National Library of Canada
Canadian Theses Service
Ottawa, Canada
K1A 0N4

Bibliothèque nationale du Canada
Services des thèses canadiennes

CANADIAN THESES

THÈSES CANADIENNES

NOTICE

The quality of this microfiche is heavily dependent upon the quality of the original thesis submitted for microfilming. Every effort has been made to ensure the highest quality of reproduction possible.

If pages are missing, contact the university which granted the degree.

Some pages may have indistinct print especially if the original pages were typed with a poor typewriter ribbon or if the university sent us an inferior photocopy.

Previously copyrighted materials (journal articles, published tests, etc.) are not filmed.

Reproduction in full or in part of this film is governed by the Canadian Copyright Act, R.S.C. 1970, c. C-30.

AVIS

La qualité de cette microfiche dépend grandement de la qualité de la thèse soumise au microfilmage. Nous avons tout fait pour assurer une qualité supérieure de reproduction.

S'il manque des pages, veuillez communiquer avec l'université qui a conféré le grade.

La qualité d'impression de certaines pages peut laisser à désirer, surtout si les pages originales ont été dactylographiées à l'aide d'un ruban usé ou si l'université nous a fait parvenir une photocopie de qualité inférieure.

Les documents qui font déjà l'objet d'un droit d'auteur (articles de revue, examens publiés, etc.) ne sont pas microfilmés.

La reproduction, même partielle, de ce microfilm est soumise à la Loi canadienne sur le droit d'auteur, SRC 1970, c. C-30.

THIS DISSERTATION
HAS BEEN MICROFILMED
EXACTLY AS RECEIVED

LA THÈSE A ÉTÉ
MICROFILMÉE TELLE QUE
NOUS L'AVONS REÇUE

NL-339 (r.86/06)

Canada

ISBN 0-315-33349-9

ACKNOWLEDGEMENTS

I would like to give my greatest thanks to my research director Dr. Howard Alper for all of the guidance, and continual understanding throughout my stay in his laboratory.

I would also like to thank:

The Chemistry Department, University of Ottawa, for teaching assistanship.

Mr. Raj Capoor for recording the proton and carbon-13 nmr spectra. Dr. Clem Kazakoff and Dr. John Krause for recording the mass spectra.

My co-workers for their friendship and helpful discussions.

TABLE OF CONTENTS

Acknowledgements ii
Table of Contents iii
List of Tables iv
List of Abbreviations v
Abstract vi
Chapter I: INTRODUCTION 1
1. Carbonylation Reactions 1
2. Routes to Lactones via Carbonylation Reactions 14
Chapter II: RESULTS and DISCUSSIONS 18
1. Carbonylation of γ,δ- and δ,ϵ-Alkenols 18
2. Carbonylation of Allylic Alcohols 24
3. Mechanism 34
Chapter III: EXPERIMENTAL 44
1. General Comments 44
2. Carbonylation of γ,δ- and δ,ϵ-Alkenols 46
3. Carbonylation of Allylic Alcohols 48
4. Carbonylation of 2-Buten-1,4-Diol 51
5. Asymmetric Carbonylation of trans-2-Hexen-1-ol 51
REFERENCES 52

LIST OF TABLES

1. Carbonylation Reactions 5

2. Spectroscopic Properties of Lactones 40

LIST OF ABBREVIATIONS

Symbol/Abbreviations	Name
$RhCl_3 \cdot 3\ H_2O$	Rhodium(III) chloride trihydrate
$RuI_2(CO)_4$	Tetracarbonyl ruthenium(II) iodide
$PdCl_2(PPh_3)_2$	Bis(triphenylphosphine) palladium(II) chloride
$H_2PtCl_6 \cdot 6\ H_2O$	Chloroplatinic acid
$SnCl_2 \cdot 2\ H_2O$	Tin(II) chloride dihydrate
$Co_2(CO)_8$	Dicobalt octacarbonyl
m/e	mass per charge
ppm	parts per million
MHz	megahertz
mmol	millimole
TLC	Thin layer chromatography
GC	Gas chromatography
GC-RT	Gas chromatography- retention time
MS	Mass spectroscopy
M	molecular ion
IR	infrared
NMR	nuclear magnetic resonance

ABSTRACT

Saturated lactones were synthesized via the oxidative cyclization of δ,γ- and γ,ε-unsaturated alcohols and allylic alcohols, in good to acceptable yields. These reactions were run under remarkably mild conditions (room temperature and atmospheric pressure), using palladium(II) chloride and copper(II) chloride as catalysts, concentrated hydrochloric acid and sodium dried tetrahydrofuran; carbon monoxide and oxygen were bubbled through the solution. These reactions enable one to synthesize lactones starting from primary, secondary, and even tertiary unsaturated alcohols.

The amounts of tetrahydrofuran, the acid concentration and the amount of copper(II) chloride were varied individually in order to obtain the most favourable reaction conditions. The reaction did not occur in absence of oxygen.

CHAPTER I

INTRODUCTION

1. Carbonylation Reactions:

Carbonylation reactions have achieved considerable importance in synthetic chemistry as means of incorporating carbon monoxide in organic compounds containing a variety of chemical functions.

The first report of such a reaction was made in 1894[1]. It was shown that the rapid absorption of ethylene and carbon monoxide by aqueous solutions of palladium(II) chloride, afforded acetaldehyde and carbon dioxide as well as metallic palladium. About half a century later, Roelen[2] who was studying the mechanism of Fischer-Tropsch synthesis with alkenes as substrates, made a major discovery in the field of carbonylation reactions: the oxo- or hydroformylation reaction, which is the synthesis of aldehydes and alcohols from alkenes, carbon monoxide and hydrogen mediated by cobalt-catalyst. In 1953, Reppe[3] reported the carbonylation of olefins in the presence of iron or nickel carbonyls or carbonyl precursors, to form acids or esters.

The next series of discoveries came with the extension of these reactions to other transition metals, especially rhodium and palladium. Processes developed included those producinq carbonyl compounds without formal incorporation of carbon monoxide. For example, Smidt[4] in 1959, reported a commercial process, the Wacker process (1), for acetaldehyde production from ethylene

$$\begin{aligned} &C_2H_4 + PdCl_2 + H_2O \longrightarrow CH_3CHO + Pd + 2\ HCl \\ &Pd + 2\ CuCl_2 \longrightarrow PdCl_2 + 2\ CuCl \\ &2\ CuCl + 2\ HCl + \tfrac{1}{2}O_2 \longrightarrow 2\ CuCl_2 + H_2O \end{aligned} \tag{1}$$

$$\overline{\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad}$$

$$C_2H_4 + \tfrac{1}{2}\ O_2 \longrightarrow CH_3CHO$$

In general, the introdution of carbon monoxide into an orqanic system, leads to the singly homologated product; thus it was observed that any reaction involving carbon monoxide and an organometallic compound results in the formation in the organic end-product of at least one -C(O)-Y fragment, where Y may arise from a reagent or part of the substrate.

There are many carbonylation reactions which are known, and they represent routes for the manufacture of unsaturated and saturated acids, esters, amides, anhydrides and lactones from different feedstocks (Table 1).

The carbonylation of unsaturated compounds usually involves the participation of compounds having an acidic hydrogen such as water, alcohols, thiols, ammonia, amines or carboxylic acids. The end-products are carboxylic acids and their derivatives. These reactions are usually carried out using catalytic amounts of group VIII metal complexes under carbon monoxide pressure or with stoichiometric amounts of metal complexes or metal carbonyls at atmospheric pressure; the addition of acid increasing the rate of the reaction.

Initial work in this area was mainly concerned with carbonylation reactions of alkynes as substrates^3, for which nickel tetracarbonyl was the catalyst of choice:

$$CH\equiv CH + CO + H_2O \xrightarrow[150°C;\ 30\ bar]{Ni(CO)_4} CH_2{=}CHCO_2H$$

Olefins are in general, more difficult to carbonylate than alkynes and both stoichiometric and catalytic reactions require high temperatures and pressures For example, it was reported that reacting olefins using carbon monoxide and water in the presence of a nickel salt as catalyst at 300°C and 6000 psi pressure, afforde the carboxylic acid^5. A few years later, Bird^6 also reported the synthesis of carboxylic acids from olefins. This time nickel carbonyl was the catalyst and the reaction was carried out under acidic conditions at temperature around 250°C, and 200 atm pressure of carbon monoxide.

Before considering carbonylation reactions of olefins in more detail, examples of the carbonylation of other substrates will be examined briefly.

From Table 1, it can be seen that a variety of products such as carboxylic acids, esters and anhydrides can be prepared by the carbonylation of alcohols, ethers and carboxylic acid esters respectively.

In 1968, Paulik[7] reported the rhodium-catalysed carbonylation of methanol to acetic acid, known as the "Monsanto process":

$$CH_3OH + CO \xrightarrow[\substack{CH_3I \text{ or } HI \\ 180^\circ C;\ 30\text{-}40 \text{ bar}}]{RhCl_3 \cdot 3\ H_2O} CH_3COOH$$

By adding an iodide promoter, it was possible to improve the reaction yield as high as 99% acetic acid at as low a pressure as 1 atm. Because of the rapidly increasing price of hydrocarbon feedstocks, the Monsanto process offers a viable alternative for the production of acetic acid.

Table 1. Carbonylation Reactions.

Type	Group formed
Hydroformylation	formyl: -C(O)-H
Hydrocarbonylation	acid: -C(O)-OH
Azacarbonylation	N-acyl: -C(O)-N-
Carbocarbonylation	ketone: -C(O)-C-
Oxacarbonylation	acyloxy: -C(O)-O-
Halocarbonylation	acid halide: -C(O)-hal

In the late 1970's, three patents[8,9,10] reported the synthesis of acetic anhydride from the carbonylation of methyl acetate. The carbonylation was done without water, affording the corresponding anhydride:

$$CH_3CO_2CH_3 + CO \xrightarrow[\text{acetic acid}]{\text{cat; } CH_3I} (CH_3CO)_2O$$

The catalyst for this reaction was either a rhodium[8.9] or nickel[10] compound with an amine or phosphine used as co-catalyst. Temperatures ranged from 175° to 200°C and pressures from 25 to 60 bar depending on the type of catalyst. The reaction is superior to the process by which acetic anhydride is obtained via the high temperature pyrolysis of acetic acid to ketene (it is derived from ethylene)[11]. It is less energy intensive and is independent of oil-based hydrocarbon feedstocks.

