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LIST OF ABBREVIATIONS

Aliquat 336	Tricaprylmethylammonium chloride
bpy	2,2′-bipyridine
β-CD	β-Cyclodextrin
COD	1,5-Cyclooctadiene
COSY	Correlation Spectroscopy
Cp	Cyclopentadienyl
CTAB	Cetyltriethylammonium bromide
CTP	Catalytic Two Phase System
d	doublet
dd	doublet of doublets
DDAB	Didecyldimethylammonium bromide
diphos	1,2-bis(diphenylphosphino)ethane
DME	Dimethoxyethane
DOCYCL	Decoupler Offset Cycling
DPPS	Diphenylphosphino-benzene-m-sulphonate
DTAC	Dodecyltrimethylammonium chloride
e.s.d.	estimated standard deviation
FAB	Fast Atom Bombardment
GC	Gas Chromatography
GC/MS	Gas Chromatography/Mass Spectrometry
HBPT	Hexabutylphosphoric triamide
1,5-HD	1,5-Hexadiene
HETCOR	Heteronuclear Correlation
IR	Infrared
m	multiplet

mmol	millimole
MS	Mass Spectrometry
NMR	Nuclear Magnetic Resonance
NOE	Nuclear Overhauser Enhancement
PEG	Poly(ethylene glycol)
PPN	Bis(triphenylphosphine)iminium
PT	Phase Transfer
PTA	Phase Transfer Agent
PTC	Phase Transfer Catalysis
q	quartet
RCT	Relayed Coherence Transfer
RPM	Revolution Per Minute
s	singlet
SET	Single Electron Transfer
TBAB	Tetrabutylammonium bromide
TBAHS	Tetrabutylammonium hydrogen sulfate
TDA-1	Tris(dioxa-3,6-heptyl)amine
TEBACl	Benzyltriethylammonium chloride
THF	Tetrahydrofuran

ABSTRACT

The first examples of the application of biphasic and phase transfer catalysis to early-transition-metal organometallic chemistry are described. These include very efficient and convenient syntheses of the (η^5-cyclopentadienyl)tricarbonylhydridovanadate anion under remarkably mild biphasic conditions. The latter is capable of effecting, under phase transfer conditions, the reduction of halides, sterically encumbered nitro compounds, and the cyclodehydration of α,β-unsaturated ketones. The reactions may proceed via electron transfer pathways.

The use of nickel cyanide under biphasic or phase transfer conditions converts vinyl epoxides to the unsaturated ketones and/or unsaturated δ-hydroxyacids. These results represent the first examples of the use of transition-metal complexes in catalytic-two-phase isomerization of vinyl epoxides. The key catalytic species is believed to be the cyanocarbonylnickel anion, participation of which has been proposed in the reaction mechanism.

O-Benzyl oxime ethers were obtained in modest yields by the exposure of benzylic bromides to nitric oxide, a palladium(0) or ruthenium complex as the catalyst, aqueous sodium hydroxide, benzene as the organic phase and a quarternary ammonium salt as phase transfer agent. This provides the first example of a catalytic reaction of halides which involves free or co-ordinated nitric oxide and is also a novel process in the area of a phase transfer catalysis utilizing nitric oxide as a reactant.

CHAPTER 1

Introduction

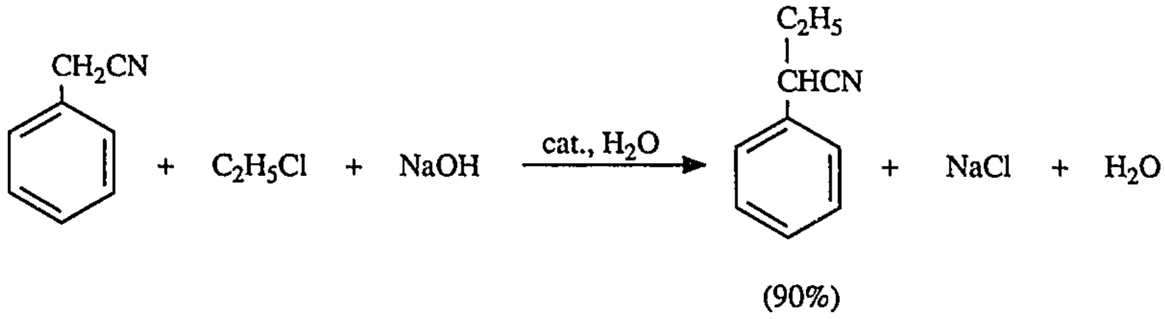
There is a broad range of organic reactions which could involve the use of ionic reagents and nonpolar substrates. In order that these reactions occur certain criteria for the reaction medium must be met, the most important of which seems to be solubility. The system should offer conditions which enable reacting species sufficient contact in order for reaction to occur at a reasonable rate. It is also important that the ionic reagents display high reactivity and good selectivity for the desired process. In addition, there is an expectation, especially when reactions are run on a large or industrial scale, that the products could be easily separated from the reaction medium. All those requirements are not easily fulfilled because they are often mutually exclusive.

Traditionally, high polarity solvents such as dimethyl sulfoxide or solvent mixtures are used in the hope of achieving solubility or at least partial solubility of the two reagents. This approach, however has limited applicability because ionic reagents could be very different from organic compounds in their solubility patterns. This method also does not meet other requirements which were specified above.

1.1 Principles of Phase Transfer Catalysis

Twenty-five years ago Mąkosza[1] described the concept of the use of a catalytic system consisting of two immiscible solvents. One of them was an aqueous solution of base and the other being an organic medium containing organic lipophilic compounds.

The following example is representative:



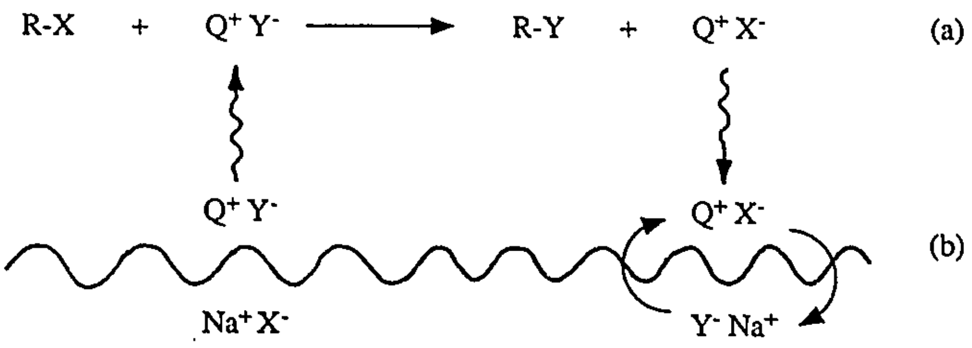
cat. = $PhCH_2(C_2H_5)_3N^+Cl^-$

This method resulted in the generation of the carbanion and its subsequent reaction with another organic substrate. What allowed these reactants to cross the barrier of insolubility, was the use of a catalyst acting as a carrier, which enabled ionic, in this case anionic, reagent residing at the interphase to reach the substrate in the organic phase. The catalyst employed was a quarternary ammonium salt. The main idea of the catalytic process was a continuous formation of lipophilic ion pairs of reacting anions (i.e., phenylacetonitrile carbanions) with lipophilic cations supplied by the catalyst (e.g., $PhCH_2(C_2H_5)_3N^+$, known as benzyltriethylammonium chloride or TEBACl). The anion, once in the organic phase, might react with an organic substrate, while liberated cation could enter another cycle. This technique was independently studied by Starks[2] and Brändström[3] with application to a broader range of anionic reagents including inorganic anions. The name of phase transfer catalysis (PTC) given by Starks[2b] has been commonly accepted and is now the most widely used term describing this phenomenon. It does not however reflect the true nature of the process involving carbanions, since they are generated at the phase boundary. This is the reason why Mąkosza to this day prefers to use the more general name of "catalytic two phase system" (CTP)[4].

From the early years of discovery a tremendous amount of development has occurred in the area of PTC. A great variety of phase transfer agents are available now with new ones being introduced constantly. Quarternary ammonium and phosphonium salts are the most popular, and one can choose from a variety based mostly on different lengths of alkyl substituents on the nitrogen or phosphorus atoms. The ionophores like crown ethers and cryptands or their acyclic analogs, poly(ethylene glycol)ethers and tris(polyoxaalkyl)amines[5], could be also used due to their tendency to complex or solvate inorganic cations. Thus generated, lipophilic cations perform similarly to the 'onium salts. Polysorbate 80[6] was recently reported to be equally effective in this area. In addition, poly(ethylene glycol)ethers, crown ethers and β-cyclodextrins have been found to act by forming inclusion complexes with organic molecules, rendering them soluble in the aqueous phase. This case is called reverse phase transfer catalysis[7]. A special category of phase transfer agents are alkylarenesulfonates and tetraarylboronates which have been applied in the acidic version of PTC[8].

Phase transfer catalysis can function in other heterogeneous two phase systems, the most important being a solid-liquid version. It involves anions in one phase (solid) and lipophilic substrates in another phase (liquid). The anions can be also generated at the interphase (e.g., surface of solid NaOH, KOH, K_2CO_3, etc.,). The most effective catalysts are again tetraalkylammonium salts or often crown ethers or cryptands with their ability to complex cations. This is a valuable method since it avoids the use of an aqueous medium thus allowing synthesis of products which would not be stable in the presence of an aqueous base. There are also reports on gas-liquid[9] and gas-solid[10] phase transfer catalysis. The liquid-liquid system is the most versatile - in particular the one involving inorganic anions, and it is the subject of this dissertation.

Initially there was a major controversy concerning the mechanism of phase transfer catalysis, especially after Starks reported his version based on the extraction principle[2b]. During two decades of mechanistic investigation it appeared evident that no general mechanism can be drawn. There are substantial differences among mechanisms of the PTC processes involving different reagents. It has been already stated that the interphase plays an important role in reactions with carbanion intermediates. The role of phase boundary is also believed to be crucial for reactions involving inorganic anions. Such processes can be exemplified by nucleophilic substitution which is shown in the Scheme 1 below.



Q^+ = quat cation

X^- = negatively charged leaving group

Y^- = reacting anion

Scheme 1

According to this scheme the observed rate of substitution can depend on two factors:

(*i*) rate of chemical reaction (a),

(*i i*) rate of ion exchange (b)

If the first process has the slowest rate, the reaction is believed to proceed according to the extraction mechanism. On the other hand if the ion exchange occurring at the phase boundary has a limiting rate, the terms of interfacial reaction[11] or diffusion controlled reaction[12] are used to differentiate it from the former case. The overall rate of the interfacial reaction depends on the speed of stirring and this criterion can be used as a verifying tool.

In parallel to mechanistic investigations there is a growing number of reports on practical applications of PTC methodology. Mostly, the reports come from the following areas:

(*i*) nucleophilic aliphatic and aromatic substitution involving organic and inorganic anions as well as addition reactions;

(*ii*) oxidation, reduction and elimination processes;

(*iii*) generation and reactions of carbenes;

(*iv*) organometallic chemistry including catalytic processes and syntheses of transition metal complexes

Literally thousands of specific examples can be found in numerous reviews[4,11,13] and monographs[14-17]. Areas (*iii*) and (*iv*) deal with species which could be very active electrophiles, reacting rapidly with water and OH^- anions. In spite of this, the typical liquid-liquid PTC system has been found to be very efficient for carbene generation[18] and for reactions in which organometallic compounds act as reactants or catalysts. The synthesis of many organometallic molecules can be also accomplished using PTC avoiding the use of strictly anhydrous conditions which require special glassware and experimental techniques. In fact, PTC conditions offer so many advantages for these processes that this method has gained widespread interest and resulted in numerous applications.

1.2 Application of Transition Metal Complexes under Phase Transfer Conditions

PTC was used for the first time in organometallic chemistry to synthesize trihalomethyl mercury[19] in a two phase CHX_3 / $(NaOH + KF)_{aq.}$ system.

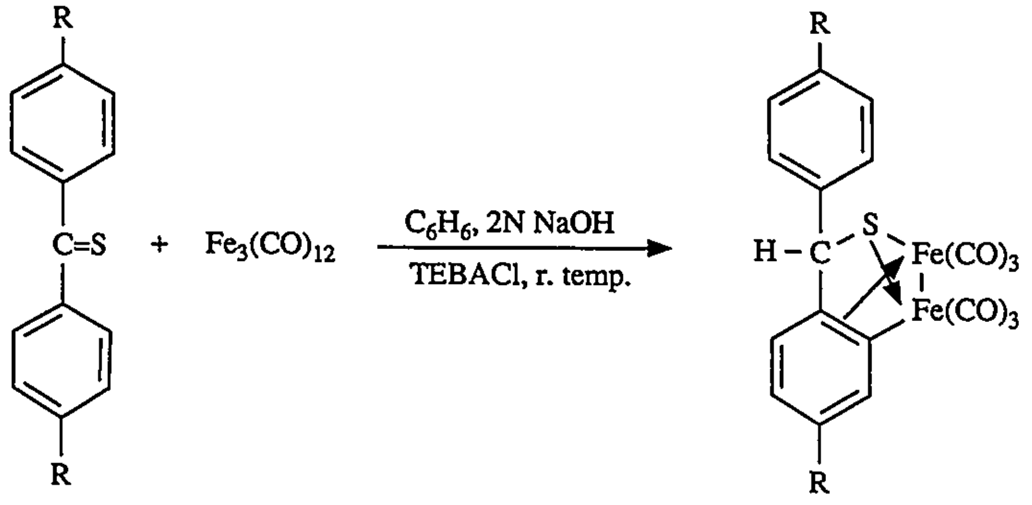
$$\mathrm{PhHgCl} \xrightarrow[\mathrm{TEBACl}]{\mathrm{CHX_3\ /\ NaOH,\ KF_{aq.}}} \mathrm{PhHgCX_3}$$

(59%)

X = Cl or Br

TEBACl = $PhCH_2N^+(C_2H_5)_3\ Cl^-$

The real breakthrough, however came after Alper[20] reported the first phase transfer and organotransition metal application, describing the ortho-metallation of thiobenzophenones in the reaction with $Fe_3(CO)_{12}$ in a two-phase benzene / 2N NaOH system.



(70%)

R = $N(CH_3)_2$, OCH_3, H, CH_3

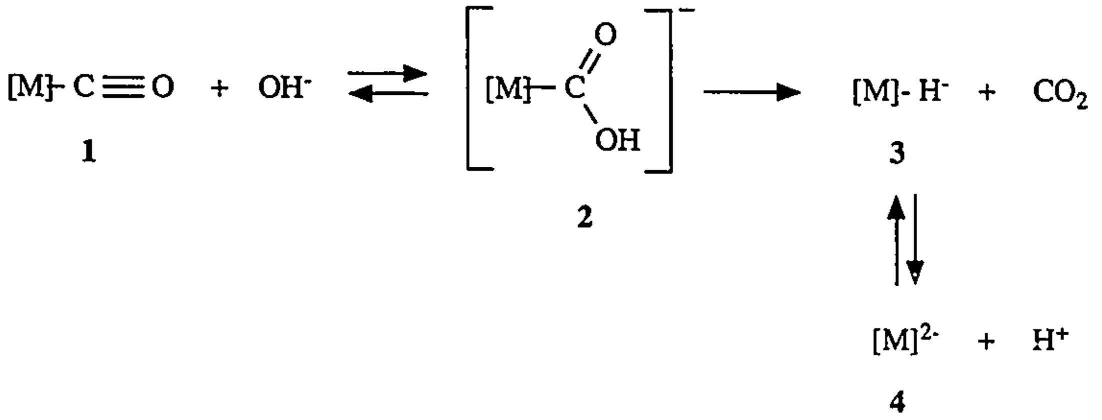
It was proposed that this reaction occurred through the transient production of anionic hydride $HFe_3(CO)_{11}^-$ by a phase transfer catalytic process, followed by nucleophilic attack of the ion pair $TEBA^+HFe_3(CO)_{11}^-$ on the thione group[20].

