

**THESIS OF THE Ph.D. DISSERTATION**

**CATALYTIC CARBONYLATION OF DIAZO COMPOUNDS.  
SYNTHESIS AND KINETICS.**

**NESZTA KUIK - UNGVÁRI**

**MSc in Chemistry**

**Supervisor:**

**DR. FERENC UNGVÁRY**

**Professor of Chemistry**



**UNIVERSITY OF PANNONIA**

**SCHOOL OF CHEMICAL SCIENCES**

**VESZPRÉM**

**2010**

## I. INTRODUCTION AND AIM OF THE WORK

The replacement of the diazo group in a diazoalkane by carbon monoxide may afford the corresponding ketene and dinitrogen.



There are many indirect and direct experimental evidences in the scientific literature regarding this transformation, which suggest multi-step reactions for the ketene formation.

In this work the cobalt-carbonyl-catalyzed dediazotation and carbonylation of diazoalkanes were examined in the case of diazomethane, ethyl diazoacetate, and (trimethylsilyl)diazomethane. In the presence of ethanol ethyl acetate, diethyl malonate, and ethyl (trimethylsilyl)acetate were formed, respectively. In the absence of ethanol the carbonylation of ethyl diazoacetate resulted in the formation of cobalt carbenoid complexes, while (trimethylsilyl)diazomethane led to (trimethylsilyl)ketene.

Ethyl diazoacetate was used as the model compound in the investigation of the mechanism of the cobalt-catalyzed carbonylation reaction. The effect of modification of the catalyst by triphenylphosphane was also investigated.

## II. EXPERIMENTAL METHODS

Handling of the complexes was carried out under an atmosphere of dry and deoxygenated argon or carbon monoxide utilizing standard Schlenk techniques. The products were purified by column chromatography, and were characterized by various analytical and spectroscopic methods such as IR, NMR, GC, GC-MS, UV-VIS, ICP-OES, single-crystal X-ray diffraction.

The kinetics were measured at different initial concentrations by following the gas volume change at atmospheric pressure using a thermostatted glass reactor at 10°C, which was connected to a thermostatted mercury-filled gas burette.

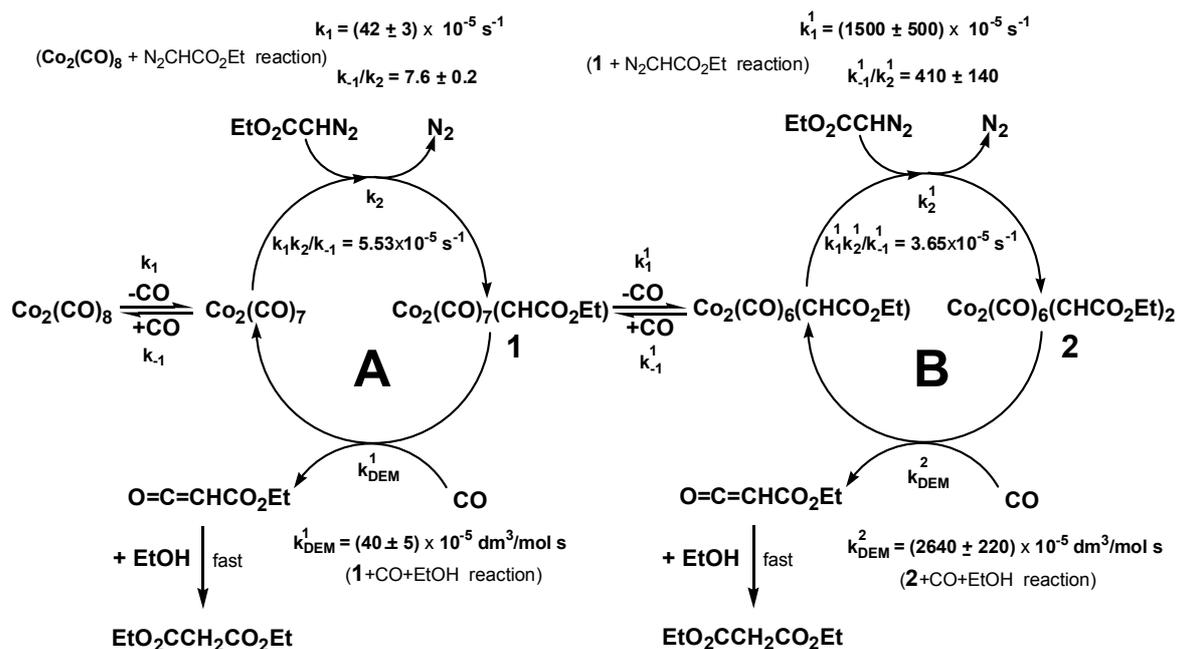
The  $^{13}\text{C}$ -exchange reactions were performed in a reactor connected to a flow-through infrared cuvette. From  $^{13}\text{C}$  enriched complexes  $^{13}\text{C}$  NMR spectra were recorded at low temperatures.