Another route to obtain acetic anhydride is via the carbonylation of dimethyl ether. When treated in the presence of nickel or nickel compound, of iodine or an iodine compound, and atrivalent organic group VA element compound and carbon monoxide, the ether afforde acetic anhydride[10]:

$$CH_3OCH_3 + CO \xrightarrow[58\ atm]{200°C} (CH_3CO)_2O$$

Ethers can be carbonylated to esters. For example, dimethyl ether yields methyl acetate[12]. The best results were found when acetic acid was used as the solvent at 200°C and 230 atm of carbon monoxide, in the presence of ruthenium catalyst and an iodide promoter.

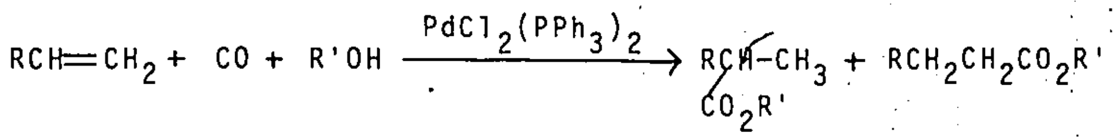
$$CH_3OCH_3 + CO \xrightarrow[\substack{200°C;\ 230\ atm \\ 3\text{-}5\ atm\ H_2;\ CH_3I}]{RuI_2(CO)_4/HI;\ 1/10} CH_3CO_2CH_3$$

Hydrogen was necessary to initiate the reaction.

The above processes are examples of carbonylation reactions of industrial importance since the products. acetic acid and acetic anhydride are major industrial chemicals used in the manufacture of vinyl acetate and cellulose acetate. Acetic acid is also an important industrial solvent.

Reactions which results in the formation of carboxylic acids are referred to as hydroxycarbonylation or hydrocarboxylation reactions. When an alcohol is used as the co-substrate instead of water, the process is called hydroesterification. These two classes of carbonylation reactions will now be examined.

Saturated esters are formed by the carbonylation of simple olefins in alcohols. Terminal olefins, and some internal ones, were carbonylated under 50 atm of carbon monoxide at about 100°C to give saturated esters in high yields[13,14]:

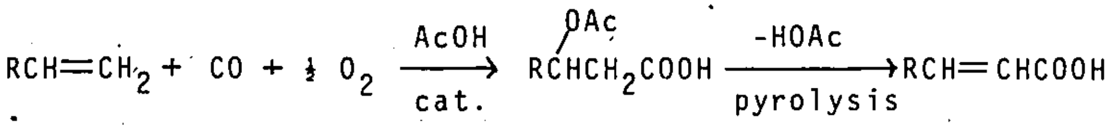


$$RCH{=}CH_2 + CO + R'OH \xrightarrow{PdCl_2(PPh_3)_2} \underset{CO_2R'}{RCH}{-}CH_3 + RCH_2CH_2CO_2R'$$

The presence of hydrochloric acid results in an increase in the rate of the reaction. The ratio between straight and branched chain esters depends of temperature. carbon monoxide pressure, phosphine ligand and the presence or absence of other additives or promoters such as hydrochloric acid.

In 1968, Bittler[15] reported the carbonylation of olefins using the same palladium catalyst as above, which allowed the reaction to occur at lower temperatures. Palladium compounds were used as the catalyst since they readily formed complexes with olefins. It was believed that the olefin could be carbonylated at a lower temperature when activated by a palladium-olefin complex. The results showed that the esters could be synthesized at temperatures below 100°C (P_{CO}: 300-700 atm).

Medema[16], in 1969, reported the palladium-catalysed oxidative-carbonylation of olefins. It was shown that the oxidative-carbonylation of olefins in the presence of palladium(II)/copper(II) as catalyst yielded β-substituted and/or α,β-unsaturated carboxylic acid derivatives; when the reaction was on allylic compounds, β,γ-unsaturated carboxylic acid derivatives were obtained.



$$RCH{=}CH_2 + CO + \tfrac{1}{2}\,O_2 \xrightarrow[\text{cat.}]{\text{AcOH}} R\overset{\text{OAc}}{\text{C}}HCH_2COOH \xrightarrow[\text{pyrolysis}]{\text{-HOAc}} RCH{=}CHCOOH$$

Ethylene undergoes oxidative-carbonylation in the presence of alcohols and a Wacker-type catalytic system to give dialkyl succinates[17]:

$$CH_2{=}CH_2 + 2\ CO + \tfrac{1}{2}\,O_2 + ROH \xrightarrow[\text{125-175 psi } O_2\text{; 85°C}]{\text{300 psi CO; 700 psi } C_2H_4} RO_2CCH_2CH_2CO_2R + H_2O$$

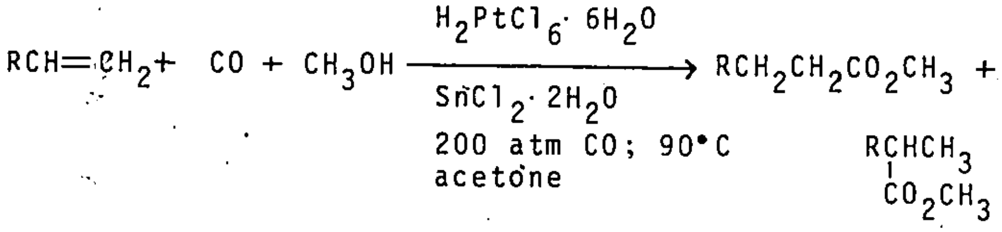
A catalytic system based on palladium(II) chloride/copper(II) chloride or palladium(II) chloride/iron(III) chloride gave rather poor results owing to the presence of hydrogen chloride. By using copper(I) chloride instead of copper(II) chloride or iron(II) chloride instead of iron(III) chloride, the succinate yields were improved.

An intensive study by Stille et al[18] on the carbonylation of alkenes catalysed by palladium and cupric chlorides, showed that at 2-3 atm of carbon monoxide and at room temperature, cis- and trans-but-2-enes undergo alkoxy-alkoxycarbonylation affording different isomers of methyl-3-methoxy-2-methyl-butanoate:

$$CH_3CH{=}CHCH_3 + 2\ CH_3OH + CO \longrightarrow CH_3(CH_3O)CHCH(CH_3)CO_2CH_3$$

It was also found by Stille and Divakaruni[19] that the stereochemistry of the dicarboxylation reaction was cis and proceeded with the direct transfer of the carbomethoxyl group from the palladium to an olefinic carbon atom in a regiospecific anti-Markownikoff direction.

In the 1970's: the study of a large variety of reactions continued but perhaps the most significant advances occurred in the area of reactions of carbon monoxide with simple molecules such as hydrogen. The interest in hydrogenation using platinum-tin (Pt-Sn) complexes was extended to carbonylation reactions, using H_2PtCl_6-$SnCl_2$. A range of terminal alkenes were found to react with carbon monoxide and methanol to give good yields (about 85%) of the corresponding linear methyl-ester[20]:



$$RCH{=}CH_2 + CO + CH_3OH \xrightarrow[\substack{SnCl_2 \cdot 2H_2O \\ 200\text{ atm CO; }90^\circ C \\ \text{acetone}}]{H_2PtCl_6 \cdot 6H_2O} RCH_2CH_2CO_2CH_3 + \underset{\displaystyle CO_2CH_3}{RCHCH_3}$$

A small amount of olefin reduction occurred (2-4% of the olefin), but isomerization of the α-olefin to internal olefins (mostly the 2-isomer) was the only major competing reaction. The reaction occurred at 200 atm of carbon monoxide and replacing methanol with water resulted in the formation of the acid rather than the ester. Linear carboxylic acid esters were also obtained of the major product from terminal olefins, when ligand-stabilized Pt(II)-group 4B metal halide complexes were used as catalysts[21,22].

In 1979, Bardi[23] reported the hydroesterification of propene to esters of butyric acid. The reaction occurs with high selectivity towards the linear isomer. using bis(triphenylphosphine) palladium dichloride and triphenylphosphine:

$$CH_3CH{=}CH_2 + CO + ROH \xrightarrow{\text{room temp.}} CH_3CH_2CH_2CO_2R$$

In 1980, there was a report[24] that cobalt carbonyl or cobalt salts can, in the presence of pyridine catalyze the formation of methyl esters of fatty acids from suitable olefins, carbon monoxide and methanol at 160°C and 160 atm.

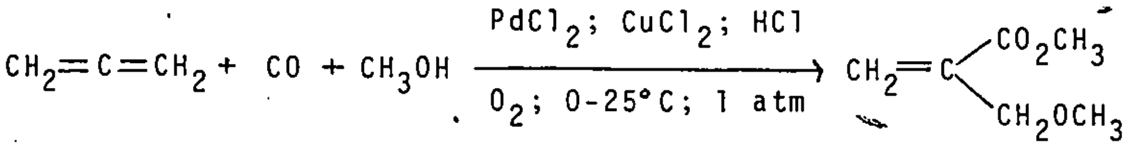
From the work mentioned, it can be seen that linear and branched chain esters or acids are formed. the linear isomer being usually the major one. These reactions also required the use of high pressures and moderate to high temperatures.

In 1984, Despeyroux and Alper[25] reported a homogeneous regiospecific palladium-based catalytic system for the hydroesterification of internal and terminal olefins under mild conditions, affording the branched chain isomer as the major product. When the above reaction was applied to alkynes[26], it was found that they reacted in a regioselective manner to give monoester from internal alkynes or diesters from terminal ones. For the diesters, the cis-isomer was the major product.