These first two processes are examples of the use of PTC technique in organometallic synthesis, and they are stoichiometric with respect to the metal reagent. As previously stated phase transfer reactions can be also used for transforming organic substances. In those cases stoichiometric processes remain economically feasible as long as the metal complexes are inexpensive. More attention is presently being directed toward developing PTC processes which can operate using catalytic quantities of often precious organometallic reagents.

The great interest in applications of PTC to transition metal chemistry has resulted in hundreds of publications and a few recent review papers[21-23].

1.2.1 Carbonylation Reactions

One of the most useful and most intensively investigated[24,25] applications of metal and phase transfer catalysis are carbonylation reactions. The success of carbonylation under PTC conditions is mainly due to the fact that metal carbonyl complexes **1**, which usually are the main participants in those reactions, can produce anionic metal carbonyls after being attacked by the hydroxide ions. Phase transfer agents facilitate this process:



Scheme 2

The hydroxycarbonyl complex **2** thus formed is generally unstable and readily decomposes to the metal hydride which in the protic medium can equilibrate with the corresponding anion. Anionic reagent **3** or **4**, with the help of cationic carriers, can interact with appropriate substrates and ensuing CO insertion leads to the carbonylation product. In the case of the former hydrido species, reduction reactions may occur which will be discussed in section 1.2.3. Other reasons which make the use of PTC carbonylation attractive include the exceptionally mild conditions of this process and simplicity in both execution and work-up as compared to many homogeneously catalyzed carbonylation reactions[26].

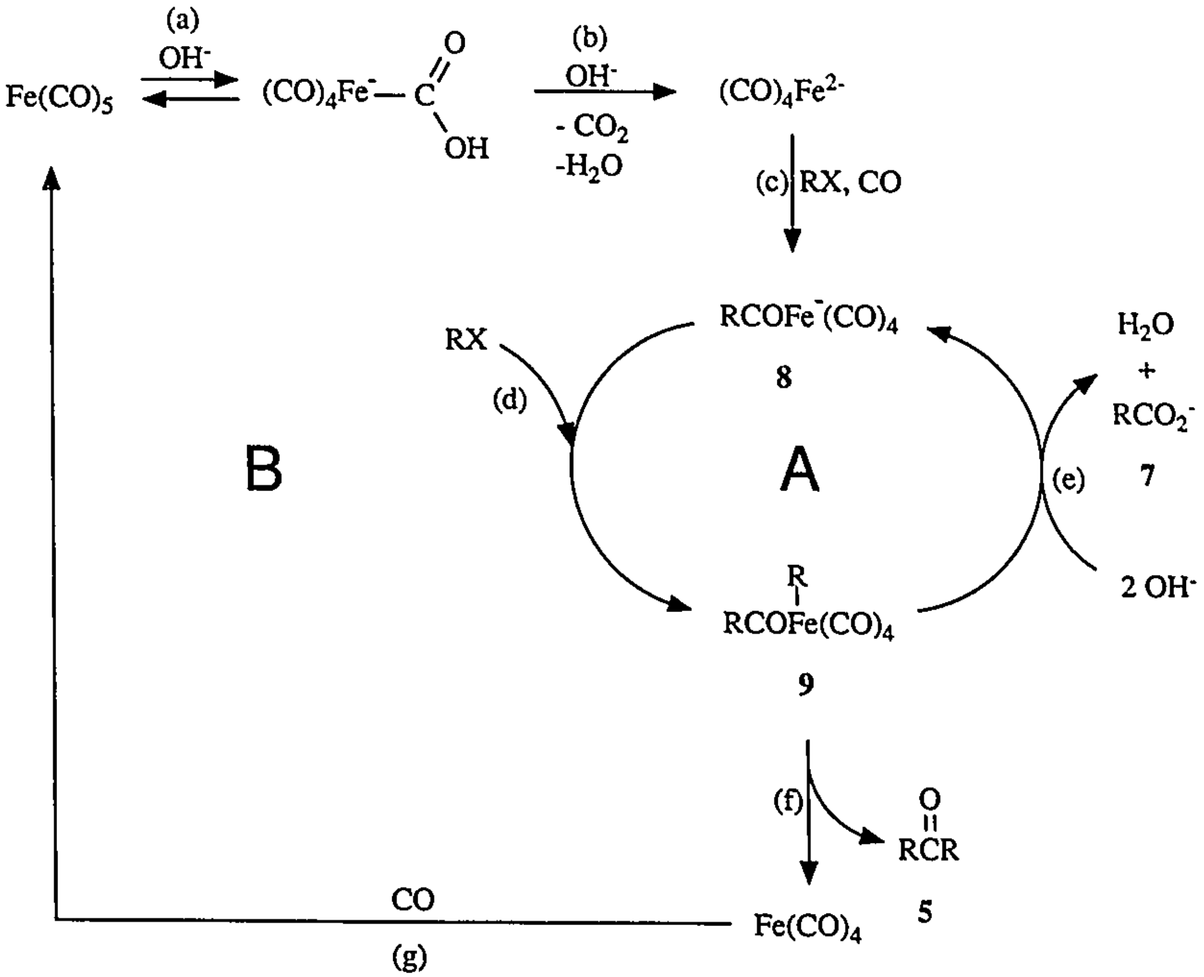
1.2.1.1 Carbonylation of Halides

The first communications on the carbonylation of halides were reported in 1977[27]. Cobalt carbonyl was used as a catalyst and it appeared to be one of the most valuable reagents for such processes[21].

Recently, elegant work of des Abbayes[28] was published concerning similar reactivity of pentacarbonyliron. It was found that benzyl halides could be converted to ketones **5** or acids **6** giving a varying ratio of products depending on the reaction conditions.

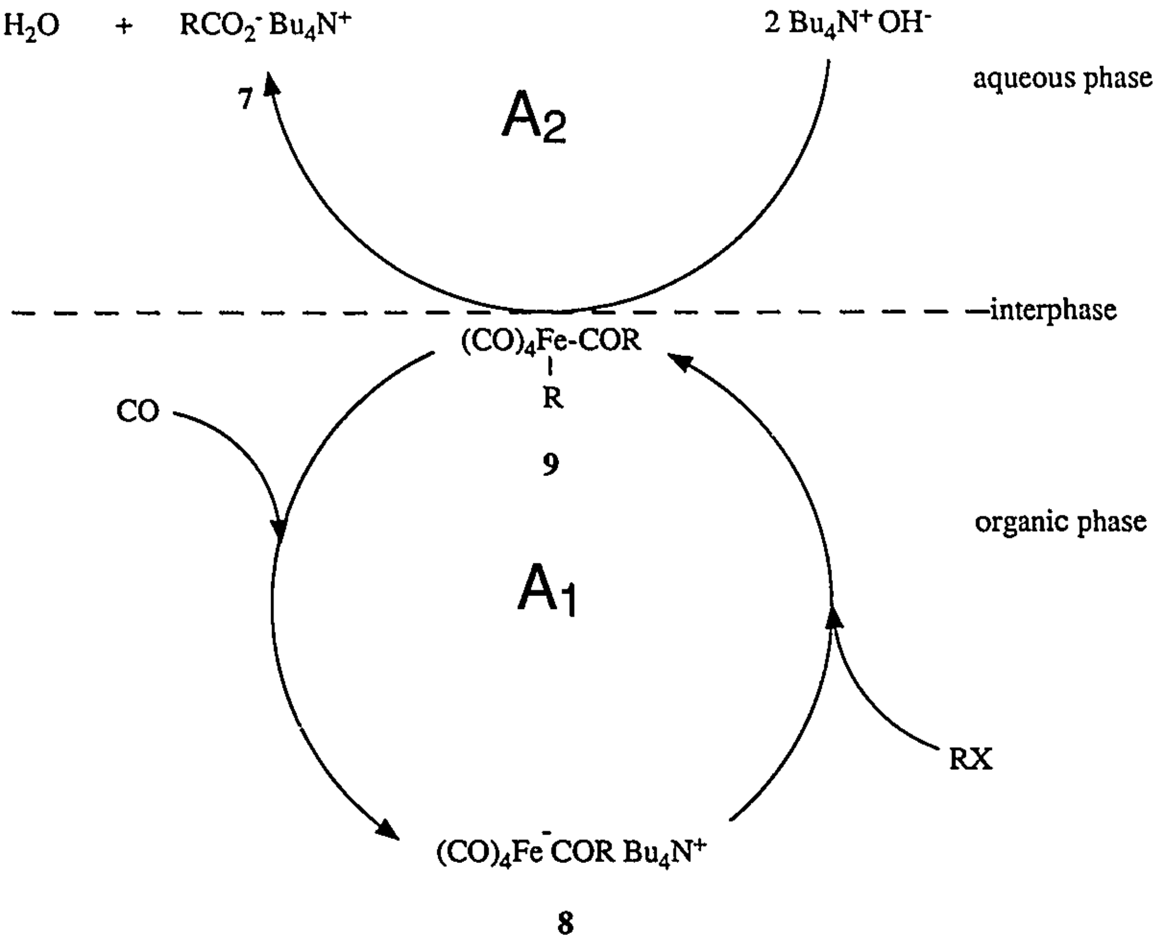
$$\mathrm{RX} \xrightarrow[(\mathrm{Bu_4N^+})_2\mathrm{SO_4}^{2-},\ \mathrm{CO}]{\mathrm{Fe(CO)_5,\ CH_2Cl_2,\ H_2O,\ OH^-}} \underset{\mathbf{5}}{\mathrm{RCOR}} + \underset{\mathbf{6}}{\mathrm{RCO_2H}}$$

The following mechanism involving two catalytic cycles has been proposed:



Scheme 3

The role of the quat (Bu_4N^+) was limited to the interfacial activity of the hydroxide anions[29], e.g., steps a, b and e, and formation of an ion pair $RCOFe(CO)_4^-Bu_4N^+$ rendering the catalyst **8** soluble in the organic phase. The ketone **5** was generated via cycle **B**, whereas the carboxylate **7** of the acid **6** was believed to result from inner cycle **A**. Formation of carboxylate was strongly affected by any factor that increased the base catalyzed cleavage of the intermediate **9** (an increase in stirring speed, aqueous concentration of the hydroxide ion or the amount of the cationic carrier). Scheme 4 illustrates the two parts of the catalytic cycle A leading to phenylacetate anion (7) in the two phase system.



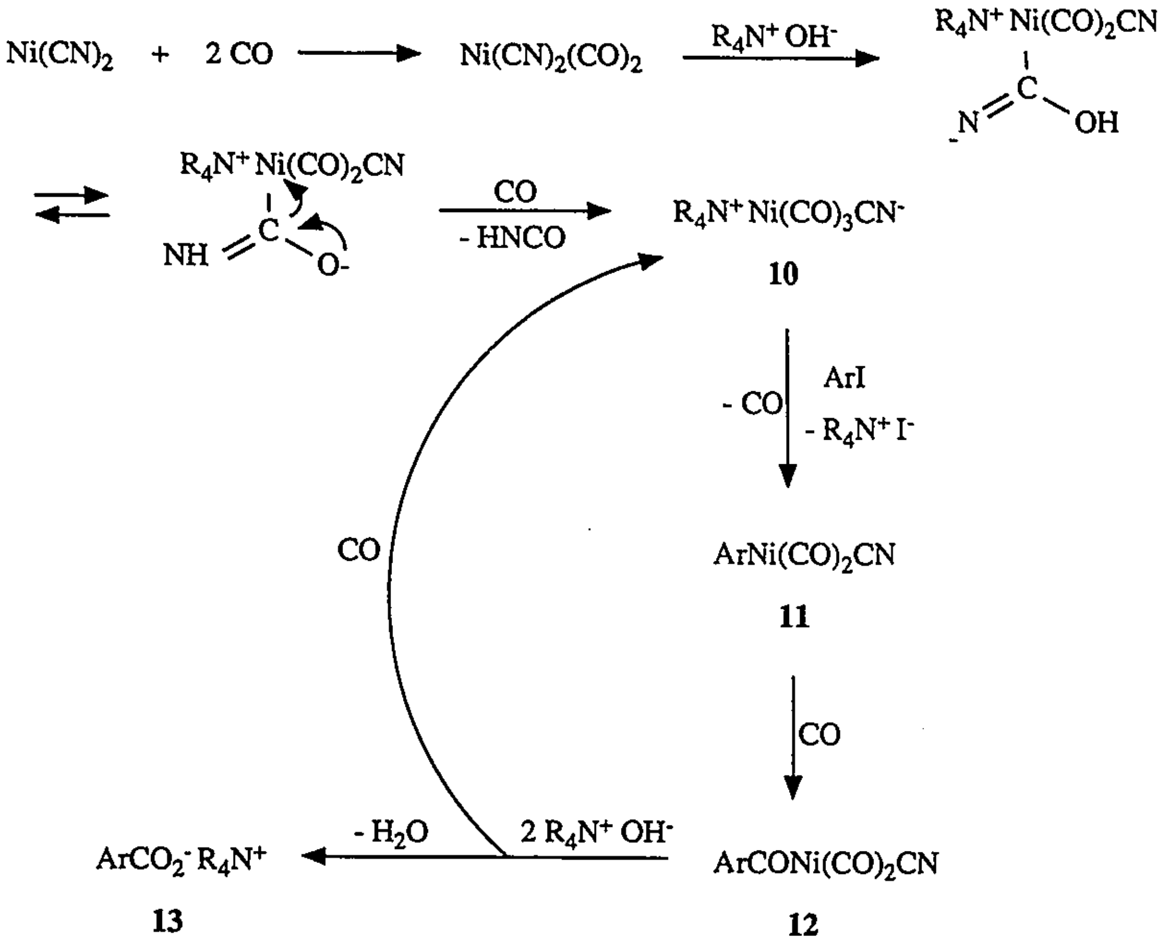
Scheme 4

Unlike benzyl halides, vinyl and aromatic derivatives are much more difficult to carbonylate. It is known that some palladium complexes are effective in carbonylation of vinyl bromides[30], as well as the cobalt carbonyl under UV irradiation for the same process involving aryl halides[31]. Recent developments in this area are summarized below.

In 1988 Alper published results on nickel cyanide and phase transfer catalyzed carbonylation of aryl iodides in the absence of light[32]. Treatment of aryl iodides with carbon monoxide, sodium hydroxide (5N), and toluene as the organic phase, cetyltrimethylammonium bromide as the phase-transfer catalyst, and nickel cyanide as the metal complex, afforded benzoic acid derivatives in 46 to 100% yields.

$$\mathrm{ArI} \quad + \quad \mathrm{CO} \quad \xrightarrow[\mathrm{PhCH_3,\ C_{16}H_{33}N(CH_3)_3^+\,Br^-}]{\mathrm{Ni(CN)_2{\bullet}4H_2O,\ 5N\ NaOH}} \quad \underset{(46 - 100\%)}{\mathrm{ArCO_2H}}$$

Bromo and chloro derivatives did not react under the described reaction conditions. It is believed that the carbonylation process (Scheme 5) was catalyzed by the *in situ* generated cyanotricarbonylnickelate ion (**10**)[33].



