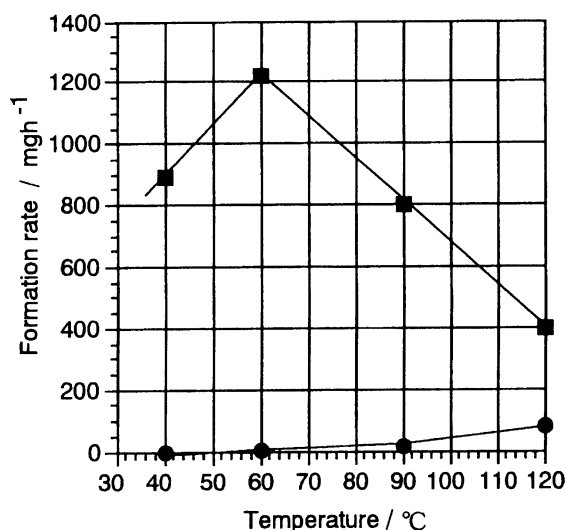
b) MN: Methyl nitrite, MCF: Methyl chloroformate.

c) MN was formed by the reaction between NOCl and MeOH. d) MN was added.

Table 3. Mass Balance of Reactants and Products^{a)}

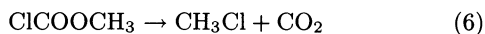
Reactant gas flow rate (in/out(consumed amount))		Product flow rate (in/out(produced amount))	
CO	MN	NO	MCF
mmol h ⁻¹		mmol h ⁻¹	
36.1/23.3 (12.8)	27.6/19.1 (8.5)	25.7/40.7 (15.0)	0.0/9.3 (9.3)

a) Reaction conditions 1% PdCl₂/Al₂O₃ 2 cm³, 60 °C, gas flow rate 30000 cm³ h⁻¹, HCl: 0.8 vol% (9.8 mmol h⁻¹), MeOH: 7.3 vol% (89.0 mmol h⁻¹).



■ : Methyl chloroformate
● : Dimethyl carbonate

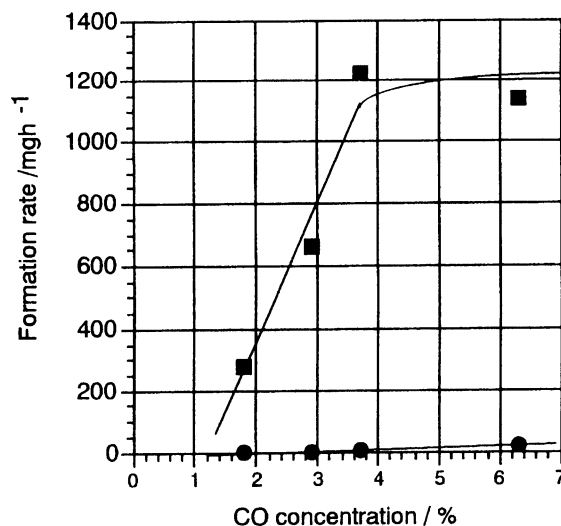
Fig. 2. Formation rate of products vs. reaction temperature. Reaction conditions: Pressure: 1 atm; Gas flow rate: 30000 cm³ h⁻¹; Catalyst: 1% PdCl₂/Al₂O₃; Catalyst volume: 2 cm³; CO: 3.5—4.0 vol%; HCl: 1 vol%; methyl nitrite: 1.5—2 vol%; NO: 2—3 vol%; MeOH: 5—8 vol%. Closed squares and circles in the figure correspond to methyl chloroformate and dimethyl carbonate, respectively.



At temperatures higher than 60 °C, dimethyl carbonate (DMC) begins to form. As already reported, similar behavior has been observed when Cl₂ was used.¹¹⁾

Effects of Reactant Concentrations. The concentrations of CO and methyl nitrite also influenced the formation rate of products. The results are shown in Figs. 3 and 4, respectively. The formation rate of chloroformate depends on the concentration of CO almost by first order. When the concentration of nitrite is lower than twice of HCl concentration, the formation rate depends on the concentration of methyl nitrite also by first order.