The same procedure was then applied to the hydrocarboxylation of alkenes[27], where water was used instead of methanol; again regiospecificity was observed. The key to success of this reaction is the use of water diluted in tetrahydrofuran (THF) since no reaction occurs using water alone.

$$RCH{=}CH_2 + CO + H_2O \xrightarrow[O_2;\ r.t.;\ 1\ atm]{PdCl_2;\ CuCl_2;\ HCl} RCH(CO_2H)CH_3$$

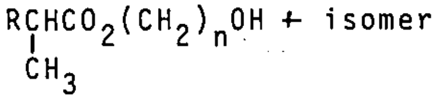
Allenes, and several substituted allenes, were found to react also under the above conditions[28]. For example, allene reacted to give methyl 2-methoxymethylacrylate:



$$CH_2{=}C{=}CH_2 + CO + CH_3OH \xrightarrow[O_2;\ 0\text{-}25°C;\ 1\ atm]{PdCl_2;\ CuCl_2;\ HCl} CH_2{=}C(CO_2CH_3)(CH_2OCH_3)$$

Fergusson and Alper[29] reported, also in 1984, the monohydroesterification of diols. Reaction of the latter with olefins under oxidative-carbonylation and acidic conditions gives hydroxy esters in good yields. The reaction was found to be regioselective:

$$RCH{=}CH_2 + HO(CH_2)_nOH + CO \xrightarrow[O_2;\ THF;\ r.t;\ 1\ atm]{PdCl_2;\ CuCl_2;\ HCl}$$



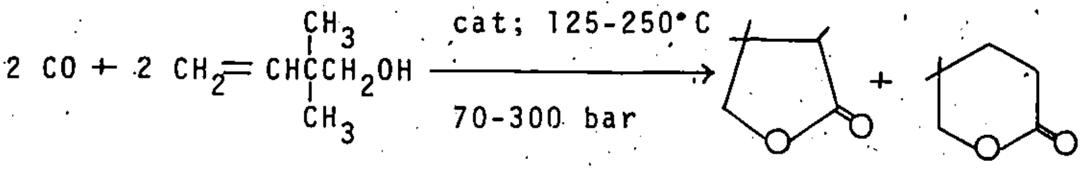
$$\underset{\displaystyle CH_3}{RCH}CO_2(CH_2)_nOH + \text{isomer}$$

Alper and Hartstock[30] recently reported the conversion of amines into carbamate esters. The same process as above was applied to aromatic amines giving fair to quantitative yields (34 to 99%) of products.

2. Routes to Lactones via Carbonylation Reactions:

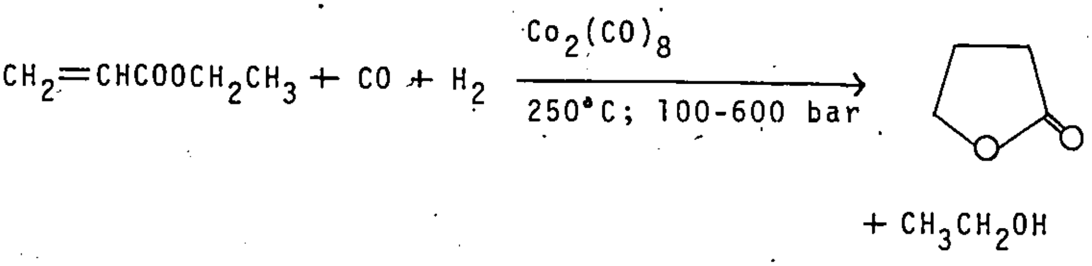
Lactones may be synthesized by many methods one of which involves the oxycarbonylation of unsaturated aliphatic hydrocarbons and their oxygenated functional derivatives. The methods are, in general, of limited utility since there are competing side-reactions.

In the presence of carbon monoxide and dicobalt octacarbonyl or rhodium chloride, as the catalyst, 2.3- and 3,4-unsaturated alcohols yield the corresponding γ- or δ-lactones[31,32,33]:

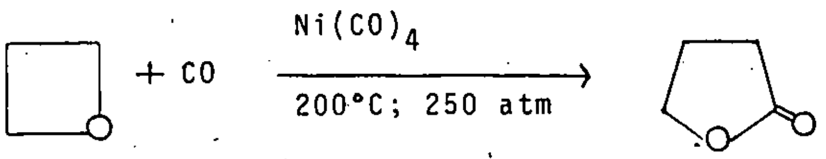


The competing reaction is the isomerization of the unsaturated alcohol to the aldehyde; eg. with allyl alcohol, only about 2% γ-butyrolactone is obtained, 50% of the starting material being isomerized to propanal. It was shown that in the presence of acetonitrile as the solvent, and pyridine as a ligand on the cobalt-catalyst, propanal formation was reduced and the lactone could be obtained in about 60% yield[33]. Unsaturated alcohols which have an alkyl substituent at the carbon adjacent to the C-OH group give better yields of lactones, since isomerization does not ensue.

Hydroformylation of esters of α,β-unsaturated carboxylic acids also provides an alternative route to γ-lactones[34]:

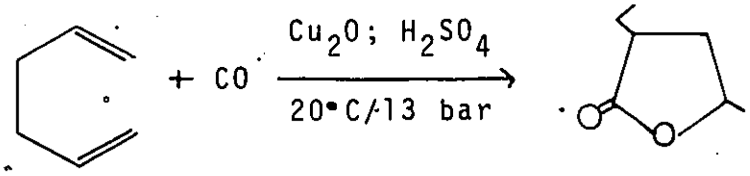


Epoxides and other heterocyclic ethers can be carbonylated to lactones. For example, oxetanes react in the presence of carbon monoxide and nickel carbonyl to give the corresponding γ-butyrolactone in good yield[35]:



55% yield

Lactones can also be synthesized via the carbonylation of unsaturated hydrocarbons. 1,5-Hexadiene gives a 95% yield of α-ethyl-γ-valerolactone at 20°C/13 bar using a copper-catalyst[36]:



The above examples indicate that lactones can be obtained from the carbonylation reaction of various substrates. However these methods require high temperatures and pressures. Also many have competing side-reactions which lowers the yield of the lactone.

The present work is concerned with the synthesis of lactones. From the process developed by Despeyroux and Alper[25], it seemed conceivable that unsaturated alcohols could undergo intramolecular oxidative-carbonylation to lactones at room temperature and atmospheric pressure. Such a regioselective lactone synthesis, if general, would represent a significant improvement over existing metal catalyzed routes to these heterocycles.

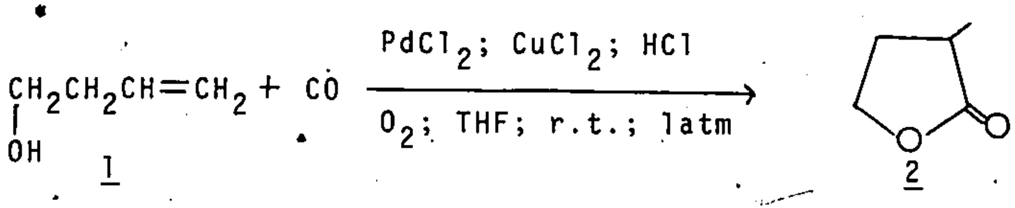
CHAPTER II

RESULTS and DISCUSSION

1. Carbonylation of γ,δ- and δ,ε-Alkenols:

Oxidative-carbonylation of a series of γ,δ- (i.e.: homoallylic) and δ,ε-unsaturated alcohols in tetrahydrofuran with palladium(II) chloride as the catalyst, in the presence of cupric chloride and acid, afforded lactones in reasonable yields. These reactions were effected at room temperature and atmospheric pressure. Typically, a 10:1 ratio of substrate to palladium catalyst was employed in these reactions, with 0,5 ml of concentrated hydrochloric acid dissolved in 60-70 ml of the solvent. The proportion of substrate to cupric chloride ranged from 5:1 to 5:4 depending on the nature of the reactant. Let us now consider each of these cyclization reactions with emphasis on the determination of the best reaction conditions and the characterization of the products. The possible mechanism for these reactions is discussed subsequently.

a. 3-Buten-1-ol:

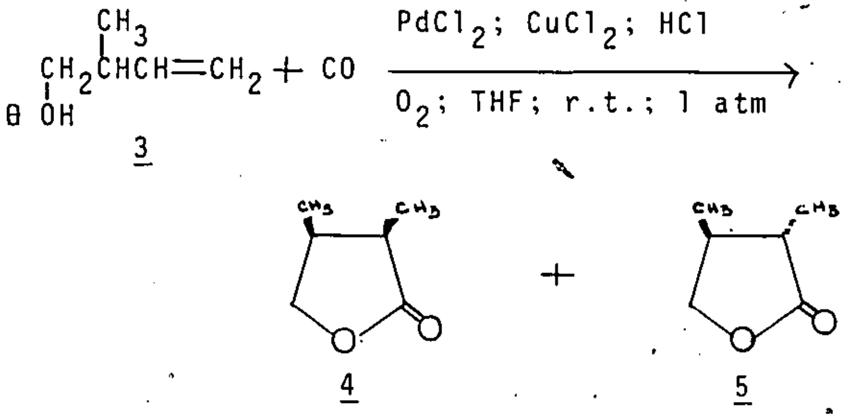


Use of 3-buten-1-ol (1) as the substrate under the usual conditions afforded α-methyl-γ-butyrolactone (2) in 60% yield. In order to determine the preferred acid concentration, the amount of hydrochloric acid was varied from 0,1 ml (15%yield) to 0,5 ml (60% yield); replacement of hydrochloric acid by 0,5 ml of acetic acid resulted in no carbonylation of the alcohol. When no cupric chloride was used a 34% yield of lactone was observed, and half of the starting material was recovered. Replacement of tetrahydrofuran by dimethoxyethane (DME) gave the lactone (2) in 38% yield together with starting material.

The structure of the lactone (2) was assigned by comparison of spectral data with an authentic sample as well as by gas chromatography. The carbonyl absorption band in the infrared spectrum (neat) at 1769 cm^{-1}, is comparable to the accepted value of 1765 cm^{-1} [37]. The proton magnetic resonance spectral data is in good agreement with literature data[38]. The principal fragmentation in the mass spectrum is expulsion of carbon dioxide.

resulting in the appearance of a base peak at m/e 56. The spectral data for 2 and the other lactones are given in Table 2.

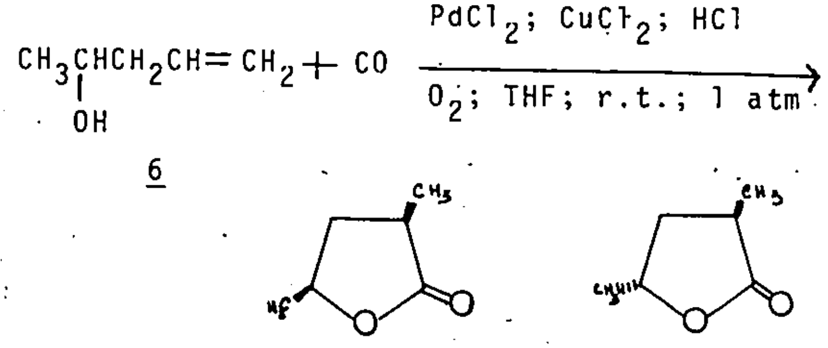
b. 2-Methyl-3-buten-1-ol:



The ratio of cupric chloride:substrate was varied for this carbonylation. At 8:10 cupric chloride:reactant, a 10% yield was found, as well as many by-products; the yield increased to 32% using a 5:10 ratio of cupric chloride:substrate, reached a maximum of 42% using a 2:10 ratio and decreased to 36% in the absence of the copper compound. Substitution of cupric acetate monohydrate for cupric chloride afforded the lactone in 50% yield as well as numerous unidentified by-products. No reaction was observed in the absence of both cupric chloride and oxygen, or oxygen alone. Thus, oxygen is necessary for this reaction. Under the usual conditions (see Chapter III:Experimental, section 2), a 42% yield of pure 2,3-dimethyl-γ-butyrolactone was obtained by fractional distillation.