Scheme 5

It was suggested that the (σ-aryl)nickel complex **11** arises by a single electron transfer process involving aryl iodide and **10** with intermediate formation of a radical pair within a solvent cage (i.e., $S_{RN}1$ reaction[34]). Carbonylation of **11** (to the acylmetal complex **12**), followed by carbon-nickel bond cleavage by base, gave the acid anion **13**.

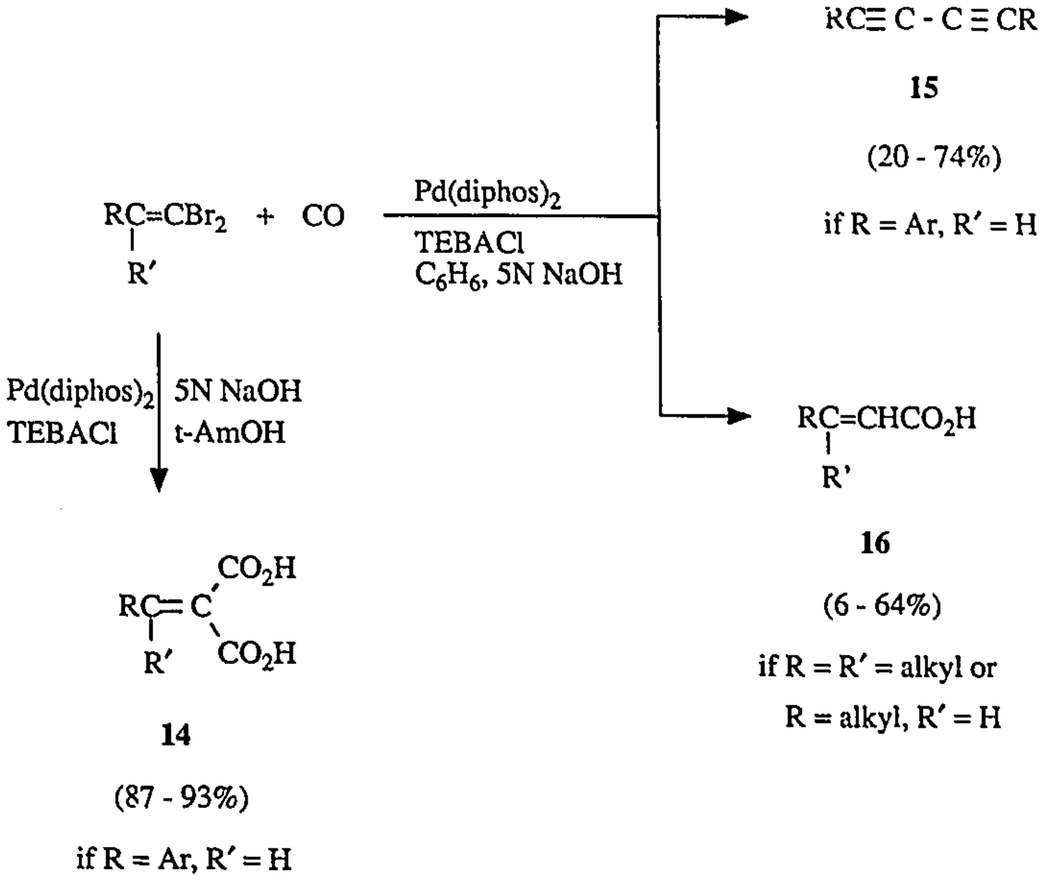
In 1989 bimetallic carbonylation of aryl iodides was reported by Brunet et al[35]. The authors in their communication stated that carbonylation of iodobenzene to benzoic acid could be performed under mild conditions (60^{0}C, 1atm. of CO) with a bimetallic $Fe(CO)_5/Co(CO)_8$ catalyst system (Scheme 6).

$$C_6H_5I \xrightarrow[\substack{Bu_4N^+\,Br^-,\ CO,\ 60\ ^0C,\ 1\ atm. \\ 2)\ H_3O^+}]{1)\ Fe(CO)_5\ /\ Co_2(CO)_8,\ NaOH_{aq.}\ /\ C_6H_6\ /\ EtOH} \underset{(65\%)}{C_6H_5CO_2H}$$

Scheme 6

The presence of iron and cobalt carbonyls, as well as the phase transfer agent were essential in order to achieve high yields of benzoic acid. Interestingly, the carbonylation of bromobenzene (which on its own was unreactive under the above reaction conditions) could be brought about in the presence of iodobenzene, with the conversion reaching 40%. Although a mechanism was not proposed at this stage, the authors speculated that perhaps a binuclear species $FeCo(CO)_8^-$ was involved in the transformations observed.

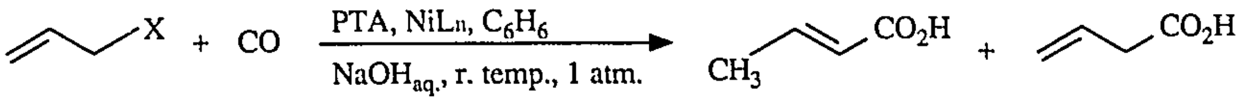
Interesting results were obtained in the area of PTC carbonylation of vinyl halides. In an extension of earlier work on palladium and phase transfer mediated CO insertion using vinyl bromides[30], Alper and co-workers[36] applied a similar system to vinylic dibromides.



Scheme 7

Scheme 7 shows how the nature of the substrate or solvent affects the scope of the reaction. While vinylic dibromides derived from aromatic aldehydes were carbonylated to unsaturated diacids **14** using tert-amyl alcohol as the organic phase, diynes **15** were formed when the same process was effected using less polar benzene as the organic solvent. In the case of substrates bearing aliphatic substituents (R and/or R′= alkyl), only products of monocarbonylation **16** were found.

The carbonylation of allyl halides can be catalyzed by nickel complexes[33,37] giving isomeric mixtures of butenoic acids (i.e., **17** and **18**).



17 **18**

a)[37] Ln = $(CO)_4$, X = Cl, PTA = Aliquat 336 (85%, **17**/**18** = 3:2),

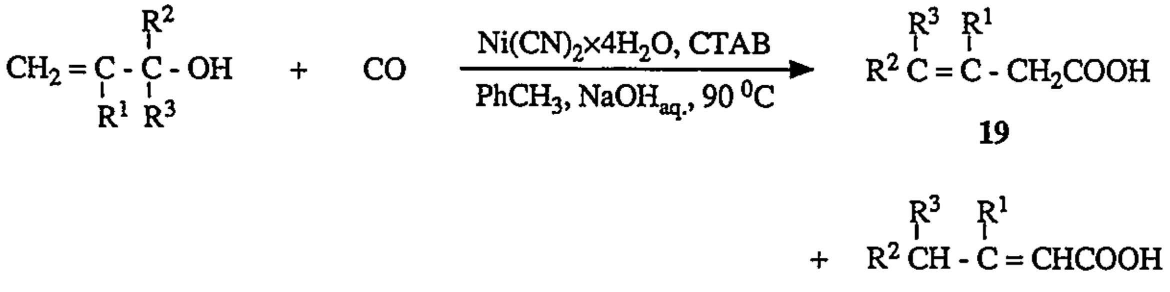
b)[33] Ln = $(CN)_2\times 4H_2O$, X = Cl, PTA = TBAHS (98%, **17**/**18** = 4:1),

c)[33] Ln = $(CN)_2\times 4H_2O$, X = Br, PTA = TBAHS (88%, **17**/**18** = 6:1)

There is evidence for the intermediacy of polynuclear nickelates $[Ni_5(CO)_{12}]^{2-}$ and $[Ni_6(CO)_{12}]^{2-}$ occurring in the first phase transfer process (a), while $Ni(CO)_3CN^-$ has been isolated as the active species in the second instance [(b) and (c)]. An advantage of this method over the former one is that it does not require the use of extremely toxic nickel tetracarbonyl.

1.2.1.2 Carbonylation of Allyl Alcohols

Recently, the direct carbonylation of allyl alcohols to acids[38] has been realized using nickel cyanide under phase transfer conditions.



$$CH_2=\underset{R^1}{C}-\overset{R^2}{\underset{R^3}{C}}-OH \quad + \quad CO \xrightarrow[PhCH_3,\ NaOH_{aq.},\ 90\,^{0}C]{Ni(CN)_2\times 4H_2O,\ CTAB} R^2\,\overset{R^3}{C}=\overset{R^1}{C}-CH_2COOH \;(\mathbf{19}) \quad + \quad R^2\,\overset{R^3}{CH}-\overset{R^1}{C}=CHCOOH \;(\mathbf{20})$$

19

20

a) $R^1 = R^2 = R^3 = H$,

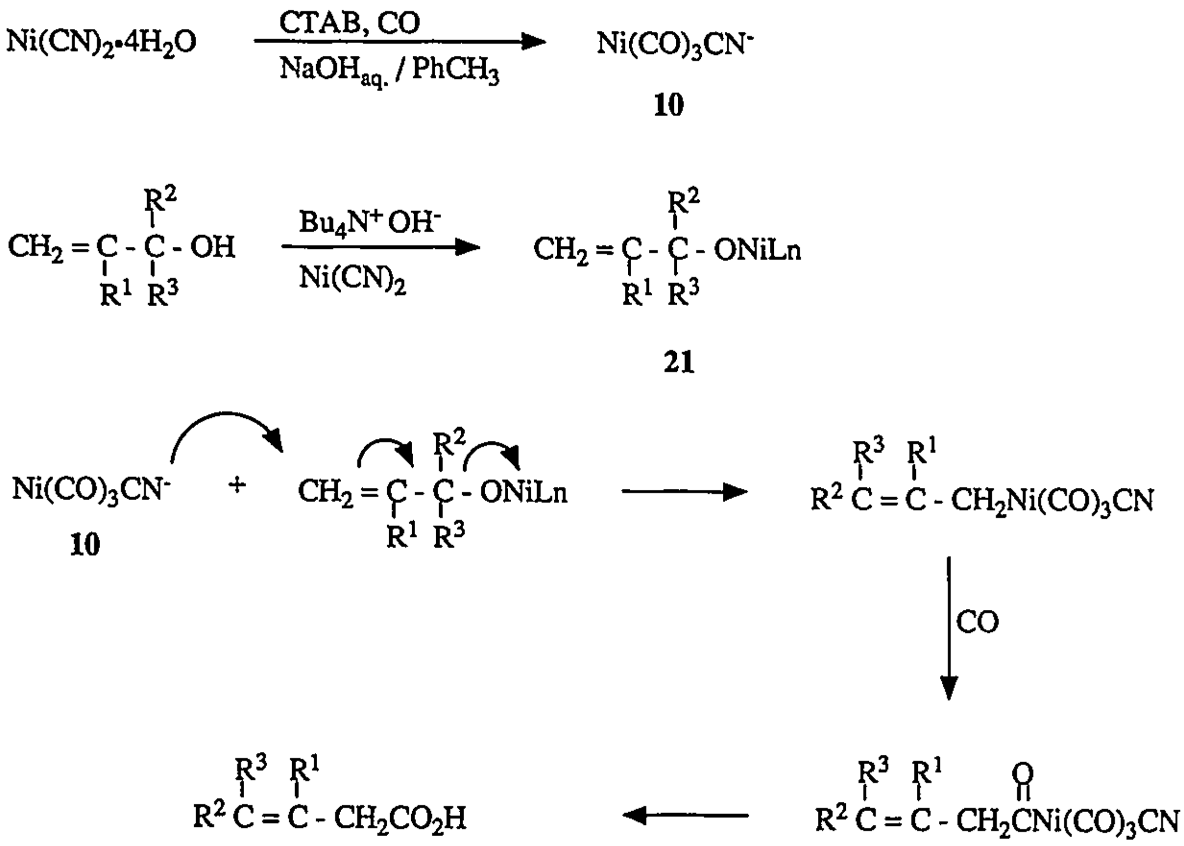
b) $R^1 = CH_3, R^2 = R^3 = H$,

c) $R^1 = R^2 = H$, $R^3 = C_2H_5$,

d) $R^1 = H$, $R^2 = R^3 = CH_3$,

e) $R^1 = H$, $R^2 = CH_3$, $R^3 = C_2H_5$

While allyl alcohol (a) gave pure crotonic acid (**20**, $R^1 = R^2 = R^3 = H$) in 68% yield, the other substrates including secondary (c) and tertiary (d, e) alcohols afforded a mixture of isomeric carboxylic acids **19** and **20**. The ratio of **19** to **20** was found to be sensitive to base concentration with more of the conjugated product **20** observed at higher base strength. The role of the base was not only to promote double bond isomerization, but it also influenced the generation of the catalytically active species $[Ni(CO)_3CN^-]$[33], and the deprotonation of the alcohol. Scheme 8 outlines a possible mechanism.



Scheme 8

Two roles have been proposed for nickel cyanide in this reaction:

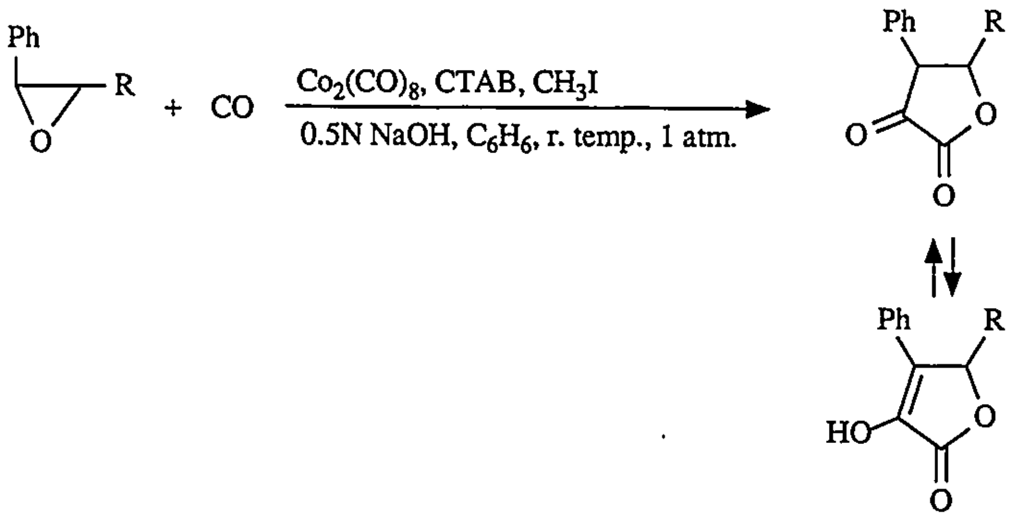
(*i*) conversion to $Ni(CO)_3CN^-$,

(*ii*) deprotonation of the alcohol by base followed by reaction with $Ni(CN)_2$ to give **21**

The described example is the only report so far claiming the successful use of PTC in transition metal catalyzed carbonylation of allyl alcohols.

1.2.1.3 Carbonylation of Epoxides

Attempted cobalt and PTC carbonylation of the styrene oxides resulted in the successive incorporation of two molecules of carbon monoxide leading to the α-keto lactone (or its enol tautomer **22**) product[39].