Effects of Nitrite/Chloride Molar Ratio. It was also found that the nitrite/chloride ratio influences the selectivity of methyl chloroformate very drastically



■ : Methyl chloroformate
● : Dimethyl carbonate

Fig. 3. Formation rate of products vs. CO concentration. Reaction conditions: Pressure: 1 atm; Temperature: 60 °C; Gas flow rate: 30000 cm³ h⁻¹; Catalyst: 1% PdCl₂/Al₂O₃; Catalyst volume: 2 cm³; HCl: 1 vol%; methyl nitrite: 1—2 vol%; NO: 2—4 vol%; MeOH: 4—8 vol%. Closed squares and circles in the figure correspond to methyl chloroformate and dimethyl carbonate, respectively.

as shown in Fig. 5. Selectivity was defined as Eq. 7.

$$\text{MCF selectivity (\%)} = \frac{\text{MCF (mmol h}^{-1}\text{)} \times 100}{\text{MCF (mmol h}^{-1}\text{)} + \text{DMC (mmol h}^{-1}\text{)}} \quad (7)$$

Interestingly, when the nitrite/Cl molar ratio is less than 2, selectivity is almost 100%. As the concentration of nitrite increases relative to HCl concentration, selectivity decreases because of the formation of carbonate. As already reported,¹¹⁾ almost the same results were obtained when Cl₂ was used.

Mechanism. A mechanism accounting for the formation of chloroformate is proposed in Scheme 1. PdCl₂ reacts with CO and methyl nitrite to form a methoxy-carbonyl complex [Pd^{IV}Cl₂(COOCH₃)(NO)]. A similar type of complex has been isolated by Bréchet as a phos-

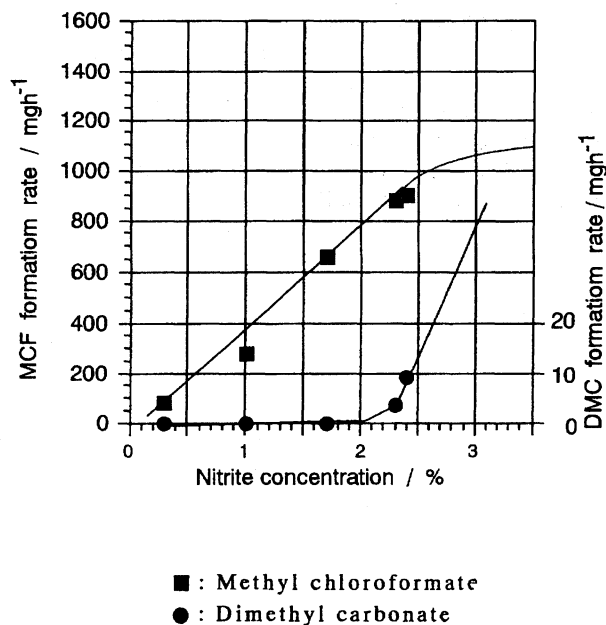


Fig. 4. Formation rate of products vs. methyl nitrite concentration. Reaction conditions: Pressure: 1 atm; Temperature: 60 °C; Gas flow rate: 30000 cm³ h⁻¹, Catalyst: 1% PdCl₂/Al₂O₃; Catalyst volume: 2 cm³; HCl: 1 vol%; CO: 1.8—3 vol%; NO: 2—4 vol%; MeOH: 6—9 vol%. Closed squares and circles in the figure correspond to methyl chloroformate and dimethyl carbonate, respectively.