The experiments under pressure were performed in a stainless-steel autoclave (total capacity = 20 cm<sup>3</sup>) containing a glass insert.

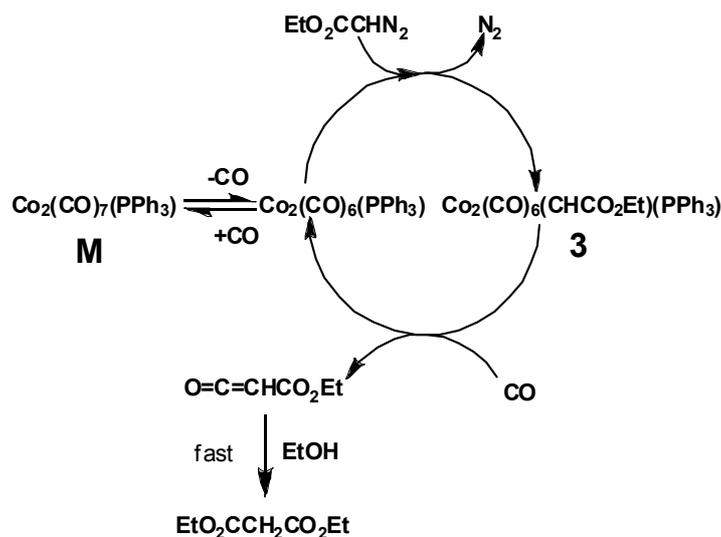
### III. NEW SCIENTIFIC RESULTS

1. The carbonylation of diazomethane at 10°C and 20 bar pressure of carbon monoxide in the presence of ethanol and octacarbonyl dicobalt as the catalyst gave ethyl acetate in mediocre yields.
2. (Trimethylsilyl)diazomethane was selectively carbonylated to (trimethylsilyl)ketene under atmospheric pressure of carbon monoxide in the presence of octacarbonyl dicobalt as the catalyst. The rate of (trimethylsilyl)ketene formation was found to be first order in both (trimethylsilyl)diazomethane and octacarbonyl dicobalt, and negative first order with respect to carbon monoxide. The observed rate constant at 10°C, in *n*-heptane solution is:  
 $k_{\text{obs}} = (0,52 \pm 0,06) \times 10^{-3} \text{ s}^{-1}$ .
3. The preparation of propanedioic acid ethyl-5-methyl-2-(1-methyl-ethyl)cyclohexyl ester in 65 % isolated yield was achieved by a convenient one-pot carbonylation of ethyl diazoacetate in the presence of (1R,2S,5R)-(-)-menthol and 1 mol %  $\text{Co}_2(\text{CO})_8$  as the catalyst. Using morpholine instead of menthol in the synthesis 3-(4-morpholinyl)-3-oxo-propanoic acid ethyl ester was obtained in 56 % isolated yield.
4. The kinetics of the catalytic carbonylation of ethyl diazoacetate in the presence of ethanol have been established using octacarbonyl dicobalt, and (ethoxycarbonyl)carbene-bridged carbonyl cobalt complexes as the catalyst precursors.
5. The composition of the cobalt complexes using various concentrations of the reagents were determined by quantitative infrared spectroscopy. If the concentration of ethyl diazoacetate [EDA] is more than 10 times of that of [CO] in the reaction mixtures, the cobalt is mainly present in form of  $\text{Co}_2(\text{CO})_6(\text{CHCO}_2\text{Et})_2$  (**2**). Rising the CO concentration diminishes the concentration of complex **2** in favor of  $\text{Co}_2(\text{CO})_7(\text{CHCO}_2\text{Et})$  (**1**) and  $\text{Co}_2(\text{CO})_8$ . At high concentrations of CO (>150 bar)  $\text{Co}_2(\text{CO})_8$  is the prevailing cobalt complex in the solution.
6. The kinetics of the assumed elementary steps in the catalytic cycle(s) have been established using  $\text{Co}_2(\text{CO})_8$  and the isolated complexes **1** and **2**.