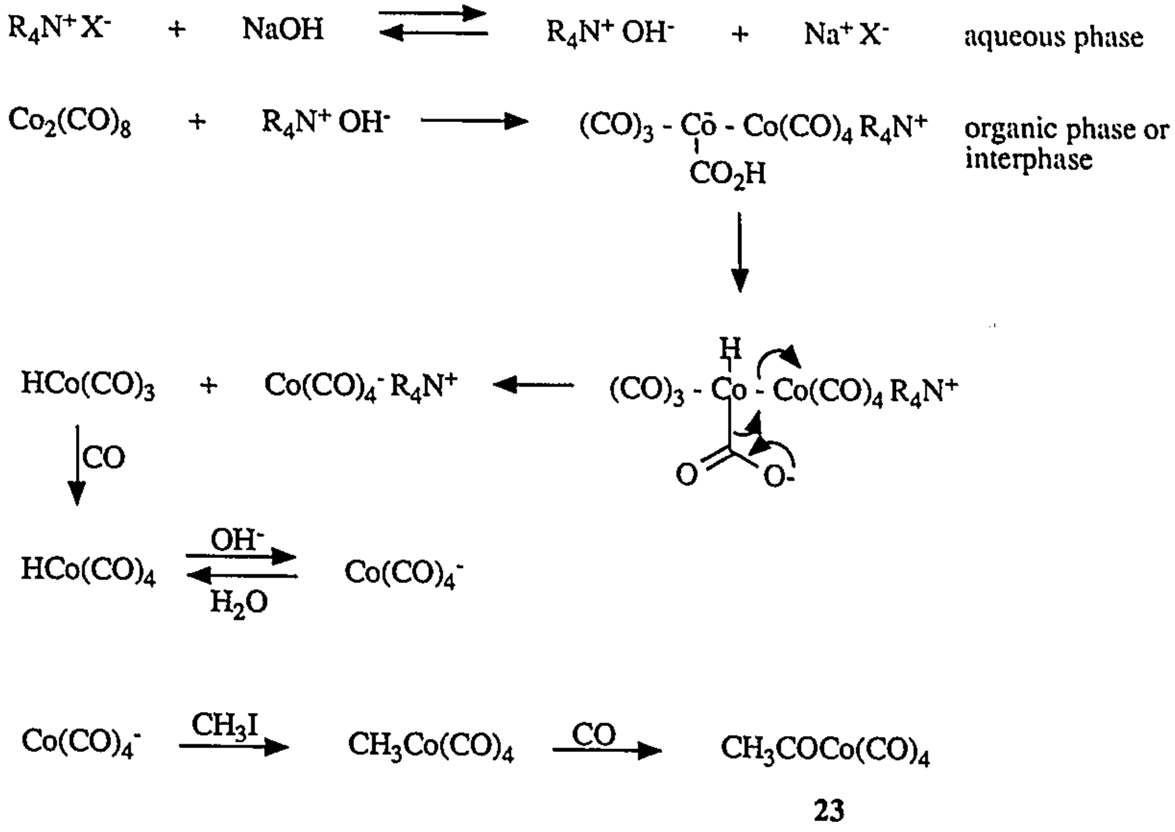


22

(34 - 65%)

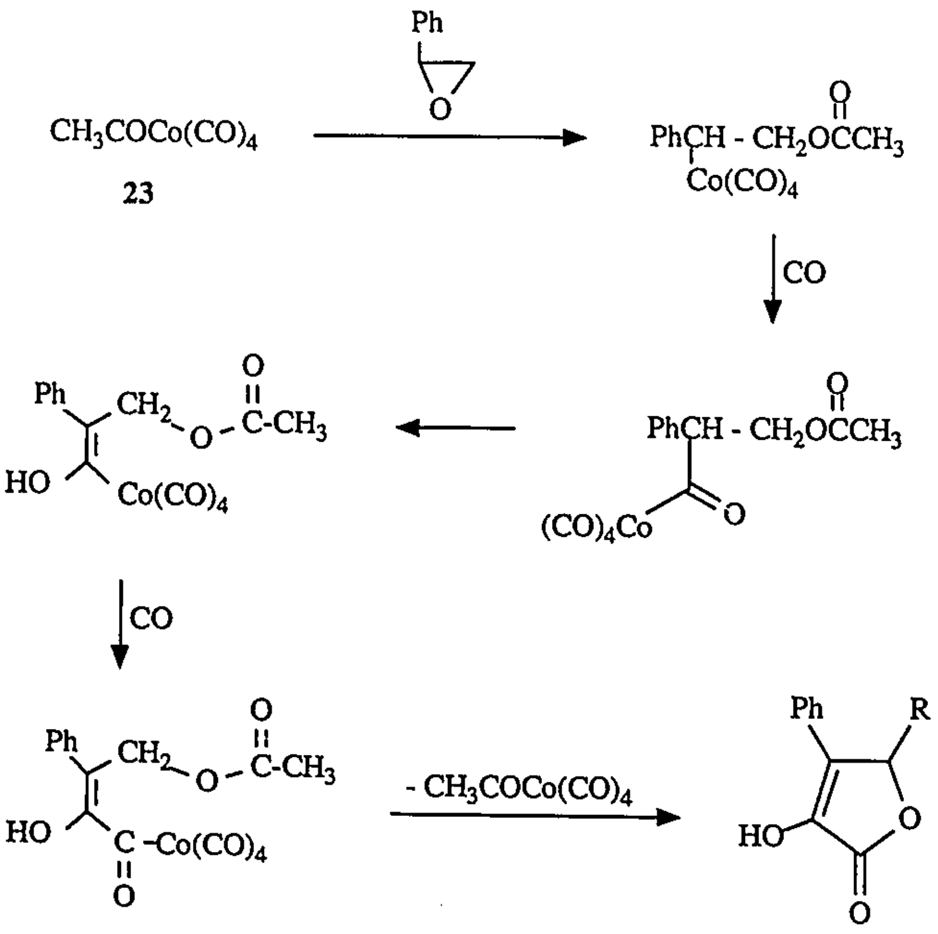
R = H, CH_3

It is believed that the key intermediate in this rare example of the double carbonylation reaction is an acylcobalt tetracarbonyl complex $CH_3COCo(CO)_4$ (**23**) the generation[21] of which is outlined in Scheme 9.



Scheme 9

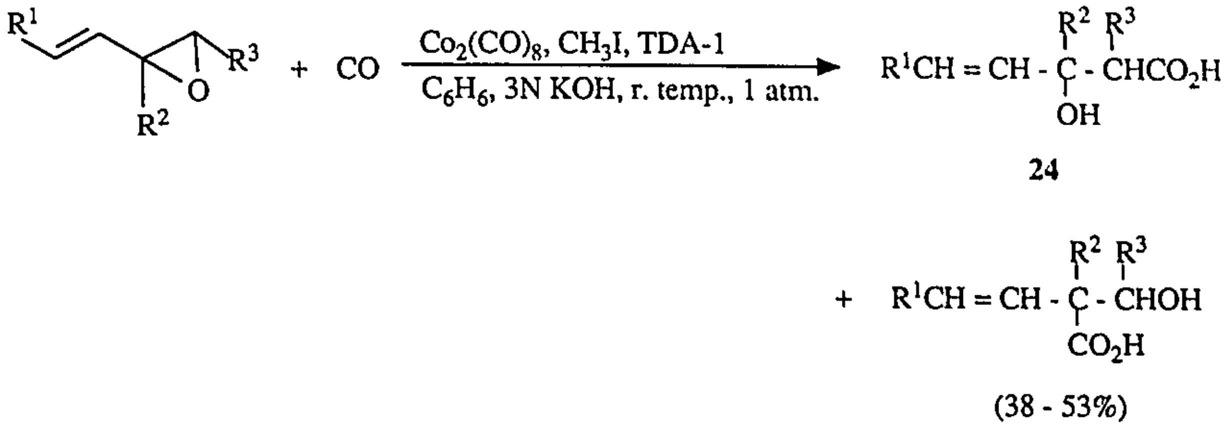
The *in situ* generated catalyst **23** adds to the epoxide and then sequential carbonylation ultimately leads to **22** (R = H) (Scheme 10).



Scheme 10

The PTC agent not only plays a role in the formation of the acylcobalt tetracarbonyl (**23**), but it promotes enolization as well.

Under the same reaction conditions vinyl epoxides experienced monocarbonylation to give hydroxy acids[40]. The best yields were obtained using TDA-1 as the phase transfer agent.



$$\mathrm{CO} \xrightarrow[\mathrm{C_6H_6,\ 3N\ KOH,\ r.\ temp.,\ 1\ atm.}]{\mathrm{Co_2(CO)_8,\ CH_3I,\ TDA\text{-}1}} R^1CH=CH-\overset{R^2}{\underset{OH}{C}}-\overset{R^3}{C}HCO_2H$$

24

$$+\ R^1CH=CH-\overset{R^2}{\underset{CO_2H}{C}}-\overset{R^3}{C}HOH$$

(38 - 53%)

TDA-1 = tris(dioxa-3,6-heptyl)amine

a) R^1-R^3 = $-(CH_2)_2-$, R^2 = H

b) R^1 = H, R^2-R^3 = $-(CH_2)_4-$,

c) R^1 = R^3 = H, R^2 = CH_3,

d) R^1 = R^2 = R^3 = H

High regioselectivity was observed for the β,γ-unsaturated acid **24**.

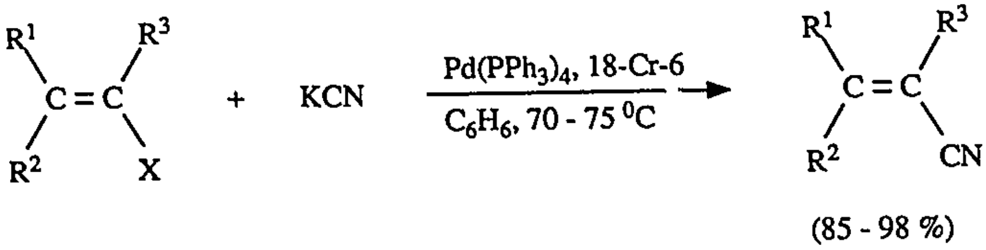
1.2.2 Nucleophilic Substitution Reactions

Phase transfer catalyzed nucleophilic substitution reactions, so common and useful in organic synthesis, have also found some important applications in organometallic chemistry. Two interesting cases exist in this field:

(*i*) nucleophilic attack on species containing an organometallic group,

(*ii*) the reverse situation where the presence of a transition metal moiety facilitates nucleophile formation enabling subsequent reactions to occur with organic substrates

In the first group both nickel catalyzed aromatic[41] and palladium mediated vinylic[42] substitutions of halogen with cyanide anions are known. The latter process was the first reported example of this kind.



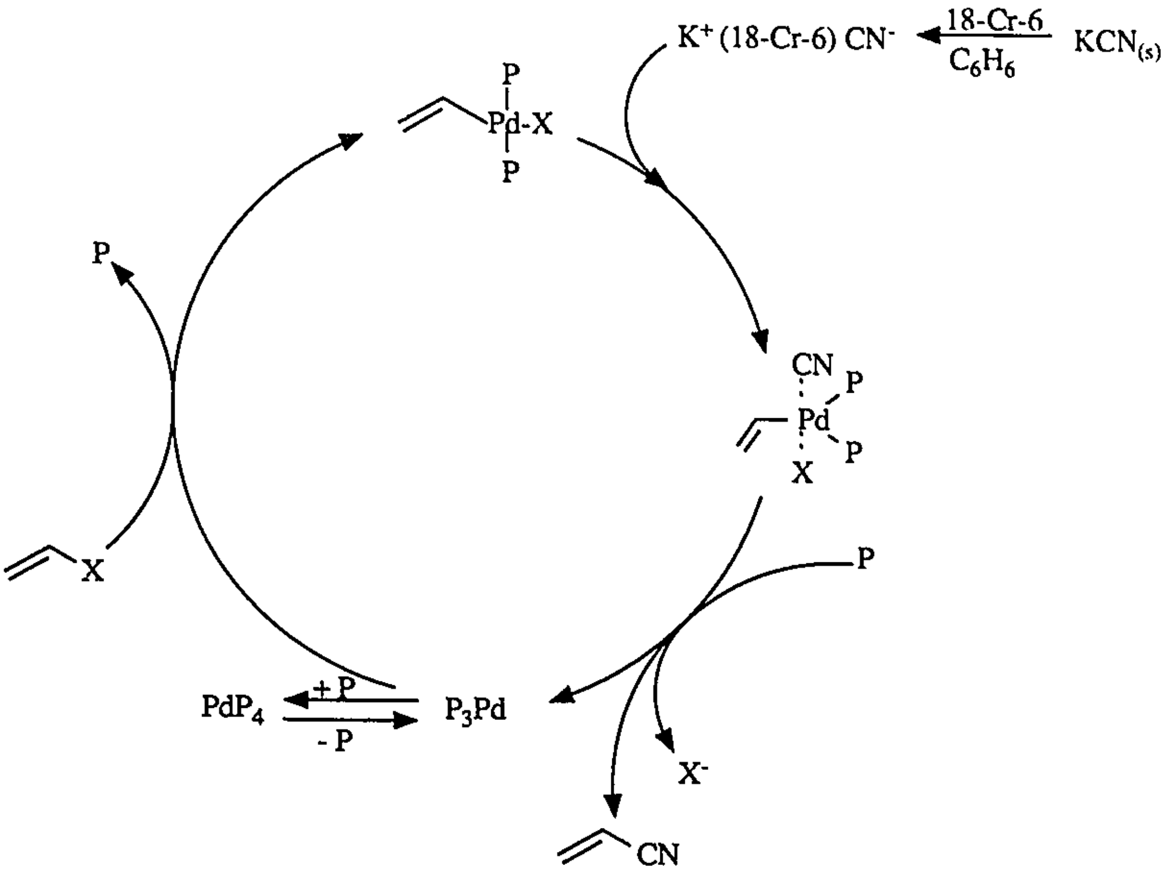
R^1 = H, Ph, Bu,

R^2 = H, Ph, CH_3,

R^3 = H, Ph,

X = Br, Cl

High isomeric purity (up to 99%) was observed. This solid-liquid system may operate according to the Scheme 11.

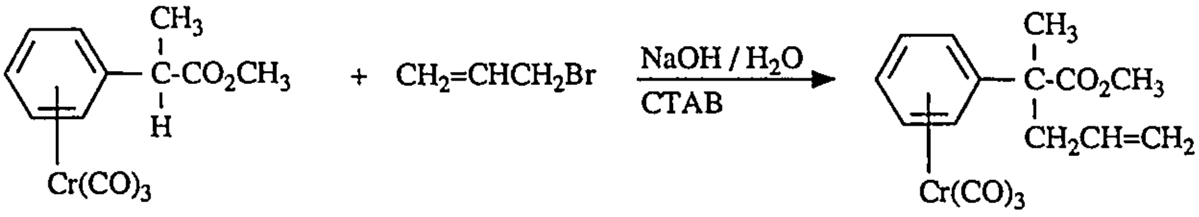


$P = PPh_3$

Scheme 11

The role of a crown ether may be to dissolve otherwise insoluble KCN in the organic solvent.

In the second case the use of chromium and iron carbonyls as complexing agents toward alkenes or arenes resulted in a dramatic change of their behavior in basic media[43,44]. For example, methyl phenylpropionate, as a chromium tricarbonyl complex **25**, was efficiently alkylated in the typical PTC system, alkylation being faster than ester hydrolysis[43].



25

The presence of a transition metal moiety could enhance the acidity of a **C-H** bond thereby facilitating carbanion formation.