Comparison of the proton magnetic resonance spectral data with that in the literature[39], indicated a 2:1 ratio of trans:cis dimethyl lactones. This was determined by looking at the doublets of the methyl groups; in the cis-isomer, they are found at 1,04 and 1,18 ppm; for the trans-isomer, at 1,16 and 1,26 ppm; therefore by comparing their relative integration, the above ratio was found. The base peak in the mass spectrum (m/e 55) corresponds to the loss of carbon dioxide and a methyl group from the molecular ion.

c. 4-Penten-2-ol:



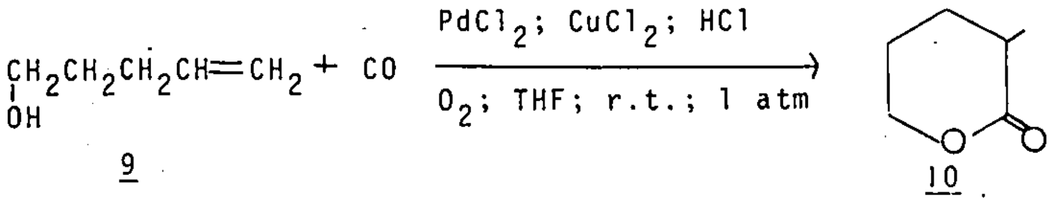
$$\underset{\text{OH}}{CH_3\overset{|}{C}H}CH_2CH{=}CH_2 + CO \xrightarrow[O_2;\ THF;\ r.t.;\ 1\ atm]{PdCl_2;\ CuCl_2;\ HCl}$$

6

7 8

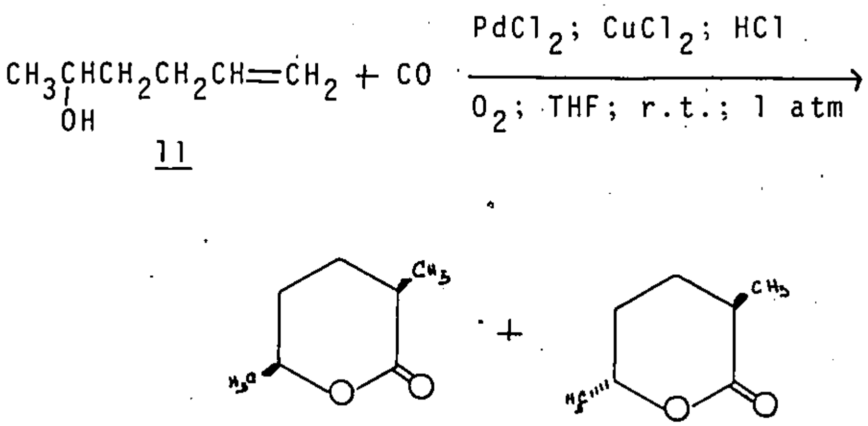
The first experiment carried out using an 8:10 ratio of cupric chloride:substrate, gave the isomeric 2,4-dimethyl-γ-butyrolactone in 30% yield. When a 2:10 ratio was used the yield improved significantly to 80%. The infrared, nuclear magnetic resonance[40] and mass spectral[41] data were in good agreement with literature values. Integration of the nuclear magnetic resonance spectrum indicated that the cis and trans lactones were present in equal amounts. This was determined by consideration of the number of protons found between 1,84 and 2,18 ppm; since only two hydrogens from the β-position of the trans-isomer are found in this region, the integration corresponds to the presence of one proton; then by looking at the region 2,35-2,92 ppm, integration revealed the presence of three hydrogens, two from the cis and one from the trans as should be found from equal amounts of each isomer.

d. 4-Penten-1-ol:



One experiment was run with the unsaturated alcohol 9, using an 8:10 ratio of cupric chloride:substrate giving the α-methyl-δ-valerolactone (10) in 75% yield. The spectral data had similar characteristics to those of the lactones already described.

e. 5-Hexen-2-ol:



$$\underset{\text{OH}}{CH_3CH}CH_2CH_2CH{=}CH_2 + CO \xrightarrow[O_2;\ THF;\ r.t.;\ 1\ atm]{PdCl_2;\ CuCl_2;\ HCl}$$

11

12 + 13

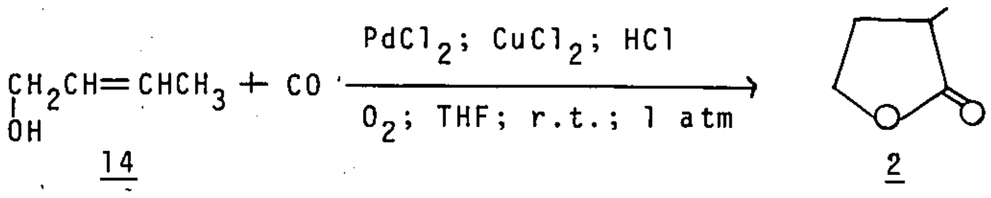
The 2:10 ratio of cupric chloride:substrate was used in the reaction of 11, affording a 38:62 mixture of cis (12) and trans (13) -2,5-dimethyl-γ-valerolactone (50% yield). The proportion of cis and trans isomers was determined by nuclear magnetic resonance spectroscopy[42]: the cis-isomer shows a doublet at 1,34 ppm and the trans at 1,32 ppm, when the relative area were compared the above ratio was obtained. The mass spectral results were in accord with literature data[41].

From these results, it can be seen that this oxidative-carbonylation, which occurs under mild conditions. is superior to other known metal-catalysed routes, which require high temperatures and pressures. For example, the synthesis of α-methyl-γ-butyrolactone is a significant improvement when compared to other methods of preparation of this lactone[5,31,43,44].

2. Carbonylation of Allylic Alcohols:

Attempts to carbonylate allylic alcohols usually results in isomerization to the corresponding aldehyde or other undesirable reactions[31,33,35,43,45,46,47,48]. These methods, when sucessful, require the use of high temperatures and pressures. The present oxidative-carbonylation method yielded lactones, in acceptable to good yields, as major products. Aldehydes were not produced in these reactions, the principal by-product being the allylic chloride probably formed by hydroxide displacement from the substrate by chloride ion of cupric chloride.

a. 2-Buten-1-ol (crotyl alcohol):



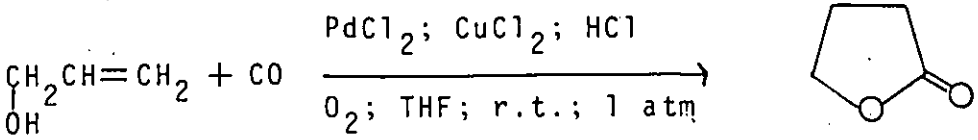
The amount of hydrochloric acid was determined from the following set of reactions: at 0,5 ml of hydrochloric acid, the lactone (2) was isolated in 50% yield; when the acid concentration was decreased to 0,2 ml, a 5% yield of 2 was obtained, while the yield was 17% using 1 ml of hydrochloric acid (in all instances, the amount of tetrahydrofuran was 60-70 ml). If water (0,32 ml) is substituted for hydrochloric acid, lactone is formed (20%) but the reaction is inferior to the use of 0.5 ml of hydrochloric acid. No lactone was obtained if glacial acetic acid (0,5 ml) and 3 Å molecular sieves are employed for the cyclization reaction.

Tetrakis(acetonitrile)palladium(II) tetrafluoroborate can function as a catalyst for the reaction but the yield of 2 is only 20-28%. Nevertheless the catalytic system does not require acid.

When the volume of tetrahydrofuran was reduced to 15-20 ml, a 28% yield of 2 was obtained, while the use of half (30-35 ml) of the normal amount of tetrahydrofuran gave the lactone in nearly the same yield (47%) as in the optimum conditions.

Since the lactone formed was the same as that obtained from the carbonylation of 3-buten-1-ol, it seemed conceivable that isomerization of the homoallylic alcohol to crotyl alcohol preceeded the oxidative cyclization reaction. Therefore the reaction of 3-buten-1-ol was run under the same experimental conditions, except that oxygen and carbon monoxide were not present. No isomerization occured.

b. Allyl alcohol:



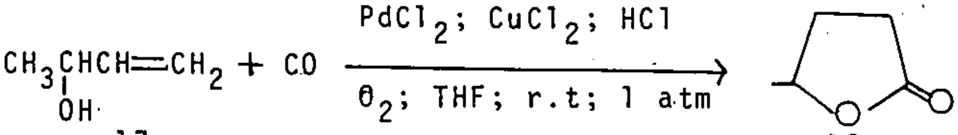
$\underset{OH}{CH_2}CH{=}CH_2 + CO \xrightarrow[O_2;\ THF;\ r.t.;\ 1\ atm]{PdCl_2;\ CuCl_2;\ HCl}$

15 16

Using the usual volume of tetrahydrofuran (60-70 ml) gave γ-butyrolactone, 16, in only 10% yield and the conversion was just 15%. However, decreasing the volume of tetrahydrofuran to 30-35 ml, resulted in a significant improvement in the yield of 16 (46%). There was no propionaldehyde produced in either case.