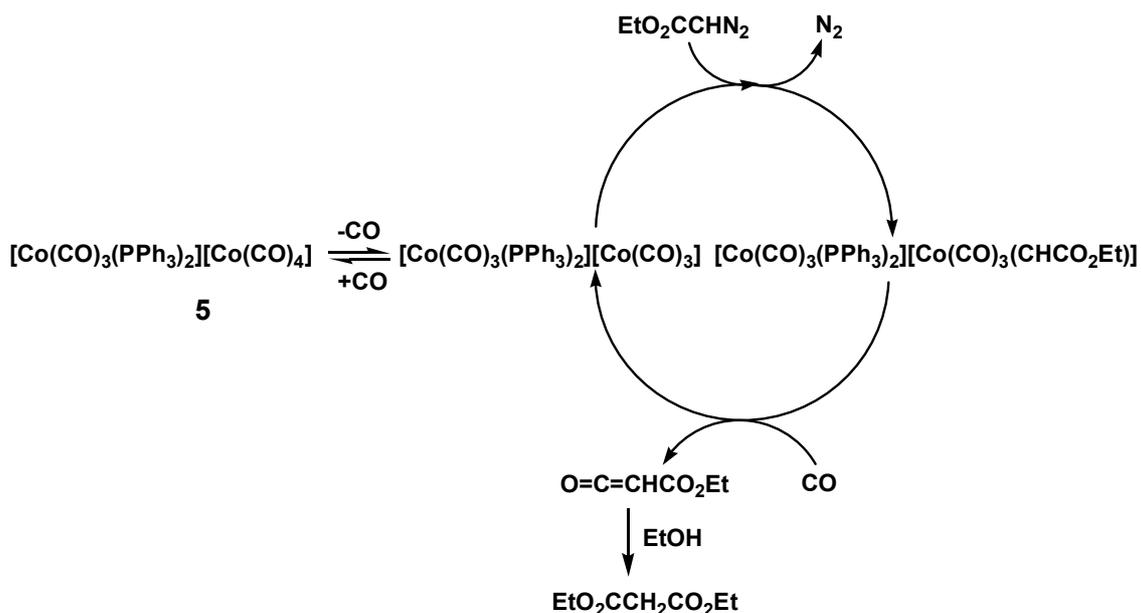
7. Based on the observation that the rising ethanol concentration does not influence the rate of the catalytic carbonylation it can be stated that the diethyl malonate product formation is the result of a fast reaction after the rate-determining carbonylation.
8. The results of the infrared spectroscopic and of the kinetic investigations support the assumption that the formation of diethyl malonate occurs in two coupled cycles **A** and **B**. In cycle **A**  $\text{Co}_2(\text{CO})_7$  and complex **1** are the working repeating species, whereas in cycle **B** the species are  $\text{Co}_2(\text{CO})_6(\text{CHCO}_2\text{Et})$  and complex **2**.
9. The mechanism of the cobalt-catalyzed ethyl diazoacetate carbonylation can be described by the scheme below. Included in the scheme are the experimentally determined rate constants measured in dichloromethane solution at 10 °C using  $\text{Co}_2(\text{CO})_8$  and the isolated complexes **1** and **2** in the kinetic measurements.