1.2.3 Reduction Reactions

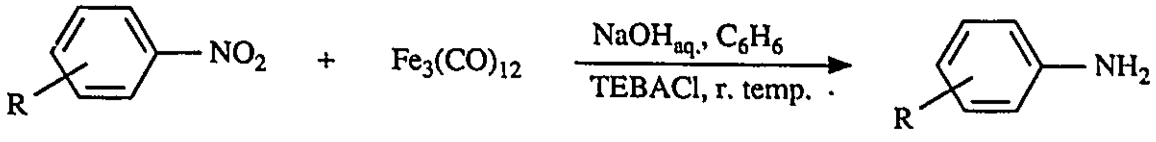
Second to carbonylation in terms of the quantity of published work is the area of reduction using metal complexes under phase transfer conditions.

Transition metal hydrides are the species usually assumed to be responsible for reduction processes. The hydride is normally generated *in situ* and, as a result, it is not very well characterized. In some cases reduction results could be repeated using well known hydrides and performing the same reaction under homogeneous conditions. This may provide insight on the initial, presumed generation of a reducing agent but the subsequent steps are often not very well understood.

As noted previously, metal hydrides could be generated by OH^- attack on a carbonyl ligand. This implies that carbon monoxide or inert nitrogen are often used as a gaseous atmosphere for reduction processes. Hydrogenation reactions which are based on the use of PTC and transition metal complexes under hydrogen gas will be included in this section as well, since they also are believed to involve active hydride species.

1.2.3.1 Reduction of Nitro Compounds

Reduction of nitroarenes to anilines were among the first examples of organometallic phase transfer processes. In 1977 Alper reported the stoichiometric reaction involving triiron dodecacarbonyl[45].



(60 - 92%)

R = p-CH_3, p-OCH_3, p-Cl, p-$COCH_3$

Two years later, in support of the hypothesis that $HFe_3(CO)_{11}^-$ was a key reagent in this process, almost identical results were obtained applying pre-synthesized $Et_4N^+HFe_3(CO)_{11}^-$ under homogeneous conditions[46].

A bimetallic system can also effect the catalytic reduction of nitro compounds[47].

$$ArNO_2 \quad + \quad CO \quad \xrightarrow[C_6H_6,\ C_{12}H_{25}N(CH_3)_3^+\,Cl^-,\ \text{r. temp., 1 atm.}]{Co_2(CO)_8\ /\ [1,5\text{-HDRhCl}]_2,\ 5N\ NaOH} \quad ArNH_2$$

(43 -98%)

$[1,5\text{-HDRhCl}]_2$ = chloro(1,5-hexadiene)rhodium(I) dimer

Ar = Ph, $CH_3C_6H_4$, p-ClC_6H_4, p-$PhC(O)C_6H_4$, 1-Naphthyl, p-$PhCH_2C_6H_4$

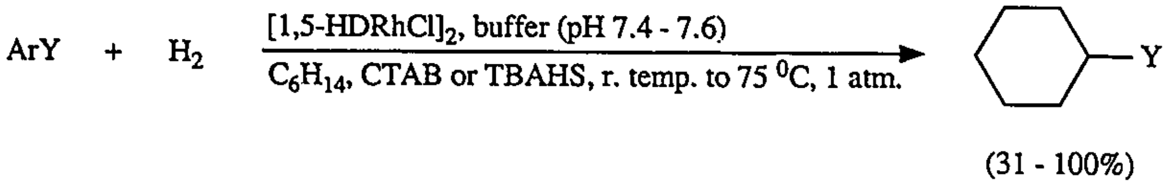
Although neither cobalt nor rhodium complexes produced aromatic amine when applied alone, the use of both catalysts and phase transfer conditions brought about formation of amines in good yields. A kinetic investigation[47b] revealed that the rhodium complex catalyzes the nitro reduction, but the presence of a phase transfer agent inhibits this reaction.

Addition of a second metal catalyst (cobalt carbonyl), reactivates the active species.

None of the reports gave full details concerning the mechanistic picture of those reduction processes, which are complex and seem to involve electron transfer pathways[24,48].

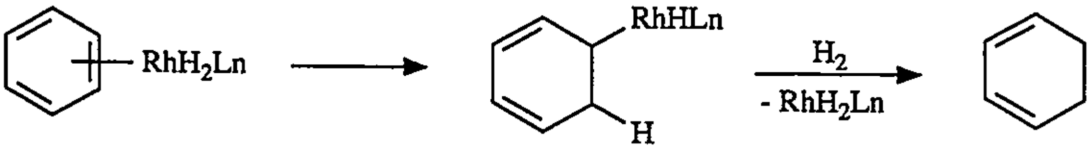
1.2.3.2 Reduction of Carbon-Carbon Double Bonds

Few reports on the application of PTC to the reduction of activated carbon-carbon double bonds (like those of α,β-unsaturated carbonyl compounds[49] or activated dienes[50]) have been described until quite recently. Alper and Januszkiewicz[51] reported the use of $[1,5\text{-HDRhCl}]_2$ for the efficient reduction not only of isolated carbon-carbon double bonds, but also of dienes and most importantly of aromatic rings.



Y = -OR, -OCOR, -COR, -COOR, $-CONH_2$

In general, good selectivity was observed for the above reactions, since functional groups as ethers, esters, amides or ketones remained unaffected. It has been proposed that reduction of arenes is a stepwise process involving an η^2-arene(hydrido)rhodium complex.



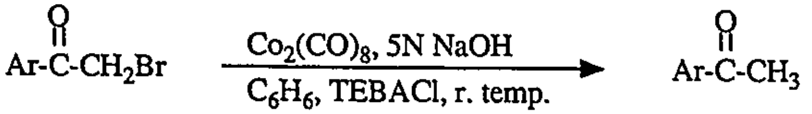
Double repetition of the above sequence would lead to the final saturated hydrocarbon (i.e., cyclohexane).

Similar results were published by Blum and co-workers[52] also using rhodium and PTC ($RhCl_3 \times 3H_2O$ / Aliquat 336).

Both rhodium based catalytic systems were later applied to the selective hydrogenation of α,β-unsaturated carbonyl compounds[53,54].

1.2.3.3 Reductive Dehalogenation

Alkyl and aryl bromides are known to undergo debromination by the use of metal complexes in a catalytic two phase system. In 1977, it was found that *in situ* generated cobalt tetracarbonyl anion promotes the debromination of α-bromoketones **26** to the corresponding ketones[55].



$$\text{Ar-}\overset{\displaystyle O}{\overset{\|}{C}}\text{-CH}_2\text{Br} \xrightarrow[C_6H_6,\ \text{TEBACl, r. temp.}]{Co_2(CO)_8,\ \text{5N NaOH}} \text{Ar-}\overset{\displaystyle O}{\overset{\|}{C}}\text{-CH}_3$$

26

(58 - 66%)

Ar = 1-Adamantyl, p-PhC_6H_4, 2-Naphthyl

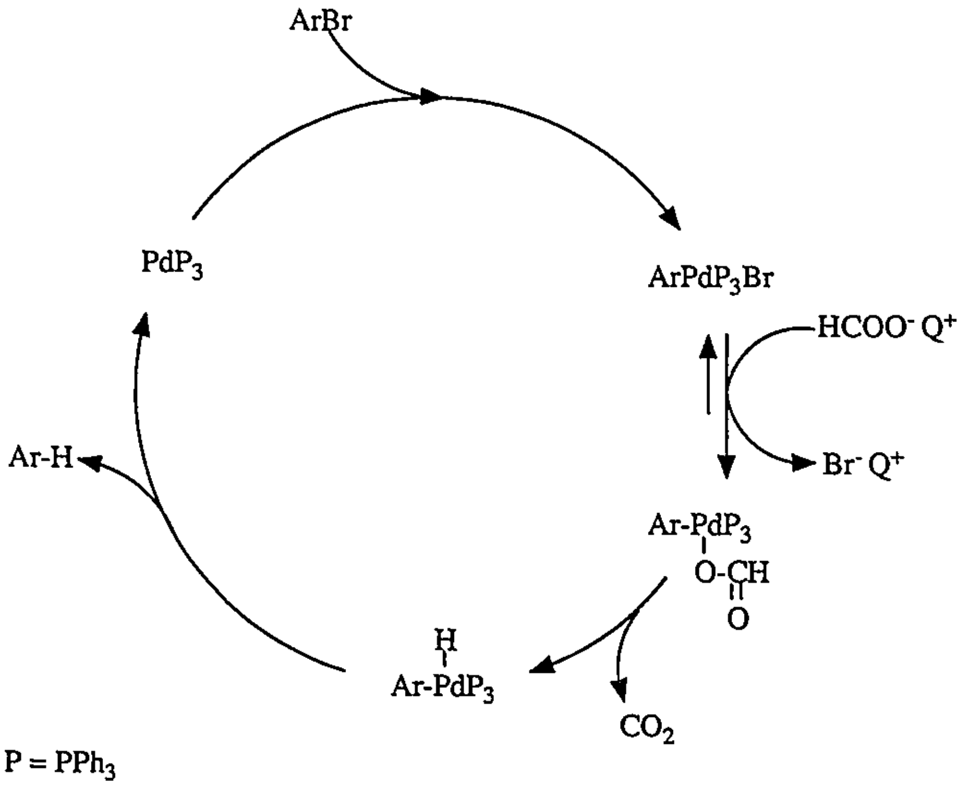
More recently Blum[56] demonstrated the use of sodium formate and catalytic amounts of palladium triphenyl phosphine complexes for the debromination of bromoarenes.

$$\text{ArBr} \quad + \quad \text{HCOONa} \xrightarrow[\text{o-Xylene, } H_2O,\ 100\ ^0C]{PdCl_2(PPh_3)_2 \text{ or } Pd(PPh_3)_4,\ Q^+X^-} \text{Ar-H}$$

(10 - 53%)

Ar = Cl-C_6H_4, CHO-C_6H_4, C_6H_5, CH_3-C_6H_4

It has been observed that the yield of this process whose mechanism is outlined in Scheme 12 increases with increasing electron-donating ability of the substituents.



Scheme 12

It is noteworthy that in both dehalogenation reactions substitution of chloro for the bromo analogs resulted in a significant decrease of reaction rate.

1.2.3.4 Reductive Desulfurization

Benzylic mercaptans can be desulfurized in a stoichiometric reaction using triiron dodecacarbonyl under phase transfer conditions[57].

$$R^1R^2R^3CSH \quad + \quad Fe_3(CO)_{12} \xrightarrow[\text{TBAHS, 60 }^0\text{C}]{\text{5N NaOH, }C_6H_6} \underset{(58 - 95\%)}{R^1R^2R^3CH}$$

R^1 = Ph, $CH_3C_6H_4$, 2,4-Cl_2-C_6H_3, p-$CH_3OC_6H_4$,
R^2 = H, Ph, $CH_3C_6H_4$,
R^3 = H, Ph

Phase transfer conditions offer remarkable flexibility in this case, because desulfurization of the same mercaptans could be also conducted in an **acidic medium**[58].

$$R^1R^2R^3CSH \quad + \quad Fe_3(CO)_{12} \xrightarrow[\text{p-}C_{12}H_{25}C_6H_4SO_3Na\text{, 60 }^0\text{C, 1 atm.}]{\text{48 - 50\% }HBF_4\text{, }C_6H_6} R^1R^2R^3CH$$

The above process is apparently biphasic since higher yields were obtained when the reaction was conducted in the absence of the phase transfer agent:

a) R^1 = p-$CH_3OC_6H_4$, $R^2 = R^3$ = H (10%; 72%*),
b) R^1 = p-ClC_6H_4, $R^2 = R^3$ = H (60%; 44%*),
c) R^1 = 2,4-Cl_2-C_6H_3, $R^2 = R^3$ = H (73%; 74%*),
d) $R^1 = R^2$ = p-$CH_3C_6H_4$, R^3 = H (94%*),
e) $R^1 = R^2$ = Ph, R^3 = H (84%*)
* no PTA used

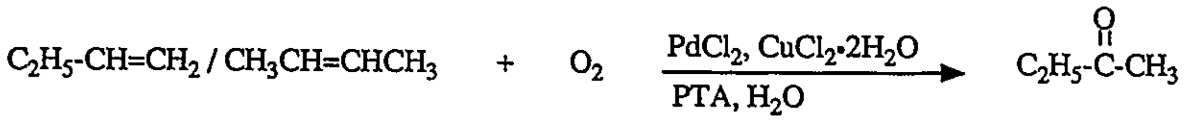
1.2.4 Oxidation Reactions

Until 1980 very little work had been done in PTC and transition metal oxidation of organic compounds[48a]. The only description relevant to this field was given in the patent literature by Starks[59] who studied olefin oxidation. During the period of last ten years significant developments have occurred in this area.

Many phase transfer catalyzed oxidation reactions are carried out in an atmosphere of molecular oxygen or using aqueous hydrogen peroxide as an oxidant.

1.2.4.1 Wacker-Type Oxidation of Olefins

Both terminal and internal olefins were oxidized to ketones when PEG-400[60] or β-cyclodextrin[61] were employed as phase transfer agents for the Wacker reaction[62]. For example isomeric butenes afforded butanone under mild conditions:



$$C_2H_5\text{-}CH{=}CH_2 \,/\, CH_3CH{=}CHCH_3 \quad + \quad O_2 \xrightarrow[\text{PTA, } H_2O]{PdCl_2,\ CuCl_2{\cdot}2H_2O} C_2H_5\text{-}\overset{\overset{O}{\|}}{C}\text{-}CH_3$$

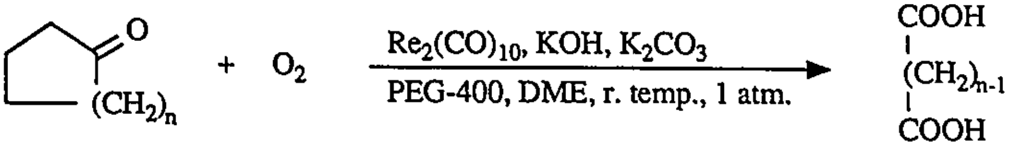
PTA = PEG-400 (71 - 82%)[62],

PTA = β-Cyclodextrin (68 - 76%)[63]

Isomerization of the starting olefin appeared to be a major obstacle in these reactions. As a result isomeric mixtures of ketones often accompanied the final product formation. Interestingly, this side reaction could be eliminated if one used tetraalkylammonium salt as a phase transfer agent having at least one long chain alkyl group (e.g., cetyltrimethylammonium bromide)[63]. In this case only terminal olefins are oxidized with significant suppression of isomerization. Although the regioselectivity was a remarkable achievement, the 48 hour reaction time was a major drawback in terms of potential commercial application.

1.2.4.2 Oxidation of Ketones

The conversion of cyclic ketones to diacids[64], like the Wacker reaction, is a process of great industrial value. When cyclic ketones were exposed to catalytic amounts of rhenium carbonyl, oxygen and solid-liquid PTC conditions, the dicarboxylic acids were obtained in good yields[65].