The carbonyl absorption band of 16 occured in the infrared at 1775 cm^{-1} in accord with the value reported in the literature[37] and the proton magnetic resonance spectrum also compared to the reference one[49], as well as to that of the authentic sample[50]. The mass spectrum showed a base peak at m/e 42, which corresponds to the loss of carbon dioxide from the molecular ion. A gas chromatograph of the product was then spiked with commercial γ-butyrolactone (Fluka Chemicals) and one peak was observed. providing further evidence for the validity of the structural assignment.

c. 3-Buten-2-ol:



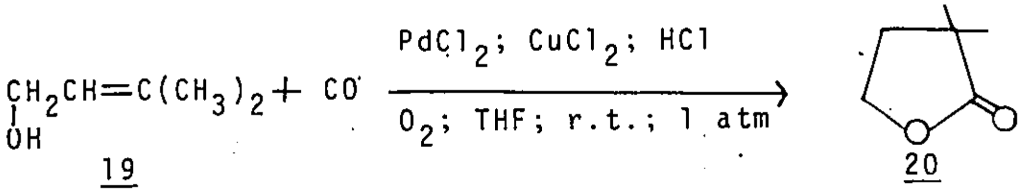
17

18

When the carbonylation reaction was run using a volume of 60-70 ml of tetrahydrofuran, only a 5% yield of lactone 18 was obtained. It was gratifying to learn that γ-valerolactone could be formed in 70% yield by simply repeating the reaction in half the volume of tetrahydrofuran. Interestingly, a further decrease in the volume of tetrahydrofuran to 15-20 ml gave unsatisfactory results (25% 18). Finally when the acid was decreased to 0,3 ml, and the ratio of cupric chloride:substrate increased to 8:10, the lactone 18 was formed in just 15% yield.

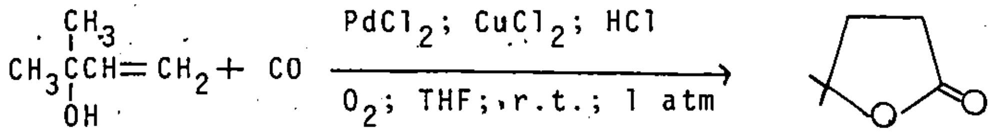
γ-Valerolactone, 18, was identified by infrared[51] nuclear magnetic resonance[52] and mass spectroscopy. The latter showed a molecular ion at m/e 100 and a base peak at m/e 56 corresponding to the loss of carbon dioxide.

d. 3-Methyl-2-buten-1-ol:



As in the previous case, reduction of the volume of tetrahydrofuran in the reaction resulted in a substantial improvement in yield of the lactone, 20 (i.e. from 15% to 45%). The α,α-dimethyl-γ-butyrolactone was checked for purity by gas chromatography and the product was identified by infrared, proton nuclear magnetic resonance and mass spectroscopy (see Table 2).

e. 2-Methyl-3-buten-2-ol:

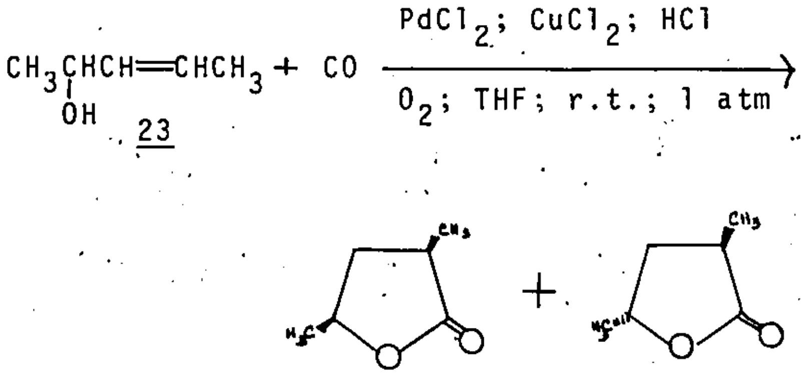


21

22

Applications of the usual reaction conditions to 2-methyl-3-buten-2-ol (21) (see Chapter III:Experimental, section 3), gave 4,4-dimethyl-γ-butyrolactone (22), in 65% yield. It was identified by infrared, proton and carbon-13 nuclear magnetic resonance as well as mass spectroscopy (see Table 2).

f. 3-Penten-2-ol:

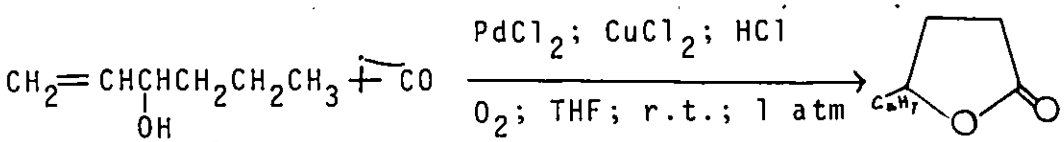


7

8

The carbonylation of this allylic alcohol was done as described (see Chapter III:Experimental, section 3), affording a 1:1 mixture of cis- and trans-2,4-dimethyl-γ-butyrolactone in 65% yield. The products were identical to those obtained from 4-penten-2-ol.

g. 1-Hexen-3-ol:

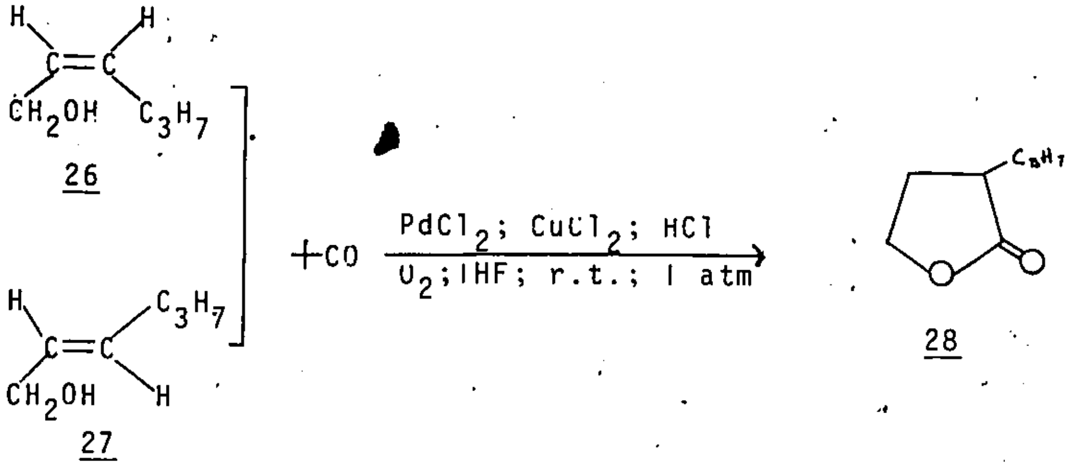


24

25

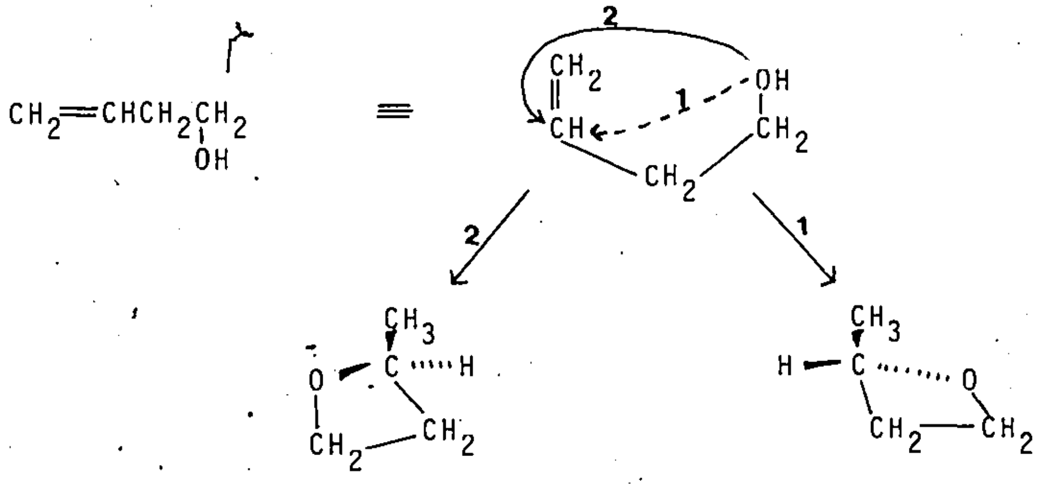
Under the usual conditions (30-35 ml of tetrahydrofuran), 4-n-propyl-γ-butyrolactone (25) was obtained in 40% yield from 1-hexen-3-ol (24); when the volume of tetrahydrofuran was increased to 40-45 ml, a lower yield of 25 was obtained (23%). The spectral data for 25 were analogous to that for γ-valerolactone (18) except that the base peak in the mass spectrum occured at m/e 85. The latter may arise by loss of the propyl radical from the molecular ion.

h. Cis- and trans-2-hexen-1-ol:



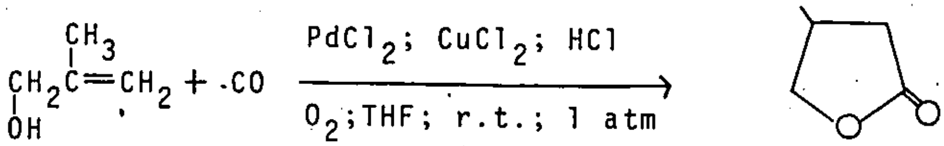
Little difference was observed in the oxidative cyclization of cis- and trans-2-hexen-1-ol to α-n-propyl-γ-butyrolactone (28). The cis-isomer, 26, as reactant afforded 28 in 30% yield while the same product was isolated in 35% yield from the trans-isomer, 27.

Since one is creating a chiral center using either isomer of 2-hexen-1-ol, it was of interest to determine whether one could achieve asymmetric induction in the reaction. Diethyl-L-tartrate has been used in several asymmetric synthesis including the epoxidation of olefins[53], and the oxidation of sulfides[54]. Consequentlty the oxidative-carbonylation of trans-2-hexen-1-ol was repeated in the presence of four equivalents of diethyl-L-tartrate (to the palladium catalyst), giving (R)-α-n-propyl-γ-butyrolactone. Careful purification of the latter afforded material having a specific rotation of -2.6° ($CHCl_3$; 0.85 g/100ml). Optically pure material has a rotation of -11°[55]; therefore the lactone was formed in 24% enantiomeric excess. It was believed from Sharpless work[56,57] that by using the (L)-tartrate enantiomer, the cyclization of the unsaturated alcohol will occur from either side of the double-bond; however, the presence of the tartrate enantiomer will favor one side to the expense of the other:



Note that while diethyl-L-tatrate is of moderate success in the attainment of asymmetric induction, β-cyclodextrin is not useful at all.

i. 2-Methyl-2-propen-1-ol:



29

30

The reaction of 2-methyl-2-propen-1-ol (29) was first effected in 60-70 ml of tetrahydrofuran and no lactone 30 was produced. The lactone was formed in modest yield (15%) by use of half of the volume of tetrahydrofuran. A further decrease in the amount of tetrahydrofuran (15 ml) gave 30 in only 5% yield. Therefore it was concluded that very little β-methyl-γ-butyrolactone (30) could be produced via the carbonylation of 2-methyl-2-propen-1-ol (29).

j. Geraniol, cinnamyl alcohol and 2-buten-1,4-diol:

Attempted carbonylation of geraniol gave only geranyl chloride. Similarly, cinnamyl alcohol afforded cinnamyl chloride and an unidentified product. It is not clear why these allyl alcohols fail to react successfully, in contrast to the similar systems already described. An allylic diol, 2-buten-1,4-diol was recovered unchanged when subjected to the usual reaction conditions.