10. The rate-determining step in the cobalt-catalyzed ethyl diazoacetate carbonylation at high CO pressure (100 bar) is the activation of ethyl diazoacetate, whereas at low CO pressure (1 bar) the reactions of complexes **1** and **2** with carbon monoxide. The effect of the [CO] on the rate of diethyl malonate formation is negative in the first case but positive in the second one. The contribution of the cycles **A** and **B** to the diethyl malonate product formation depends on the concentration ratio [EDA]/[CO]. If this ratio is  $<0.1$ , mainly cycle **A** is the source of diethyl malonate. If this ratio is  $>0.1$ , the bulk of diethyl malonate production occurs by cycle **B**.
11. In a dichloromethane solution, under an atmospheric pressure of  $^{13}\text{CO}$ , complex **2** does not exchange its CO ligands for  $^{13}\text{CO}$ . In the presence of excess ethanol, diethyl malonate with natural isotopic distribution is formed in accord with the assumption that for the formation of the diethyl malonate precursor (ethoxycarbonyl)ketene, the source of carbon monoxide is the coordinated CO in complex **2** and not the free  $^{13}\text{CO}$  from the gas phase.
12. Kinetic and infrared spectroscopic investigations have shown that triphenylphosphane substituted cobalt carbonyls such as  $\text{Co}_2(\text{CO})_6(\text{CHCO}_2\text{Et})(\text{PPh}_3)$  (**3**),  $\text{Co}_2(\text{CO})_7(\text{PPh}_3)$  (**M**), and  $[\text{Co}(\text{CO})_3(\text{PPh}_3)][\text{Co}(\text{CO})_4]$  (**5**) are an order of magnitude more active catalysts of the ethyl diazoacetate carbonylation in dichloromethane solution at  $10\text{ }^\circ\text{C}$  and atmospheric pressure of CO than  $\text{Co}_2(\text{CO})_8$ .
13. Kinetic and spectroscopic evidences support that the formation of diethyl malonate using  $\text{Co}_2(\text{CO})_7(\text{PPh}_3)$  (**M**) as the catalyst precursor occurs in a catalytic cycle through  $\text{Co}_2(\text{CO})_6(\text{PPh}_3)$  and  $\text{Co}_2(\text{CO})_6(\text{CHCO}_2\text{Et})(\text{PPh}_3)$  (**3**) as the repeating species depicted in the scheme below.



14. In dichloromethane solution at 10 °C under atmospheric pressure of  $^{13}\text{CO}$  the complex  $[\text{Co}(\text{CO})_3(\text{PPh}_3)_2][\text{Co}(\text{CO})_4]$  (**5**) exchanges its CO ligands in the  $[\text{Co}(\text{CO})_4]^-$  part for  $^{13}\text{CO}$  with an initial rate of  $0.88 \times 10^{-3} \text{ s}^{-1}$ . In 2 hours >75% of the CO ligands in the  $[\text{Co}(\text{CO})_4]^-$  part are replaced by  $^{13}\text{CO}$ , whereas practically no CO exchange occurs in the  $[\text{Co}(\text{CO})_3(\text{PPh}_3)_2]^+$  part of the complex. Under CO in the presence of ethyl diazoacetate, the intensity of the  $\nu(\text{CO})$  band of the  $[\text{Co}(\text{CO})_4]^-$  part at  $1899 \text{ cm}^{-1}$  gradually decreases parallel to the increase of a new  $\nu(\text{CO})$  band at  $1637 \text{ cm}^{-1}$ . The new band might indicate the presence of an intermediate complex in the assumed catalytic cycle depicted below.



## IV. SIGNIFICANCE OF THE SCIENTIFIC RESULTS

Ketenes are important and versatile intermediates in synthetic chemistry. Their preparation by catalytic carbonylation of diazoalkanes opens new applications especially in cases of ketenes which can not be isolated by the usual methods. The cobalt-catalyzed selective carbonylation of ethyl diazoacetate seems to be suitable for one-pot domino reactions. Anchoring the catalyst complexes to polymers, such as polystyrene-bound triphenylphosphane, promises easy recycling of the catalyst and environmentally friendly applications.