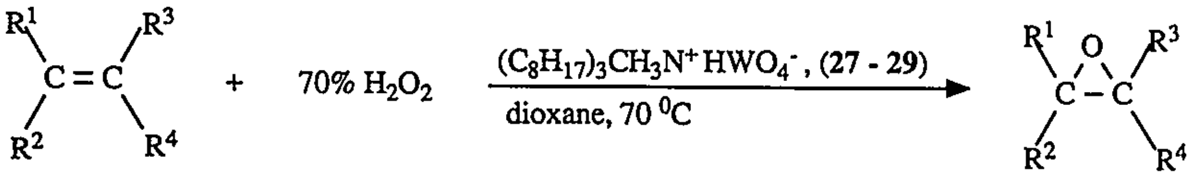


(36 - 86%)

n = 2-6

1.2.4.3 Other Oxidations

Simple, non-functional olefins can be epoxidized using hydrogen peroxide and lipophilic quarternary ammonium tungstate complexed by appropriate (**27**-**29**) lipophilic neutral or anionic phosphorus ligands[66].



$O=P(C_8H_{17})_3$ — **27**

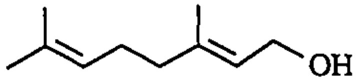
$Ph\text{-}PO_3H_2$ — **28**

$C_{12}H_{25}PO_3H_2$ — **29**

a) $R^1 = R^2 = H, R^3\text{-}R^4 = \text{-}(CH_2)_4\text{-}$ (100%),

b) $R^1 = R^2 = R^3 = H, R^4 = C_6H_{13}$ (70%),

c) $R^1 = R^2 = R^3 = H, R^4 = Ph$ (80%),

d)  (87%)

This highly efficient system was also found to be regioselective. In case of a geraniol (d) as a substrate a 9:1 ratio in favor of the 2,3-epoxide was observed, with no indication of diepoxidation.

Very recently Sasson[67] reported the effect of phase transfer catalysis on the oxidation of aniline.

$$PhNH_2 \quad + \quad 30\%\ H_2O_2 \quad \xrightarrow[\text{1,2-dichloroethane, 90 }^0\text{C}]{RuCl_3,\ DDAB} \quad \underset{(60\%)}{PhNO_2}$$

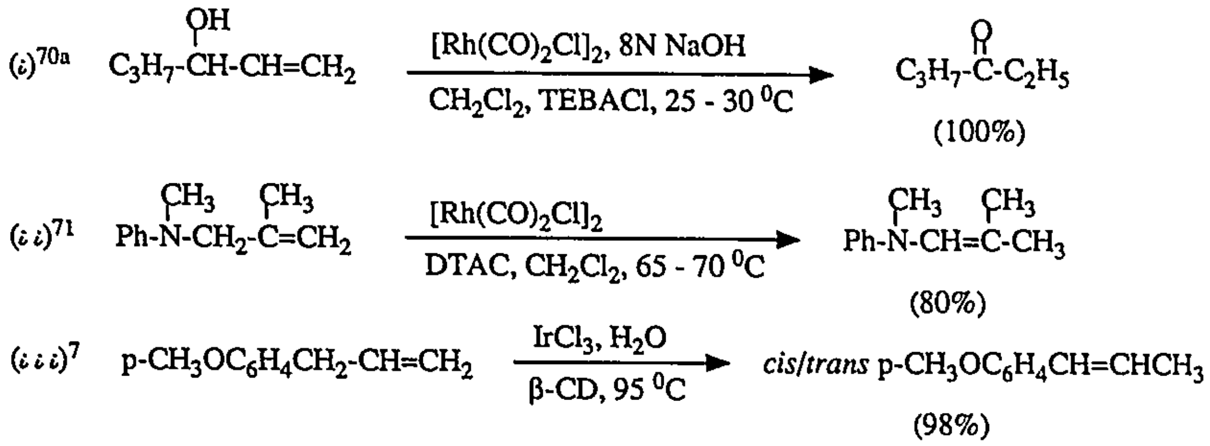
DDAB = Didecyldimethylammonium bromide

Small amounts of azo and azoxybenzene accompanied product formation. If the same process was performed in the absence of both PT and metal catalysts, then the main product was azoxybenzene (90% yield). The quarternary ammonium salt may possibly be involved in the formation of the active oxidation complex, together with $RuCl_3$ and H_2O_2.

1.2.5 Isomerization Reactions

Although isomerization reactions have been quite popular recently with respect to investigation of the mechanistic aspects of "classical" phase transfer catalysis[11,12], there are only a limited number of reports claiming the successful use of PTC in transition metal catalyzed isomerization processes, these usually involving allylic rearrangement.

Allylic alcohols (*i*)[68], amines (*i i*)[69] and aromatic (*i i i*)[7] substrates were isomerized under mild conditions using phase transfer techniques and transition metal catalysts (Scheme 13).



(*i*)[70a] $C_3H_7\text{-}\overset{OH}{CH}\text{-}CH{=}CH_2 \xrightarrow[CH_2Cl_2,\ TEBACl,\ 25-30\ ^0C]{[Rh(CO)_2Cl]_2,\ 8N\ NaOH} C_3H_7\text{-}\overset{O}{\overset{\|}{C}}\text{-}C_2H_5$ (100%)

(*i i*)[71] $Ph\text{-}\overset{CH_3}{N}\text{-}CH_2\text{-}\overset{CH_3}{C}{=}CH_2 \xrightarrow[DTAC,\ CH_2Cl_2,\ 65-70\ ^0C]{[Rh(CO)_2Cl]_2} Ph\text{-}\overset{CH_3}{N}\text{-}CH{=}\overset{CH_3}{C}\text{-}CH_3$ (80%)

(*i i i*)[7] $p\text{-}CH_3OC_6H_4CH_2\text{-}CH{=}CH_2 \xrightarrow[\beta\text{-}CD,\ 95\ ^0C]{IrCl_3,\ H_2O}$ *cis/trans* $p\text{-}CH_3OC_6H_4CH{=}CHCH_3$ (98%)

DTAC = Dodecyltrimethylammonium chloride

β-CD = β-Cyclodextrin

Scheme 13

Example (*i i i*) is particularly interesting because it represents an example of reverse phase transfer catalysis. It is believed that the function of β-CD in this system is to enhance the accessibility of the organic substrate to the aqueous catalyst by inclusion complex formation. In addition it seemed to be responsible for lowering the activation energy. Formation of a ternary intermediate between p-allylanisole, β-CD and $IrCl_3$ would account for the latter phenomenon.

1.2.6 Synthesis of Organometallic Compounds

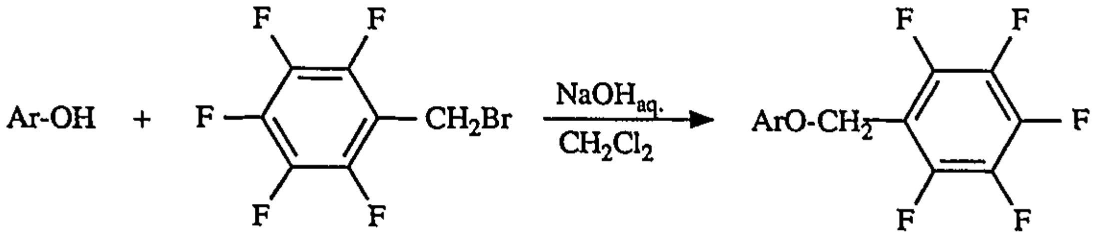
Some examples of the application of PTC to the synthesis of organometallic complexes have already been given (Section 1.2). Furthermore, this methodology provides a simple and convenient entry into a variety of organometallic species including π-allyl complexes, carbonyl complexes, metallocycles, and transition metal clusters[17].

Recent study on chloro-hydrido complexes of ruthenium, iridium[70] and platinum[71] have shown the great power of phase transfer technique when applied to base mediated α-elimination of HCl from a transition metal atom. An interesting application is the synthesis of iridium polyhydride complex[70]:

$$(P\,{}^{i}Pr_3)_2Ir(H)Cl_2 \quad + \quad H_2 \quad \xrightarrow[20\,^{0}C,\ 1atm.,\ 5\ -\ 30\ min.]{C_6H_6,\ 50\%\ NaOH,\ TEBACl} \quad \underset{(95\%)}{(P\,{}^{i}Pr_3)_2IrH_5}$$

1.3 Concept of a Biphasic System

During transition metal catalyzed reactions the concentration of the metal complex is usually low, and it may appear therefore that the biphasic system assures a sufficient amount of active species in that phase where substrates are present, so that the catalysis could be accomplished without necessity of a phase transfer agent. Indeed in some phase transfer and transition metal catalyzed processes it has been observed that reactions occur in high yield even without the 'onium salts[72]. For example, such results were obtained for the nickel-catalyzed cyanation of aryl halides[72a], nickel and palladium-catalyzed formation of sulfides from halides and thiolates[72b], iron pentacarbonyl reduction of α,β-unsaturated compounds[72c] as well as cases noted above. One explanation of this biphasic phenomenon is that organometallic complexes can act as phase transfer agents[72,73]. While it may be reasonable in such reactions, this theory certainly cannot be used to explain the unusual behavior of phenolates which undergo *quantitative* pentafluorobenzylation in the biphasic reaction medium without the use of any phase transfer catalyst, and without the presence of any metal complexes.



ArOH = Δ^9-Tetrahydrocannabinol,
α-Naphthol,
Estradiol

It was shown by Rosenfeld[74] that this analytically important process can be accomplished with ease using phenols, while carboxylic acids were found to be totally inactive, and quarternary ammonium salts had to be added in order to facilitate the esterification. It was argued that under the described conditions, which use high concentrations of alkali, there was no difference in the degree of ionization between the phenol and the carboxylic acid. The possibility of the formation of an ester and its subsequent hydrolysis by strong base was experimentally tested and ruled out. To account for all of the observations, the theory of hard and soft acids and bases[75] was invoked. It is quite possible that the phenolate anion and the pentafluorobenzyl bromide are a matching set of a soft Lewis acid and base. The significance of this fact may have important implications, which could be extended beyond the scope of this simple reaction.

The question of anion activation versus its solubility has been put forward on several occasions in order to explain the mechanism of phase transfer catalysis[76]. Although the balance between those two phenomena is not easy to foresee, it seems that the benefits of the former can easily outweigh the loss of the latter. It is also known that the reactivity of the anions is strongly dependent on their degree of solvation[77]. Therefore, if catalytic species are weakly solvated, their limited solubility in the organic phase where the substrates reside should not be an important factor, as far as the efficiency of the catalytic process is concerned. Naturally, the highest concentration of the active species would be at the interface, and this is where the reaction would take place. Generally, strong agitation should be an aid in increasing the rate of such reactions. Similar phenomena in biphasic reactions were also reported by the Mąkosza group[78].

The biphasic system described here has the important feature of heterogeneous catalysis, that of ease of catalyst recovery. This can be accomplished by simple separation of two liquid layers. The need for such a system is due to the realization that many homogeneous processes, although highly effective in catalysis, could not be economically applied in industry (catalysts used are often based on precious metals). It was highly desirable to design a new system which could combine the virtues of both homogeneous and heterogeneous catalysis. Some advantages of homogeneous catalysis[79] are worthwhile emphasizing:

(*i*) dissolved species have well defined active sites;
(*ii*) accessibility of the metal atoms is easy;
(*iii*) the modification of the steric, and/or electronic environment of the metal center can be realized quite readily

Disadvantages include:

(*i*) separation problems;
(*ii*) thermal, oxygen, and moisture sensitivity of the organometallic species;

(*iii*) corrosive properties toward chemical reactors

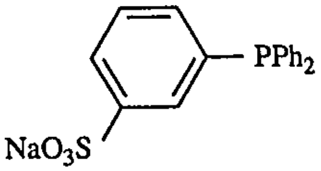
There have been several approaches toward heterogenation of homogeneous processes[80]. The methods which are being explored involve the attachment of a normally soluble catalyst to an insoluble support[81], selectively permeable membranes[82], micelle forming surfactants[83], and electrode mediated processes[84]. None of those methods however offers the simplicity of a biphasic system. This system could be simply defined as a mixture of two immiscible liquids, which *does not* require the presence of a phase transfer agent.

1.4 Application of Transition Metal Complexes under Biphasic Conditions

Although theoretically there are many possibilities of immiscible liquid systems such as the one successfully applied by Parshall[85], who used a combination of a molten salt and organic substrate, the aqueous-organic biphasic system offers the most versatility. There are basically two types of conditions under which this system could be functioning:

(*i*) water soluble substrates and organic soluble complexes,
(*ii*) water soluble transition-metal complexes and organic soluble substrates

Some organic substrates like alcohols and to a higher extent diols are water soluble and they have indeed been applied in biphasic catalysis together with organic soluble metal complexes. For example butene diol was effectively hydrogenated by hydrogen and chlorotris(triphenylphosphine)rhodium(I) in a benzene-water mixture[86]. As most organic compounds are hydrophobic, it is preferable to have the catalyst in the aqueous phase and the substrate in the organic phase. This is the area where research of biphasic catalysis is presently being directed, the most extensively exploited being water soluble transition metal complexes based on sodium diphenylphosphinobenzene-m-sulphonate (DPPS) **(30)**.

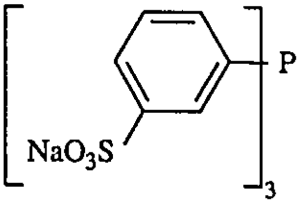


30

Triphenylphosphine comprises a constituent of many complexes known for their catalytic activity under homogeneous conditions. Introducing a highly polar substituent such as sulphonate renders the complex soluble in aqueous medium at any pH, thus opening the possibility of conducting catalysis under biphasic conditions and taking full advantage of the benefits it offers. Many practical applications have resulted by pursuing this idea, and several reviews are available on this subject[23,87,88]. Aside from the previously mentioned examples of phase transfer reactions which can be realized without the presence of a phase transfer agent (page 32), there are other documented cases of biphasic catalysis. The following processes are of considerable interest.

1.4.1 Biphasic Reduction Reactions

The vast majority of existing publications covering this subject describe the utilization of a biphasic system for the hydrogenation of a variety of unsaturated species. Both rhodium[89] and ruthenium[90] derivatives of a DPPS and other modified phosphine ligands such as the trisodium salt of tris(m-sulphonatophenyl)phosphine[91] (**31**) or [2-(diphenylphosphino)ethyl]-trimethylammonium nitrate, known as amphos nitrate[92] (**32**), have been successfully applied in this area.



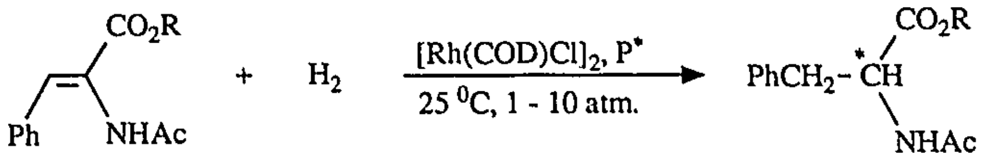
31

$Ph_2PCH_2CH_2N(CH_3)_3^+ NO_3^-$

32

With respect to their chemical properties, sulphonated triphenylphosphines resemble the parent PPh_3, and thus metal complexes containing those ligands show only minor differences in the electronic states of their central metal atoms[87,89a]. This does not preclude, however, that water soluble complexes strictly parallel the reactivity of their unmodified, homogeneously used counterparts. Some unexpected results have been obtained. For example, $RhCl(DPPS)_3$ was used by Joo and co-workers[89b] as a catalyst[89a] for the hydrogenation of unsaturated fatty acids. Interestingly, it was found that fumaric acid was reduced at a much higher rate than maleic acid. This was unusual when compared to the results with $RhCl(PPh_3)_3$ used in the hydrogenation of maleate and fumarate esters under homogeneous conditions[93] where the reverse order of reactivity was observed. A detailed mechanism has not been proposed, but it was concluded, based on a detailed kinetic study, that water - a highly polar solvent - acted probably as a proton acceptor and was responsible for the different mechanistic pathway of this process as compared with the homogeneous reaction.