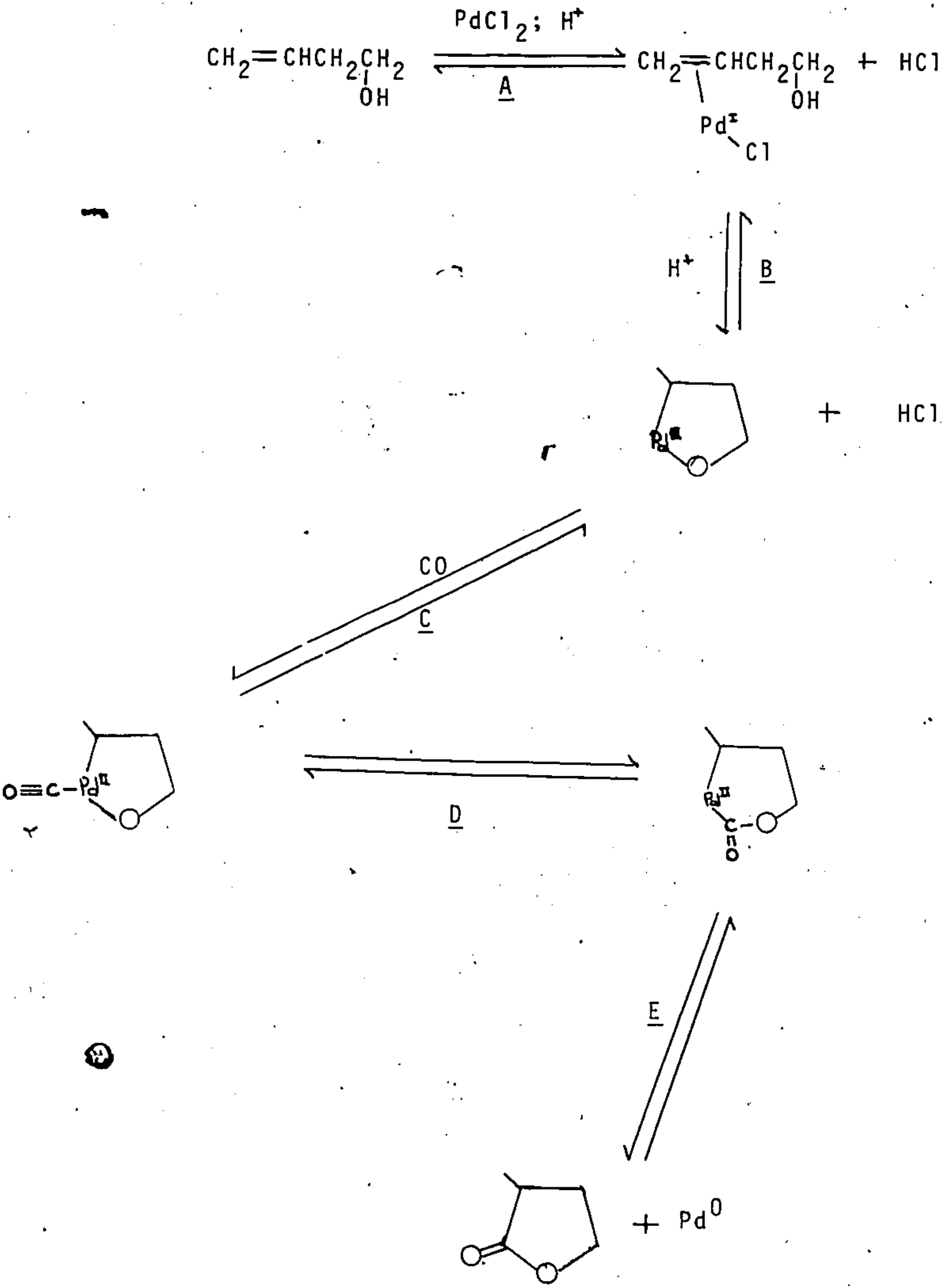
3. Mechanism:

Now that the carbonylation reactions of different substrates has been discussed, and how different factors were varied to obtain good to acceptable yields of products, a mechanism will be proposed trying to take into account these observations.

The carbonylation of 3-buten-1-ol (1) will be used as a model, (see p.35).

From the proposed mechanism, it can be seen that the first step, A, would be palladation of the carbon-carbon double bond, releasing one of the chloride ions (as hydrochloric acid). However, this step gives rise to a complex in which palladium has an oxidation number of one, which is rarely encountered. Step A does take into account the fact that acid is required for the reaction or at least the solution has to be acidic enough to provide some proton source. It was reported that addition of more than 0,5 ml of acid would lower the yield of lactone; maybe this could indicate that there is an equilibrium and that too much acid would shift the equilibrium to the left.

The second step, B, may involve bond formation between a carbon of the double bond, the palladium and oxygen. In the case of a terminal double bond, the formation of the bond occurs at the non-terminal carbon,


PdCl2; H+
A
CH2=CHCH2CH2OH
CH2=CHCH2CH2OH
PdII
Cl
+ HCl
H+
B
PdII
+ HCl
CO
C
O≡C–PdII
D
PdII
C
O
E
+ Pd0

i.e. following the Markownikoff rule; except in the case of terminal allylic alcohols, where formation of a four-membered ring would occur if the bond formation took place following the Markownikoff rule. This would involve too much strain on the system; therefore in this case, the bond formation would be at the terminal carbon resulting in a five-membered ring lactone. For internal double bonds, formation of a five-membered ring lactone was also favoured.

Addition of carbon monoxide to the coordinatively unsaturated complex (step C) would occur, followed by ligand migration (carbonyl insertion, step D). The latter is postulated to occur by migration of the palladium oxygen bond to the carbonyl carbon, since recent studies by Bryndza[58] showed that carbonyl insertion occurs preferentially between the metal-oxygen bond rather than between the metal-carbon bond, when both are present.

After carbon monoxide insertion, reductive-elimination takes place (step E), giving rise to the lactone and palladium (0).

The palladium(0) is reoxidized to palladium(II) chloride in a similar way to that proposed for the Wacker process[59]:

$$Pd^0 + 2\ CuCl_2 \longrightarrow PdCl_2 + 2\ CuCl_2$$

$$2\ CuCl + 2\ HCl + \frac{1}{2}\ O_2 \longrightarrow 2\ CuCl_2 + H_2O$$

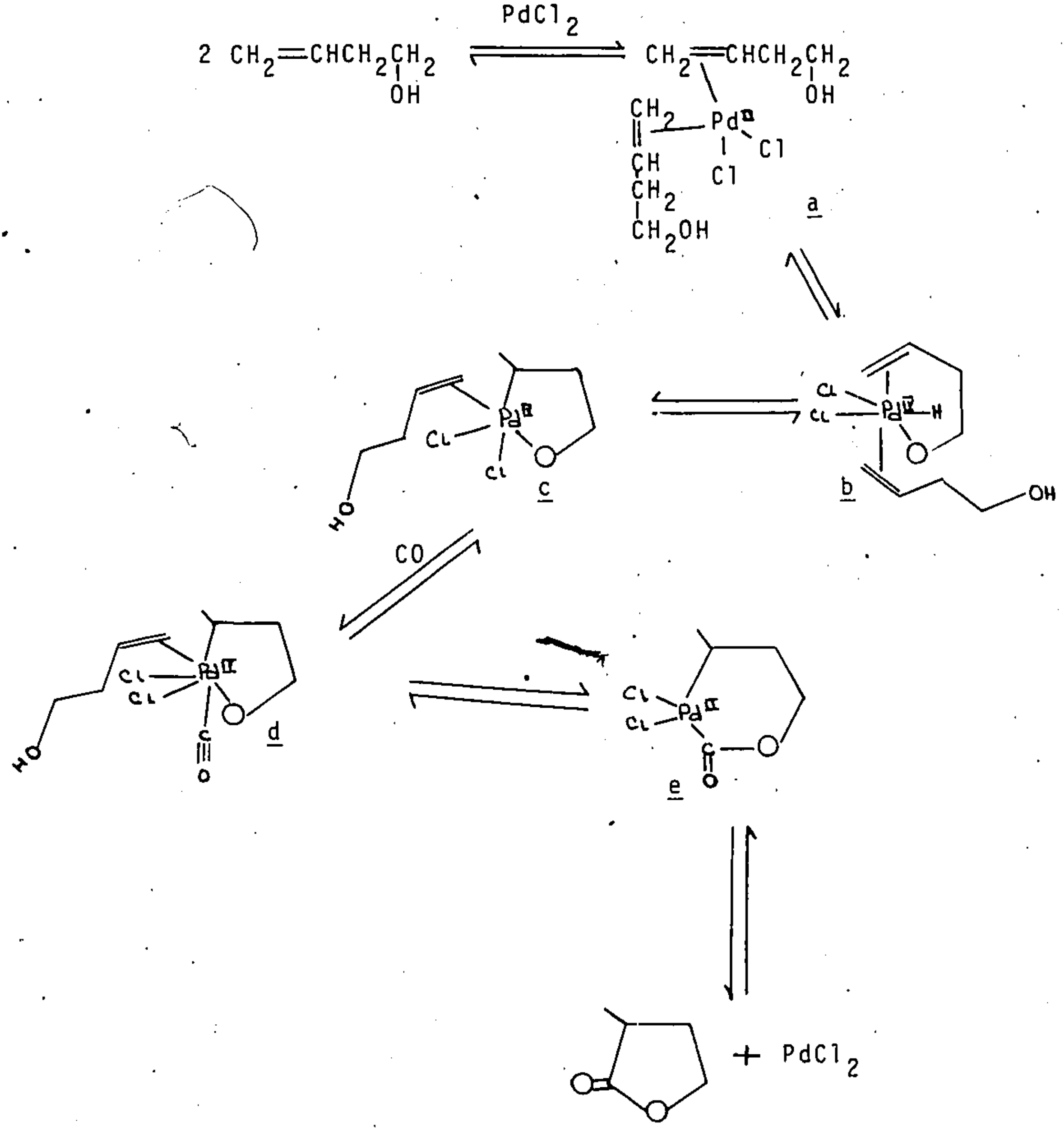
A reaction occured when no copper(II) chloride was present, indicating that either the reaction stops after all the palladium(II) chloride has been consumed (i.e. 10% conversion) or that the palladium(0) could be reoxidized in the following way:

$$Pd^0 + 2\ HCl + \frac{1}{2}\ O_2 \longrightarrow PdCl_2 + H_2O$$

Oxygen may be able to reoxidize the palladium(0) to palladium(II) chloride in the presence of acid.