## V. SCIENTIFIC PUBLICATIONS AND PRESENTATIONS.

### PUBLICATIONS RELATED TO THE THESIS

#### PUBLICATIONS

1. **N. Ungvári**, F. Ungváry  
Carbonylation of diazoalkanes, in *Modern Carbonylation Methods*  
*Kollár, L.(Ed.), Wiley-VCH, Weinheim, Chapter 8, pp 199-221, 2008.*
2. **N. Ungvári**, T. Kégl, F. Ungváry  
Octacarbonyl dicobalt-catalyzed selective carbonylation of (trimethylsilyl)-  
diazomethane to obtain (trimethylsilyl)ketene.  
*J. Mol. Catal. A Chem.* **219** (2004) 7-11.
3. E. Fördös, **N. Ungvári**, T. Kégl, F. Ungváry  
Reactions of  $^{13}\text{CO}$  with ethoxycarbonylcarbene-bridged dicobalt carbonyl complexes:  
[ $\mu_2$ -{ethoxycarbonyl(methylene)}- $\mu_2$ -(carbonyl)-bis(tricarbonyl-cobalt) (*Co-Co*)] and  
[di- $\mu_2$ -{ethoxycarbonyl(methylene)}-bis(tricarbonyl-cobalt) (*Co-Co*)].  
*Eur. J. Inorg. Chem.*, (2006) 1875-1880.
4. **N. Ungvári**, E. Fördös, T. Kégl, F. Ungváry  
Mechanism of the cobalt-catalyzed carbonylation of ethyl diazoacetate.  
*Inorg. Chim. Acta* **363** (2010) 2016-2028.

5. **N. Ungvári**, E. Fördös, J. Balogh, T. Kégl, L. Párkányi, F. Ungváry:  
Triphenylphosphane-modified cobalt-catalysts for the selective carbonylation of ethyl diazoacetate.  
*Organometallics*, **29** (2010) 3837-3851.

## PRESENTATIONS

1. **N. Ungvári**, F. Ungváry  
Reaction of  $^{13}\text{C}$  with ethoxycarbonylcarbene-bridged dicobalt carbonyl complexes.  
*XVI<sup>th</sup> International Symposium on Homogeneous Catalysis*, Florence, Italy, July 6-11, 2008. Book of Abstracts P 221.
2. **N. Ungvári**, F. Ungváry  
Reaction of  $^{13}\text{C}$  labeled carbon monoxide with ethoxycarbonylcarbene-bridged dicobalt carbonyl complexes.  
(Jelzett szén-monoxid reakciója etoxikarbonil-karbén-hidas karbonil-kobalt komplexekkel.)  
*XLII. Colloquium on Chemical Complexes* Mátrafüred, May 23-25, 2007.

## VI. FURTHER SCIENTIFIC PUBLICATIONS

1. E. Fördös, **N. Ungvári**, T. Kégl, L. Párkányi, G. Szalontai, F. Ungváry  
Structure of  $\text{Co}_2(\text{CO})_6(\text{dppm})$  and  $\text{Co}_2(\text{CO})_5(\text{CHCO}_2\text{Et})(\text{dppm})$  ( $\text{dppm} = \text{Ph}_2\text{PCH}_2\text{PPh}_2$ ) and exchange reaction with  $^{13}\text{CO}$ : An experimental and computational study.  
*Inorg. Chim. Acta*, **361** (2008) 1832-1842.
2. **N. Ungvári**, E. Fördös, T. Kégl, F. Ungváry  
Reactions of triphenylphosphane-substituted ethoxycarbonylcarbene-bridged dicobalt carbonyl complexes with carbon monoxide or  $^{13}\text{CO}$ : An experimental and theoretical study.  
*Inorg. Chim. Acta* **362** (2009) 1333-1342.