Recently the biphasic system has been successfully applied in the area of asymmetric catalysis. Water soluble sulphonated chiral phosphines (P*) have been prepared and used as constituents of optically active rhodium complexes. For example the complex $[Rh(COD)Cl]_2$ used together with (35) or (36) appeared to be an effective catalyst precursor for the enantioselective hydrogenation of enamides (33)[94].



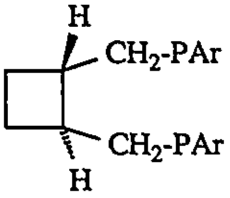
33

34

(S) or (R)

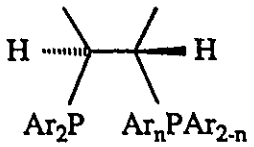
COD = 1,5-Cyclooctadiene

$P^* =$



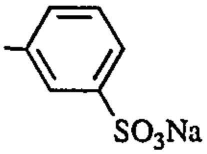
35

;



36

Ar =



a) R = H, P^* = **35** (42% e.e of (S)-**34**),

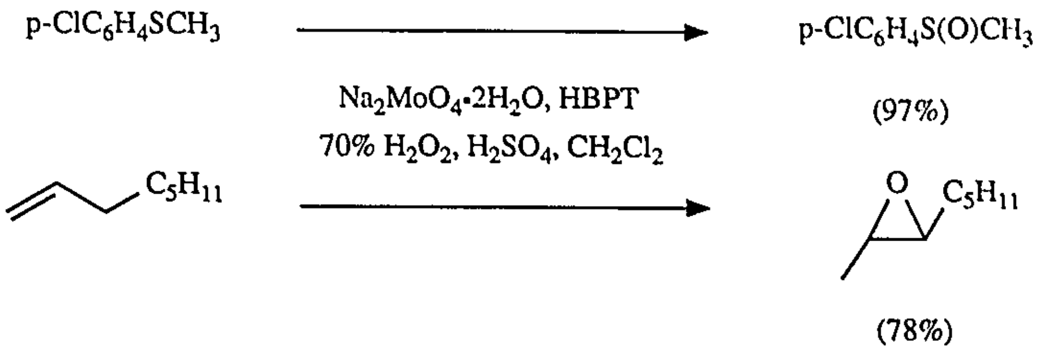
b) R = H, P^* = **36** (88% e.e of (R)-**34**),

c) R = CH_3, P^* = **35** (23% e.e of (S)-**34**),

d) R = CH_3, P^* = **36** (86% e.e of (R)-**34**)

1.4.2 Biphasic Oxidation Reactions

While the preceding section described a method, in which organic soluble species was made water soluble by the attachment of a hydrophilic ligands, the biphasic oxidation attempts seem to be based on the reverse approach. A group of Italian workers developed an oxidation procedure where the neutral Mo(VI) or W(VI) peroxo complexes formed in aqueous solution were extracted by a lipophilic, monodentate, neutral ligand into an organic phase containing substrates[95]. This process employs hydrogen peroxide and is effective in the catalytic oxidation of sulfides and the epoxidation of olefins.



HBPT = $[(CH_3(CH_2)_3)_2N]_3P{=}O$

Scheme 14

The above reaction conditions closely resemble the system previously described under paragraph 1.2.4.3, the main difference being that the present situation does not require a cationic carrier which was essential in the former case.

1.4.3 Biphasic Isomerization Reactions

Reports concerning biphasic isomerization are even more scarce than those related to phase transfer processes. They refer to terminal - internal olefin isomerization observed during attempted biphasic hydrogenation[89a,92] or hydroformylation[96] reactions. Since they were seen as side reactions they are not synthetically useful and will not be discussed further.

1.5 Objectives of the Present Research

1.5.1 Phase Transfer Catalyzed Synthesis of $HVCp(CO)_3^-$ and its Application to Reduction Reactions

There is a growing interest in the application of transition metal complexes to reduction reactions. A significant portion of this area concerns metal hydrides and in particular anionic metal hydrides which also have been the subject of recent attention[97]. With reference to the latter, phase transfer techniques can offer a convenient synthetic approach if one starts with an appropriate metal carbonyl precursor. Several such attempts have already proven successful[98]. There are no examples, however, of the use of phase transfer catalysis in reactions involving early transition metal complexes.

With chemistry of (η^5-cyclopentadienyl)tricarbonylhydridovanadate anion fairly well established[99], and noting that quarternary ammonium (Q) or bis(triphenylphosphine)iminium (PPN) cations have been effective in stabilizing reactive anions[100], we have sought to develop synthetic methods which would yield vanadium hydrido salts directly: e.g., starting from commercially available $CpV(CO)_4$.

In case of success it would also be interesting to learn whether $HVCp(CO)_3^-$ effected reductions, performed under phase transfer conditions, could afford the same or different products than the homogeneous reactions.

1.5.2 Catalytic Carbonylation of Vinyl Epoxides

In the broad area of transition metal catalyzed carbonylation reactions, vinyl epoxides remain relatively unexplored. This is despite their ready availability and a few quite promising results obtained to date. One such reaction, described in paragraph 1.2.1.3, utilizes cobalt carbonyl and methyl iodide under phase transfer conditions. As a result β-hydroxy acids are formed in rather modest yields[40].

In an attempt to improve these results we decided to investigate a nickel cyanide based catalytic system. It is known to be a superior catalyst to cobalt carbonyl in effecting a variety of carbonylations, including those of halides[32,33,101] and allyl alcohols[38]. Our aim was to see if we could obtain unsaturated hydroxy acids in high yields by reaction of vinyl epoxides using catalytic amounts of $Ni(CN)_2$ under CO and mild phase transfer conditions.

1.5.3 Phase Transfer Catalyzed Nitric Oxide Reactions

The key step of carbonylation reactions is the insertion of carbon monoxide via a ligand migratory pathway[102]. It has been shown by Bergman and co-workers[103] that co-ordinated nitric oxide can undergo migratory insertion into a metal-carbon bond. Recently the first examples of such processes with application to stoichiometric synthesis have been presented[104].

Because of the success of carbonylation under PTC conditions it seemed conceivable to us that metal and phase transfer catalysis could be utilized to effect novel reactions of organic substrates with nitric oxide.

CHAPTER 2

Results and Discussion

The common feature of the three separate projects described in this thesis is the application of transition-metal complexes for organic transformations under phase transfer or biphasic conditions.

Section 2.1 describes the synthesis of (η^5-cyclopentadienyl)tricarbonylhydridovanadate anion employing biphasic conditions. This section also describes the reactivity of $HVCp(CO)_3^-$ towards such compounds as halides, aromatic nitro compounds and α,β-unsaturated ketones.

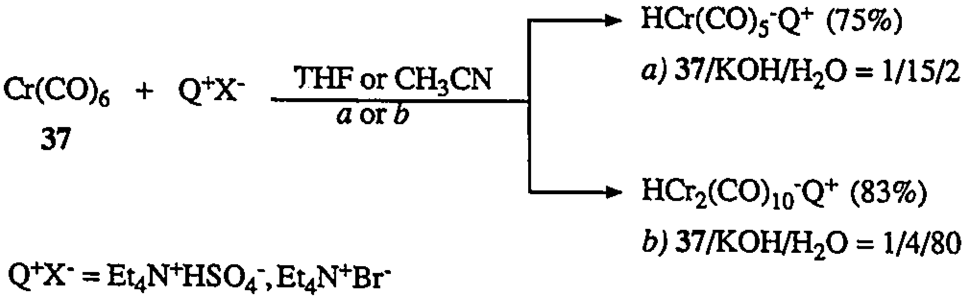
Section 2.2 describes the second project involving the catalytic carbonylation of vinyl epoxides. An application of nickel cyanide as an active catalyst precursor proved fruitful by employing catalytic two phase system. In several instances presence or absence of phase transfer agent led to different product distribution.

Finally, section 2.3 describes the phase transfer and transition-metal catalyzed reactions of nitric oxide resulting in carbon-nitrogen bond formation.

2.1 Synthesis and Reactivity of $HVCp(CO)_3^-$ in an Aqueous-Organic Two-Phase System

2.1.1 Biphasic Generation of $HVCp(CO)_3^-$

Some of the known preparative methods utilizing phase transfer techniques for the synthesis of ionic transition metal hydrides avoid the use of an aqueous medium[98a,98c]. This happens when hydrides are sensitive to water, and in this case a solid-liquid version of PTC is considered when designing a synthesis. On the other hand, the presence of water appeared to be essential in the preparation of water sensitive hydrido metal carbonyl anions $HM(CO)_5^-$ (M = Cr, Mo, W) by an ion-pair extraction technique[98d]. Conducting the experiment in water did not cause the conversion of mononuclear hydrides to the corresponding μ-hydrides. Moreover, its presence appeared to be necessary to make the reaction proceed at a reasonable rate. This was the case when a one to two molar excess of water was added, while considerable amounts of KOH (over tenfold relative to **37**) were present. However, when less base was used and the reaction mixture was diluted with a large excess of water the binuclear hydride formation was observed.



Scheme 15

The ion pair extraction technique, which is simply a phase transfer process requiring stoichiometric amounts of a cationic carrier, has also been adopted for the synthesis of a known anionic vanadium hydride $HVCp(CO)_3^-$ (**39**). In contrast to Scheme 15, the present method is based on a liquid-liquid system.

$$\underset{\mathbf{38}}{CpV(CO)_4} + Q^+X^- \xrightarrow[N_2,\ \text{r. temp. to } 60\ ^0C]{C_6H_6,\ 5N\ NaOH} \underset{\mathbf{39}}{HVCp(CO)_3^-Q^+}$$

$Q^+ = Bu_4N^+, PPN^+$

$X^- = HSO_4^-, Cl^-$

The reaction of tetrabutylammonium hydrogen sulfate (TBAHS) with cyclopentadienylvanadium tetracarbonyl was found to occur at atmospheric pressure and room temperature to afford the desired anionic vanadium hydride (see Table 1 for yields). What is remarkable about this synthesis is the fact that the product did not suffer decomposition despite being in contact with the aqueous phase, even when the reaction was run overnight. This was an interesting observation taking into account the experimental conditions given by Bergman[99]. His approach was based on homogeneous, strictly anhydrous generation of $CpV(CO)_3^{2-}$ and subsequent hydrolysis avoiding excess water which could apparently cause decomposition. Although Bergman did not describe the reactivity of $HVCp(CO)_3^-$ with water, he showed that protonation of **39** results in the series of events depicted in Scheme 16:

$$\begin{tikzcd} \underset{\mathbf{39}}{HVCp(CO)_3^-} \arrow[r, "H^+"] & {[CpV(CO)_3H_2]} \arrow[r, "-H_2"] & \underset{\mathbf{40}}{[CpV(CO)_3]} \arrow[d, "\mathbf{39}"] \\ & & \underset{\mathbf{41}}{[Cp(CO)_3V\text{-}H\text{-}V(CO)_3Cp]^-} \end{tikzcd}$$

Scheme 16

In this reaction, the ligating property of hydride **39** was discovered, which allows it to enter the vanadium coordination sphere of **40** and form the binuclear hydride **41**. The hydride **41** is spectroscopically different from its parent complex **39** having a slight (0.1 ppm) upfield ^1H NMR shift of the cyclopentadienyl proton signals. In addition, it should have a much stronger shielding of its hydride hydrogen than that of **39**.

Puttfarcken and Rehder also synthesized **39** having tetraethylammonium as a counterion[105]. The experimental procedure was essentially the same as Bergman's except that in the final stage of the synthesis the product was washed with water !

The following experiment was very informative because it showed not only that mononuclear **39** is stable in alkaline aqueous solution, but it also revealed that the two-phase synthesis of this hydride is biphasic in nature (i.e., it does not require the presence of a phase transfer agent). When 5N NaOH and benzene containing $CpV(CO)_4$ were stirred at 60 ^{0}C for two hours, the orange organic layer lost its colour and a red-orange colour appeared in the aqueous phase. Addition of bis(triphenylphosphine)iminium chloride (PPN^+Cl^-) caused an almost immediate (1-2 minutes) precipitation of a yellow-brown solid which had spectroscopic properties identical to those of PPN^+-**39** reported by Bergman[99] (IR of PPN^+-**39** shows two carbonyl stretching bands at 1890 and 1780 cm^{-1}, while ^1H NMR reveals a strongly shielded metal hydride signal around -6.5 ppm., both in THF). This solid was stable during work-up, provided that the aqueous solution used for washing was kept alkaline (≥ 5% NaOH). Although PPN^+-**39** when in contact with distilled water experienced slight but visible effervescence, the final samples of this product still showed a reasonably high purity as judged by spectroscopic methods. The results of the synthesis of $HVCp(CO)_3^-Q^+$ are summarized in Table 1.

Table 1

Synthesis of $HVCp(CO)_3^-$ under Biphasic Conditions

Reference #	Q^+	X^-	Temp., ^{0}C	Time, h	Yield, %
3.2.1	Bu_4N^+	HSO_4^-	23	12	87
3.2.2	PPN^+	Cl^-	60	2	68

2.1.2 Phase Transfer Catalyzed Reactions of $HVCp(CO)_3^-$

2.1.2.1 Reduction of Halides

Having synthesized **39** under biphasic conditions, it was of great interest to explore its reaction with reducible substrates. The reactions with halides were examined initially, since these processes had been examined under homogeneous conditions.

The readiness with which **39** transfers its hydrogen to some organic halides, initially observed by Bergman in homogeneous reactions, is not normal behavior of metal carbonyl anions. This reactivity seems to be more typical of neutral systems having phosphorus ligands. Nevertheless, Bergman's experiments provided some insight into the nature of those unusual reactions which are consistent with free radical intermediates. Bergman also proposed two mechanisms to explain how these radicals are formed. In the equations below "In·" stands for a general radical initiator.

$$(i)\quad \underset{\mathbf{39}}{HVCp(CO)_3^-} + In\cdot \longrightarrow InH + \underset{\mathbf{42}}{CpV(CO)_3^{\cdot -}}$$

$$HVCp(CO)_3^{\cdot -} + RX \longrightarrow \underset{\mathbf{43}}{CpV(CO)_3X^-} + R\cdot$$

$$R\cdot + \underset{\mathbf{39}}{HVCp(CO)_3^-} \longrightarrow RH + \underset{\mathbf{42}}{CpV(CO)_3^{\cdot -}}$$

$$(ii)\quad \underset{\mathbf{39}}{HVCp(CO)_3^-} + RX \longrightarrow \underset{\mathbf{44}}{HVCp(CO)_3} + R\cdot + X^-$$

$$\underset{\mathbf{44}}{HVCp(CO)_3} + R\cdot \longrightarrow RH + \underset{\mathbf{40}}{CpV(CO)_3}$$

$$\underset{\mathbf{40}}{CpV(CO)_3} + X^- \longrightarrow \underset{\mathbf{43}}{CpV(CO)_3X^-}$$

Scheme 17

The first process (*i*) requires a free radical initiator to produce the 17-electron radical anion **42** which has a strong affinity for one-electron ligands. Abstraction of a halogen from the organic halide would lead to **43** along with radical R·. The latter reacts with hydride **39** abstracting its hydrogen to give a dehalogenated product and releases **42** which propagates the chain reaction.