An alternative pathway to the formation of lactones is that where the palladium would go from an oxidation number of two to four and back to two, (see p.38).

First there would be palladation of two olefins; ring closure of one of the unsaturated alcohol ligands would give rise to complex b, where palladium has an oxidation number of four. Proton transfer from the palladium to the terminal carbon of the double bond, gives rise to complex c. Addition of carbon monoxide to the unsaturated complex c, would form d; followed by car-


2 CH2=CHCH2CH2OH
PdCl2
CH2=CHCH2CH2OH
CH2=CH–CH2–CH2OH
PdII
Cl
Cl
a
Cl
Cl
PdIV
H
O
OH
b
HO
PdII
Cl
Cl
O
c
CO
HO
Cl
Cl
PdII
O
C
O
d
Cl
Cl
PdII
C
O
O
e
+ PdCl2

bonyl insertion into the palladium-oxygen bond to regenerate palladium(II). Palladium(II) chloride would then be released along with the lactone.

From the present scheme, it can be seen that hydrochloric acid would not play a direct role in the reaction but would be necessary to reoxidize the palladium(0) to palladium(II), which could arise from other cycles.

Table 2. Spectroscopic Properties of Lactones.

Reactants	Products	Yield (%)	IR, ν_{CO} (cm^{-1})	^1H nmr ($CDCl_3$) (ppm)	GC-RT	MS (m/e)	
						M	Base
3-buten-1-ol	α-methyl-γ-butyrolactone	60	1769 (neat)	1.25 (d;3H) 2.00-2.50 (m;3H) 3.90-4.45 (m;2H)	3.93^a	100	56
2-buten-1-ol	α-methyl-γ-butyrolactone	50					
2-methyl-3-buten-1-ol	2,3-dimethyl-γ-butyrolactone	42	1765 (neat)	cis: 1.04 (d;3H) 1.18 (d;3H) trans: 1.16 (d;3H) 1.26 (d;3H) both: 2.00-2.77 (m;2H) 4.80-4.95 (m;2H)	3.08 3.33 ^{a}	114	55
4-penten-2-ol	2,4-dimethyl-γ-butyrolactone	80	1770 (neat)	1.24-1.58 (m;12H) 1.84-2.18 (m;2H) 2.37-2.92 (m;5H) 4.36-4.72 (m;3H)	5.29 5.48 ^{a}	114	42

Table 2. (cont'd)

Reactants	Products	Yield (%)	IR, ν_{CO} (cm^{-1})	^1H nmr ($CDCl_3$) (ppm)	GC-RT	MS M	MS Base
4-penten-1-ol	α-methyl-γ-valerolactone	75	1770 (neat)		6.56[a]	114	42
5-hexen-2-ol	2,5-dimethyl-δ-valerolactone	50	1750 (neat)	1.20-1.40 (m;12H) 2.20-2.50 (m;10H) 4.00-4.60 (m;12H)	7.36 7.90 [a]	128	42 56
allyl alcohol	γ-butyrolactone	46	1775 ($CHCl_3$)	2.48 (t;2H) 2.18-2.32 (m;2H) 4.12 (t;2H)	4.56[b]	86	42
3-buten-2-ol	γ-valerolactone	70	1775 ($CHCl_3$)	1.40 (d;3H) 1.17-1.90 (m;2H) 2.16-2.58 (m;2H)	5.06[b]	100	56
3-methyl-2-buten-1-ol	α,α-dimethyl-γ-butyrolactone	45	1770 ($CHCl_3$)	1.38 (s;6H) 2.58 (t;2H) 4.30 (t;2H)	2.18[c]	114	43

Table 2. (cont'd)

Reactants	Products	Yield (%)	IR, ν_{CO} (cm^{-1})	^1H nmr ($CDCl_3$) (ppm)	GC-RT	MS M	MS Base
2-methyl-3-buten-2-ol[d]	4,4-dimethyl-γ-butyrolactone	65	1770 ($CHCl_3$)	1.44 (s;6H) 2.08 (t;2H) 2.64 (t;2H)	5.85[b]	114	43
3-penten-2-ol	2,4-dimethyl-γ-butyrolactone	65	1765 ($CHCl_3$)	1.19-1.38 (m;6H) 1.84-2.13 (m;2H) 2.37-2.92 (m;3H) 4.28-4.70 (m:2H)	2.00[c]	114	42
1-hexen-3-ol	4-n-propyl-γ-butyrolactone	40	1770 ($CHCl_3$)	0.93 (t;6H) 1.30-1.92 (m;4H) 2,24-2.35 (m;2H) 2.5 (t;2H) 2.42-2.52 (m;2H)	8.58[b]	128	85

Table 2. (cont'd)

Reactants	Products	Yield	IR, ν_{CO}	^{1}H nmr ($CDCl_3$)	GC-RT	MS	
		(%)	(cm^{-1})	(ppm)		M	Base
cis-2-hexen-1-ol	α-n-propyl-γ-butyrolactone	30	1765 ($CHCl_3$)	0.94 (t;3H) 1.80-2.00 (m;3H) 2.32-2.60 (m;3H) 4.34 (t;2H)	5.53^c	128	86
trans-2-hexen-1-ol^e	α-n-propyl-γ-butyrolactone	35					

a: 3% ov-17: 80°C/3min $\xrightarrow{10°C/min}$ 220°C

b: 3% ov-17: 80°C/3min $\xrightarrow{10°C/min}$ 250°C

c: ov-101: 80°C/3min $\xrightarrow{10°C/min}$ 280°C

d: ^{13}C-nmr: 27.73; 29.36; 34.67; 84.51; 176.68 ppm

e: ^{13}C-nmr: 13.78; 20.54; 28.61; 32.40; 39.01; 66.49; 176.60 ppm

CHAPTER III

EXPERIMENTAL

1.General Comments:

Infrared spectra were recorded on a Perkin-Elmer 783 spectrometer. Proton Magnetic Resonance spectra were taken on a Varian EM 360A or Varian XL-300 spectrometer, with tetramethylsilane (TMS) as the internal standard. Carbon-13 Magnetic Resonance spectra were determined on a Varian XL-300 spectrometer at 75.43 MHz.

Mass spectra were obtained with a VG-7070E mass spectrometer. Routine gas chromatography was carried out with a Varian 3400 and Varian Vista 6000 gas chromatographs having a flame ionisation detector and hydrogen/air as the carrier gas.

Starting materials for the carbonylation reactions were obtained from Aldrich Chemicals Co., except allyl alcohol which was purchased from Fisher Scientific Co. and was freshly distilled prior to use.

Tetrahydrofuran (THF) was dried over sodium and benzophenone. Palladium(II) chloride was obtained from Aesar or Strem Chemicals; and copper(II) chloride was purchased from either Aldrich Chemical Co.. or Alfa Products. Concentrated hydrochloric acid was used from Fisher Scientific Company. Carbon monoxide and oxygen were supplied by Air Products.

Column chromatography was performed with silica gel 60 (E. Merck A.G., West Germany), and Bio-silica gel from Bio-Rad Laboratories.

2.Carbonylation of γ,δ- and δ,ε-Alkenols:

The following general procedure was used: carbon monoxide was bubbled through dry tetrahydrofuran (THF) (60-70 ml), palladium(II) chloride ($PdCl_2$) (0,140 g; 0,78 mmol) was added, followed by 0,5 ml of concentrated hydrochloric acid and copper(II) chloride ($CuCl_2$) (0.84 g: 6,2 mmol was used for 3-buten-1-ol and 4-penten-1-ol; 0,21 g; 1,6 mmol was used in the other cases). Oxygen bubbling commenced, the substrate (7.8 mmol) was added and the reaction mixture was stirred overnight at room temperature. The solution was filtered and the tetrahydrofuran (THF) was removed in vacuo to give the crude product.

The following particular conditions were used in the individual cases.

a. 3-Buten-1-ol:

For the reaction of this substrate, the amount of hydrochloric acid was varied and 0,5 ml was found to give the best results. When replaced by acetic acid, no reaction took place. In the absence of copper(II) chloride, there was a reaction but a lower yield was obtained.

After extraction of the crude product with ether, it was passed through a chromatographic column (silica gel 60) ($CHCl_3$ as eluant); α-methyl-γ-butyrolactone was obtained in 60% yield.

b. 2-Methyl-3-buten-1-ol:

A decreased in the copper(II) chloride:substrate ratio from 8:10 to 2:10 resulted in an increase in the yield from 20 to 43%. When no oxygen was present, there was no reaction.

The best result was 45% yield of products consisting of a mixture of 33:67 cis:trans-2,3-dimethyl-γ-butyrolactone. The lactone was purified by fractional distillation.

c. 4-Penten-2-ol:

The general procedure was followed. The isomeric 2,4-dimethyl-γ-butyrolactones were purified by fractional distillation. An 80% yield was obtained with a 1:1 ratio of cis and trans isomers.

d. 4-Penten-1-ol:

The general procedure was applied. Purification by ether extraction gave α-methyl-γ-valerolactone in 75% yield.

e. 5-Hexen-2-ol:

2,5-Dimethyl-δ-valerolactone was purified by column chromatography using Celite, Bio-Silica and Silica gel as adsorbents and 3:1/chloroform:ethyl acetate as eluant.

A 50% yield of isomeric lactones was obtained with 38% being the cis-isomer and 62% the trans-isomer.