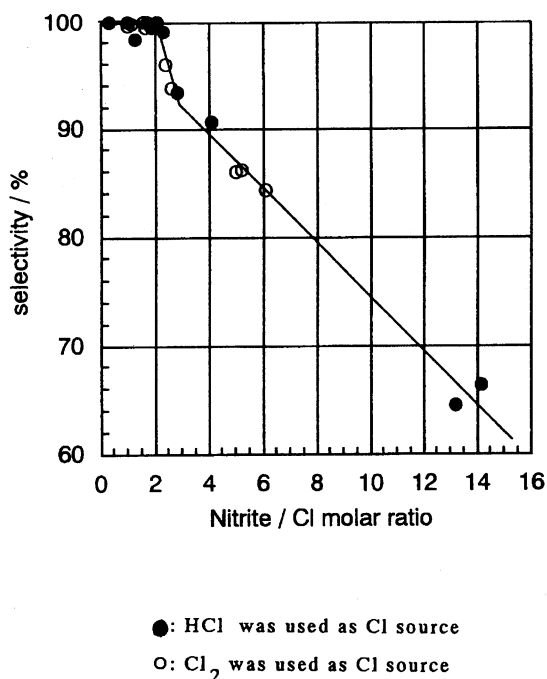
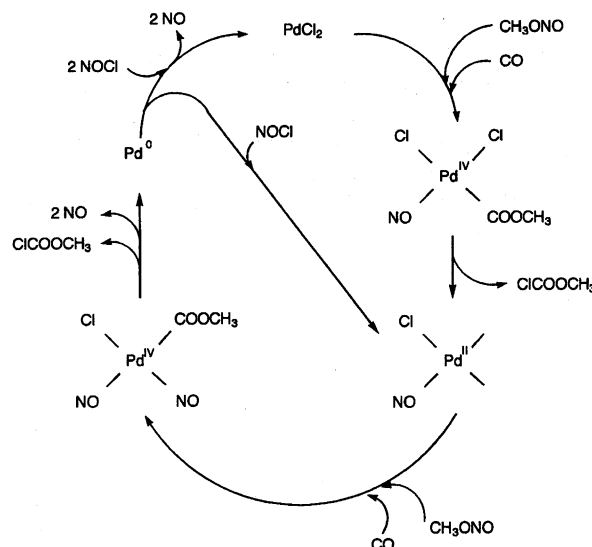


Fig. 5. Selectivity of methyl chloroformate vs. nitrite/Cl molar ratio. The results when HCl was used are indicated as closed circles. Open circles correspond to the results when Cl₂ was used.



Scheme 1. Proposed catalytic mechanism for the formation of chloroformate.

phine adduct $[\text{Pd}^{\text{IV}}\text{Cl}_2(\text{COOBU})(\text{NO})(\text{PPh}_3)]$ as an active intermediate of catalytic oxidative carbonylation of olefins.¹³⁾ From the complex, methyl chloroformate is produced through reductive elimination to form an unsaturated complex $[\text{Pd}^{\text{II}}(\text{NO})\text{Cl}]$, which reacts with CO and methyl nitrite to form another methoxycarbonyl complex. Then additional chloroformate is produced together with NO to form Pd. Pd^0 is reoxidized by NOCl to reproduce PdCl_2 or unsaturated complex $[\text{Pd}^{\text{II}}(\text{NO})\text{Cl}]$. This mechanism is consistent with the fact that high nitrite concentrations cause the formation of carbonate. It can be explained that an excess amount of nitrite reacts with methoxycarbonyl complex $[\text{Pd}^{\text{IV}}\text{ClX}(\text{COOCH}_3)(\text{NO})]$ ($\text{X}=\text{Cl}$ or NO) to produce carbonate. When the nitrite/chloride molar ratio is less than 2, all of the nitrite can be converted to a methoxycarbonyl group on Pd and to chloroformate by successive reductive elimination with Cl.

Another Support. Finally, when 2 cm³ of 1% PdCl₂/SiO₂ was used as the catalyst, methyl chloroformate was formed at a rate of 935 mg h⁻¹ under the reaction conditions of gas flow rate 30000 cm³ h⁻¹, temperature 90 °C, HCl 1 vol%, methyl nitrite 2.5 vol%, CO 4.5 vol%, methanol 7.7 vol% and NO 1.5 vol%.

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