3. Carbonylation of Allylic Alcohols:

The following general procedure was used: carbon monoxide was bubbled through tetrahydrofuran (THF) (60-70 ml for 2-buten-1-ol; 30-35 ml for the other cases), palladium(II) chloride (0.140 g: 0.78 mmol) was added followed by 0.5 ml of concentrated hydrochloric acid and copper(II) chloride (0.210 g; 1.56 mmol). Oxygen bubbling commenced, the allylic alcohol (7.8 mmol) was added and the reaction mixture was stirred overnight at room temperature. The solution was filtered, the tetrahydrofuran (THF) was evaporated in vacuo to yield the crude product.

a. 2-Buten-1-ol (crotyl alcohol):

When the above procedure was followed, α-methyl-γ-butyrolactone was obtained in 50% yield after TLC purification (using 3:1/hexane:ether as eluant).

b. Allyl alcohol:

The best result was obtained when the volume of tetrahydrofuran was decreased to 30-35 ml. The γ-butyrolactone was purified by TLC (eluant: 3:1/hexane: ether) and a 45% yield was found.

c. 3-Buten-2-ol:

The general procedure was followed. The γ-valerolactone was obtained in 70% yield after TLC purification (eluant: 3:1/hexane:ether).

d. 3-Methyl-2-buten-1-ol:

The general procedure was followed; a 45% yield of the α,α-dimethyl-γ-butyrolactone was obtained, after TLC purification (eluant: 3:1/hexane:ether).

e. 2-Methyl-3-buten-2-ol:

The general procedure was followed. 4,4-Dimethyl-γ-butyrolactone was obtained in 65% yield after TLC purification (eluant: 3:1/hexane:ether).

f. 3-Penten-2-ol:

The general procedure was used; 2,4-dimethyl-γ-butyrolactone was obtained in 65% yield after TLC purification (eluant: 3:1/hexane:ether). A 1:1 cis: trans isomer ratio was found.

g. 1-Hexen-3-ol:

The general procedure was used. After TLC purification (eluant: 3:1/hexane:ether), 4-n-propyl-γ-butyrolactone was obtained in 40% yield.

h. Cis- and trans-2-hexen-1-ol:

The general procedure was used. α-n-Propyl-γ-butyrolactone was obtained in 30% yield from the cis-isomer and 35% from the trans-isomer; after TLC purification (eluant: 3:1/hexane:ether).

i. 2-Methyl-2-propen-1-ol:

The carbonylation of this allylic alcohol was not successful; the volume of tetrahydrofuran was varied and the best result was 15% yield when 30-35 ml of tetrahydrofuran was used.

j. Geraniol:

There was no carbonylation reaction of this allylic alcohol under the described procedure.

k. Cinnamyl alcohol:

When this reaction was carried out following the general procedure, low GC yields were observed; attempts to purify the product were unsuccessful.

4.Carbonylation of 2-Buten-1,4-Diol:

The general procedure of section 3 was followed. There was no lactone formation.

5.Asymmetric Carbonylation of trans-2-Hexen-1-ol:

The same procedure as described in section 3 was followed; after addition of the substrate, 0.65 g (0.003 mol) of diethyl-L-tartrate was added.

After TLC purification (eluant: 3:1/hexane:ether). the optically active α-n-propyl-γ-butyrolactone was obtained. The optical rotation was measured and it was found to be -2.6° ($CHCl_3$; 0.85 g/ 100 ml). Since the specific rotation of optically pure (R) lactone is -11°[55], the percent enantiomeric excess is 24%. A proton nuclear magnetic resonance spectrum of the product was recorded using tris-3-[(heptafluoropropyl hydroxymethylene)-d-camphorato], europium(III) derivative (Aldrich Chemical Co.), as shift reagent. A shift in the position of the proton at the chiral center was observed.

When diethyl-L-tartrate was replaced by β-cyclodextrin, no optical rotation was observed in the lactone formed.

REFERENCES.

1. F.C. Phillips, Am Chem J, 1894, 16, 255.
2. O. Roelen, Angew Chem A, 1948, 60, 62.
3. W. Reppe, Liebigs Ann Chem, 1953, 582, 1.
4. J. Smidt, W. Hafner, R. Jira, J. Sedleimeier, R. Sieber. R. Ruttinger, H. Kojer, Angew Chem, 1959, 71, 176.
5. D.R. Levering and A.L. Glasebrook, J Org Chem, 1958, 23, 1836.
6. C.W. Bird, Chem Rev, 1962, 62, 283.
7. F.E. Paulik and J.F. Roth, JCS Chem Commun, 1968, 1578.
8. N. Rizkalla, German Patent 2,610,036, 1976; Chem Abstr. 85, 159463e (1976).
9. H. Kuckertz, German Patent 2,450,965, 1976; Chem Abstr. 85, 62675n (1976).
10. I Tomiya and Y. Kijima, British Patent 2,007.666 1979; Chem Abstr. 91, 38935a (1979).
11. R.A.Sheldon, Chemicals from Synthesis Gas, D. Reidel Publishing Co., Dordrecht, Holland, 1983; p.145.
12. G. Braca, G. Sbrana, G. Valentini, G. Andrich and G. Gregorio, J Am Chem Soc, 1978, 100, 6238.
13. J. Tsuji, M. Morikawa and J. Kiji, Tet Lett, 1963, 1437.

14. E.N. Frankel and F.L. Thomas, J Am Oil Chem Soc, 1973, 50, 39.

15. K. Bittler, N.V. Kutepow, D. Neubauer and H. Reis, Angew Chem Int Ed Eng, 1968, 7, 329.

16. D. Medema, R. van Helden and C.F. Kohll, Inorg Chim Acta, 1969, 3, 255.

17. D.M. Fenton and P.J. Steinwand, J Org Chem, 1972, 37, 2034.

18. a) D.E. James, L. Hines and J.K. Stille, J Am Chem Soc, 1976, 98, 1806.
    b) J.K. Stille, D.E. James, L.F. Hines, J Am Chem Soc, 1973, 95, 5062.
    c) D.E. James and J.K. Stille, J Am Chem Soc, 1976, 98, 1810.

19. J.K. Stille and R. Divakaruni, J Org Chem, 1979, 44, 3474.

20. L.J. Kehoe and R.A. Schell, J Org Chem, 1970, 35, 2846.

21. J.F. Knifton, J Org Chem, 1976, 41, 793.

22. J.F. Knifton, J Org Chem, 1976, 41, 2885.

23. R. Bardi, A. DelPra, A.M. Piazzesi, L. Toniolo, Inorg Chim Acta, 1979, 35, L345.

24. P. Hofmann, K. Kosswig and W. Schaefer, Ind Eng Chem Prod Res Dev, 1980, 19, 330.

25. B. Despeyroux and H. Alper, Ann NY Acad Sci, 1984, 415, 148.

26. H. Alper, B Despeyroux and J.B. Woell, Tet Lett. 1983, 24, 5691.

27. H. Alper, J.B. Woell, B. Despeyroux and D.J.H. Smith, JCS Chem Commun, 1983, 1270.

28. H. Alper, F.W. Hartstock and B. Despeyroux, JCS Chem Commun, 1984, 905.

29. S.B. Fergusson and H. Alper, JCS Chem Commun. 1984, 1349.

30. H. Alper and F.W. Hartstock, JCS Chem Commun, 1985, 1141.

31. J. Falbe, H.S. Schulze-Steinen and F. Korte, Chem Ber, 1965, 98, 886.

32. J. Falbe, Angew Chem, 1966, 78, 532.

33. A. Matsuda, Bull Chem Soc Jpn, 1968, 41, 1876.

34. D.T. Thomson in "Transition Metals in Homogeneous Catalysis", ed. G.N. Schrauzed, Dekker, NY, 1971; chap.5, p.147.

35. H. Nienburg, G. Elsehnig, DE Offen 1,066,572, 1959; Chem Abstr. 55, 10323h (1961).

36. Y. Soma, H. Sano, Japan Kokai 74-61,166, 1974; Chem Abstr. 81, 120010x (1974).

37. J. Falbe, N. Huppes and F. Korte, Chem Ber, 1964 97, 863.

38. Charles J. Pouchert, The Aldrich Library of NMR Spectra, Ed:II, USA 1983; 591A.

39. G.S.Y. Ng, L-C Yuan, I.J. Jakovac and J.B. Jones, Tetrahedron, 1984, 40, 1235.

40. S.A.M. Tayyev Hussain, W.D. Ollis, C. Smith, J. Fraser-Stoddart, JCS Perkin I, 1975, 1480.

41. E. Honkanen, T. Moisio and P. Karvonen, Acta Chem Scand, 1969, 23, 531.

42. W.H. Pirkle and P.E. Adams, J Org Chem, 1979, 44, 2169.

43. A.P. Dunlop, D.G. Manley and J.P. O'Halloran, US Patent 3,065,243, 1962; Chem Abstr. 58, 8912f (1963).

44. B. Fell, Angew Chem, 1965, 77. 813.

45. R.F. Heck in "Organic Synthesis via Metal Carbonyls" ed. I. Wender and P. Pino, Wiley NY. 1968; vol.1, p.373.

46. C.W. Bird, Transition Metals Intermediates in Organic Synthesis, Logos Press, NY, 1967; p.149.

47. P. Pino in "Organic Synthesis via Metal Carbonyls" ed. I. Wender and P. Pino, Wiley NY, 1977; vol.2, p.233.

48. J. Falbe, Angew Chem, 1962, 74, 900.

49. J.P. Lowry and N.V. Riggs, Tet Lett, 1964, 2911.

50. Charles J. Pouchert, The Aldrich Library of NMR Spectra, Ed:II, USA 1983; 590c.

51. Charles J. Pouchert, The Aldrich Library of IR Spectra, Ed:III' USA 1981; 407G.

52. Charles J. Pouchert, The Aldrich Library of NMR Spectra, Ed:II, USA 1983; 590D.

53. J.G. Hill, K.B. Sharpless, C.M. Exon, R. Regenye, Org Syn, 1984, 63, 66.

54. P. Pitchen, E. Dunach, M.N. Deshmukh and H.B. Kagan, J Am Chem Soc, 1984, 106, 8188.

55. A.I. Meyers, E.D. Mihelich, J Org Chem, 1975, 40, 1186.

56. T. Katsuki, K.B. Sharpless, J Am Chem Soc, 1980, 102, 5674.

57. K.B. Sharpless, S.S. Woodard, M.G. Finn, Pure and Appl Chem, 1983, 55, 1823.

58. H.E. Bryndza, Organometallics, 1985, 4, 1686.

59. E.W. Stern, Catalysis Rev, 1968, 1, 74.