The other pathway for the generation of free radicals (*ii*) is the "outer-sphere" electron transfer mechanism. In this case, direct electron transfer between hydride **39** and the starting material would afford the 17-electron vanadium hydride **44** and an organic radical anion which rapidly dissociates to R· and X^-. In the next step, hydrogen atom abstraction from **44** would result in final product formation together with coordinatively unsaturated **40**, and ultimately **43** after interception of the halide ion. The first mechanism, in Bergman's opinion, was the most likely to operate in the observed vanadium hydride and organic halide reactions.

Prior to conducting a series of dehalogenations using different halides, the reaction conditions were optimized based on the reactivity of 2-bromomethylnaphthalene which was chosen as the model reactant. The best yields of 2-methylnaphthalene were obtained using 5N NaOH (compare 3.3.1, 3.3.9 and 3.3.10 in Table 2). Tetrabutylammonium hydrogen sulfate was superior amongst the tested phase transfer catalysts, while the absence of any of these agents resulted in poor product yields (3.3.1 and 3.3.5 - 3.3.8). Although higher yields resulted when the reaction was carried-out under carbon monoxide, this probably was not a result of the regeneration of an active species since the quantity of product formed was still strongly related to the stoichiometry of the vanadium carbonyl used (3.3.2 - 3.3.4 vs. 3.3.12 - 3.3.13). Reactions at higher temperatures (60 ^{0}C) improved reaction rates and the yields of final products in comparison to reactions performed at room temperature.

Table 2

Effect of Reaction Conditions on the Yield of 2-Methylnaphthalene[a]

Reference #	Phase transfer agent[b]	Reactn time, h	Yield of 2-Methylnaphthalene, %
3.3.1	A	0.23	76
3.3.2	A	0.23	66[c]
3.3.3	A	0.23	32[d]
3.3.4	A	3.0[e]	0
3.3.5	B	0.23	69
3.3.6	C	3.0	22
3.3.7	D	3.0	0
3.3.8	none	3.0	7
3.3.9	A	3.0	14[f]
3.3.10	A	0.17	72[g]
3.3.11	A	3.0	60[h]
3.3.12	A	0.23	92[i]
3.3.13	A	0.23	50[i,j]

[a] Only changes to standard reaction conditions (halide/38 = 1:1, C_6H_6, 5N NaOH, N_2, TBAHS, 60 ^{0}C) are indicated.

[b] A = $(C_4H_9)_4N^+HSO_4$, B = $C_{12}H_{25}N(CH_3)_2(C_2H_5)^+Br^-$, C = $PhCH_2N(C_2H_5)_3{}^+Cl^-$, D = PEG-400. [c] Halide/38 = 1:0.8.

[d] Halide/38 = 1:0.3. [e] No 38 used. [f] 2N NaOH. [g] 8N NaOH. [h] Room temperature. [i] Carbon monoxide atmosphere.

[j] Halide/38 = 1:0.5.

Other results obtained using the two-phase system were comparable both in terms of yields and reaction times to those of the previously described homogeneous reactions. The advantage of the described system, however, is that an active agent can be generated *in situ* and what required several steps in the former process could be achieved in a one pot reaction. Generally, an induction period (40-50 minutes) was used before addition of reactant.

$$\mathrm{RX} + \underset{\mathbf{38}}{\mathrm{CpV(CO)_4}} \xrightarrow[\text{TBAHS, r. temp. to 60 }^{0}\text{C}]{\mathrm{C_6H_6}\text{, 5N NaOH, }\mathrm{N_2}\text{, 1 atm.}} \mathrm{RH}$$

Reaction times, products and yields for individual dehalogenation reactions are shown in Table 3.

Benzylic chlorides or bromides (R = $ArCH_2$ or Ar_2CH, X = Cl, Br) gave the reduced material in 44-76% yield. The presence of electron-donating (OCH_3) or withdrawing (Cl) substituents on the arene ring of a benzyl halide did not have much influence on the yield of the final product. Other activated halides, including chloromethyl phenyl sulfone and 2-chloroacetophenone were also dehalogenated by **38** under phase transfer conditions. While vinyl and aromatic bromides again led to exchange of halogen and hydrogen atoms, the corresponding chlorides appeared to be inert under the same reaction conditions. The reaction can also be applied to aliphatic halides [e.g., bromooctane (3.3.25 in Table 3)].

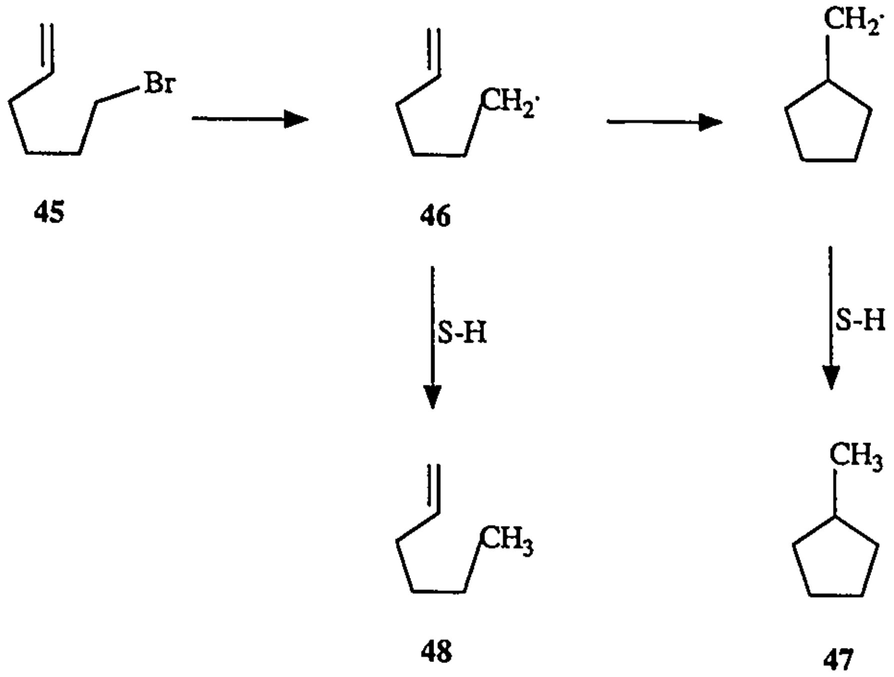
Table 3

Vanadium and Phase Transfer Catalyzed Dehalogenation of RX[a]

Reference #	Halide	Reactn time, h	Product	Yield[b], %
3.3.14	1-(chloromethyl)naphthalene	0.3	1-methylnaphthalene	74
3.3.15	bromodiphenylmethane	6	diphenylmethane	62
3.3.16	p-chlorobenzyl chloride	6	p-chlorotoluene	44
3.3.17	p-methoxybenzyl chloride	2	p-methylanisole	50
3.3.18	o-methylbenzyl chloride	0.3	o-xylene	47[c]
3.3.19	chloromethyl phenyl sulfone	2.5	methyl phenyl sulphone	76[c]
3.3.20	o-chloroacetophenone	0.5	acetophenone	39
3.3.21	o-bromoacetophenone	0.08	acetophenone	54
3.3.22	β-bromostyrene	4	styrene	88
3.3.23	2-bromonaphthalene	25	naphthalene	72
3.3.24	bromocyclohexane	16	cyclohexane	66
3.3.25	1-bromooctane	18	octane	60

[a] All reactions were run according to conditions specified in Table 2, except where noted otherwise. [b] Yields were determined by GC vs internal standard. [c] Reaction at room temperature.

The phase transfer dehalogenation reactions probably involve electron transfer processes as is likely the case in Bergman's homogeneous reactions. To confirm this hypothesis, 6-bromo-1-hexene (**45**) was used as a reactant which could generate radicals and then give a cyclization product.



S-H = hydrogen atom source (e.g., **39** or solvent)

Scheme 18

The ratio of **48** to **47** was found to be 0.77 which is consistent with the intermediacy of a radical species **46**[99a]. The validity of such a cyclizable radical probe has recently been discussed by Ashby[106].

2.1.2.2 Reduction of Aromatic Nitro Compounds

Knowing that the vanadium hydride under phase transfer conditions could be an active reducing agent toward organic halides, the two-phase system was employed for other reduction reactions. It was found that the hydride **39** generated *in situ* is an excellent reagent for the reduction of aromatic nitro compounds to the corresponding amines.

$$\underset{\mathbf{49}}{\mathrm{ArNO_2}} + \underset{\mathbf{38}}{\mathrm{CpV(CO)_4}} \xrightarrow[\text{TBAHS, r. temp. to } 60\,^{0}\mathrm{C}]{\mathrm{C_6H_6},\ 5\mathrm{N\ NaOH},\ \mathrm{N_2},\ 1\ \text{atm.}} \mathrm{ArNH_2}$$

Utilization of the same reaction conditions as those employed for the dehalogenation reaction resulted in the isolation of aromatic amines in 66 to 99% yields from nitro reactants (Table 4).

Particularly interesting are the results found using sterically encumbered nitro aromatics. *Ortho*-substituted 2-isopropyl and 2,6-dimethylnitrobenzenes (3.4.9 and 3.4.12 in Table 4, respectively) were reduced affording almost quantitative yields of amines, while nitrobenzene or nitrotoluenes gave appreciably lower yields. This kind of behavior is unique if compared to other metal and phase transfer systems known for effecting the conversion of nitro compounds to amines[45,47,107].

This reductive system can tolerate some functional groups such as ether or olefin. However, if the latter is conjugated with the carbonyl group, it is reduced together with the nitro moiety (3.4.14).

Table 4

Reduction of Nitroarenes by $CpV(CO)_4$ under Phase Transfer Catalysis Conditions[a]

Reference #	49	Reactn. time, min	Product	Yield[b], %
3.4.1	nitrobenzene	15	aniline	75[c]
3.4.2	nitrobenzene	180	aniline	68[d]
3.4.3	o-nitrotoluene	20	o-toluidine	83
3.4.4	m-nitrotoluene	25	m-toluidine	82
3.4.5	p-nitrotoluene	40	p-toluidine	88
3.4.6	o-nitroanisole	20	o-anisidine	85
3.4.7	m-nitroanisole	20	m-anisidine	77
3.4.8	p-nitroanisole	45	p-anisidine	74
3.4.9	o-isopropylnitrobonzene	20	o-isopropylaniline	99(82)
3.4.10	o-nitrobiphenyl	60	o-aminobiphenyl	94(80)
3.4.11	m-nitrobiphenyl	60	m-aminobiphenyl	87(68)
3.4.12	2,6-dimithylnitrobenzene	60	2,6-dimethylaniline	98
3.4.13	p-nitrostilbene	10	p-aminostilbene	(76)
3.4.14	$4\text{-}NO_2C_6H_4CH{=}CHCOPh$	30	$4\text{-}NH_2C_6H_4CH_2CH_2COPh$	66[e]

[a] All reactions were run according to conditions specified in Table 2, except where noted otherwise. [b] By GC yields, except those in parentheses which are isolated yields. [c] 78% yield after 80 minutes. [d] Reaction at room temperature. [e] Substrate/$CpV(CO)_4$ = 1:2.

The most effective phase transfer catalyst was TBAHS, as in the case of dehalogenation reactions. Almost equally effective was tetrabutylammomium bromide (TBAB) while the use of TEBACl, 18-Crown-6 or PEG-400 was not beneficial for p-toluidine formation (Table 5).

Table 5

Effect of the PT-Catalyst on the Yield of p-Toluidine Obtained from p-Nitrotoluene

Reference #	PT-Catalyst	Yield of p-toluidine, %
3.4.5	Tetrabutylammonium hydrogen sulfate	88
3.4.16	Tetrabutylammonium bromide	82
3.4.17	Benzyltriethylammonium chloride	14
3.4.18	18-Crown-6[a]	0
3.4.19	PEG-400	0
3.4.20	none	11

[a] Solid-liquid PTC.

By analogy to the previously discussed dehalogenation reactions, which occurred by a free radical mechanism, one could expect that the reduction of nitroaromatic compounds also involves an electron transfer process. The first step may be radical anion formation, especially knowing that nitro compounds are good electron acceptors. Nitroaromatic radical anions are relatively stable intermediates in aqueous alkaline solutions. It is known[108], that in non-alkaline medium, protonation followed by decomposition results in the decay of the radical anion $ArNO_2^{\cdot -}$ (**50**). Another reason for the decomposition of **50** would be its engagement in subsequent electron transfer reactions - the subject of a recent kinetic investigation[109]. It was found that sterically encumbered **50** transfers its electrons more slowly as compared to the unhindered analogue. In the former, as a result of substitution, the nitro group rotates away from the plane of a phenyl ring. In fact, two methyl substituents in the 2,6 positions can force the NO_2 group to be in a plane almost perpendicular to that of the aromatic ring[109]. This implies that delocalization of an unpaired spin over the arene ring is severely restricted. In addition to lower reduction potential exerted by such compounds they experience increased solvent reorganization around the radical anion center. The latter phenomenon was believed to be the major reason for the unexpected stability of the *ortho*-substituted nitroaromatic radical anions. Another factor contributing to this stability might be associated with the geometrical orientations of **50** and the potential electron acceptor. It seems quite likely that unhindered radical anions may transfer electrons at any geometrical orientation (e.g., through oxygens, nitrogen, and *ortho* or *para* carbons). The same process involving hindered **50** implies that the acceptor approaches oxygen atoms at the nitro group, and this approach would be somewhat restricted by the *ortho* substituents.

Some of the above mentioned remarks also pertain to the reactivity of the vanadium hydride under phase transfer conditions. When, for example, a mixture of nitrobenzene and 2,6-dimethylnitrobenzene (1:1 ratio) was treated with an equimolar amount of **38** for 30 minutes under the usual phase transfer conditions, aniline was the only amine detected (72% yield), while 2,6-dimethylnitrobenzene was recovered in the same quantity as introduced. This result could be explained by the fact that the reduction potential of 2,6-dimethylnitrobenzene ($E_{1/2}$ = -0.73 V) is lower than that of nitrobenzene ($E_{1/2}$ = -0.62 V)[114]. The higher susceptibility to one-electron transfer of the latter may result in the total inertness of 2,6-dimethylnitrobenzene during the reduction process, as was monitored by gas chromatography. The reduction potential was apparently not the only factor governing this reduction process. This was evident when two nitroaromatic substrates having almost the same reduction potentials were applied in another competition experiment. The use of 1:1:1 nitrobenzene ($E_{1/2}$ = -0.62 V), o-isopropylnitrobenzene ($E_{1/2}$ = -0.61 V) and **38** resulted in both aniline and o-isopropylaniline formation in the ratio of 2.4:1. This result suggests that steric effects play a role in the reaction.

Some comparisons of the reactivities of differently substituted nitro compounds were made. For example, comparison of the extent of reaction (measured as a function of amount of product formed vs. time) for two substrates, p-nitrotoluene and 2,6-dimethylnitrobenzene, indicates that the initial reaction rate for the former was greater than that for the latter. As reaction progressed with time, however, 2,6-dimethylnitrobenzene experienced greater reduction than p-nitrotoluene (Figure 1). In the series of nitrotoluenes and nitroanisoles (3.4.5 - 3.4.9 in Table 4) *para* derivatives required longer reaction times for complete reduction, while *ortho* substituted compounds displayed reactivity comparable to those of *meta* analogues.

At this stage one could only speculate about the mechanism of these reduction processes. Three points however are worth considering:

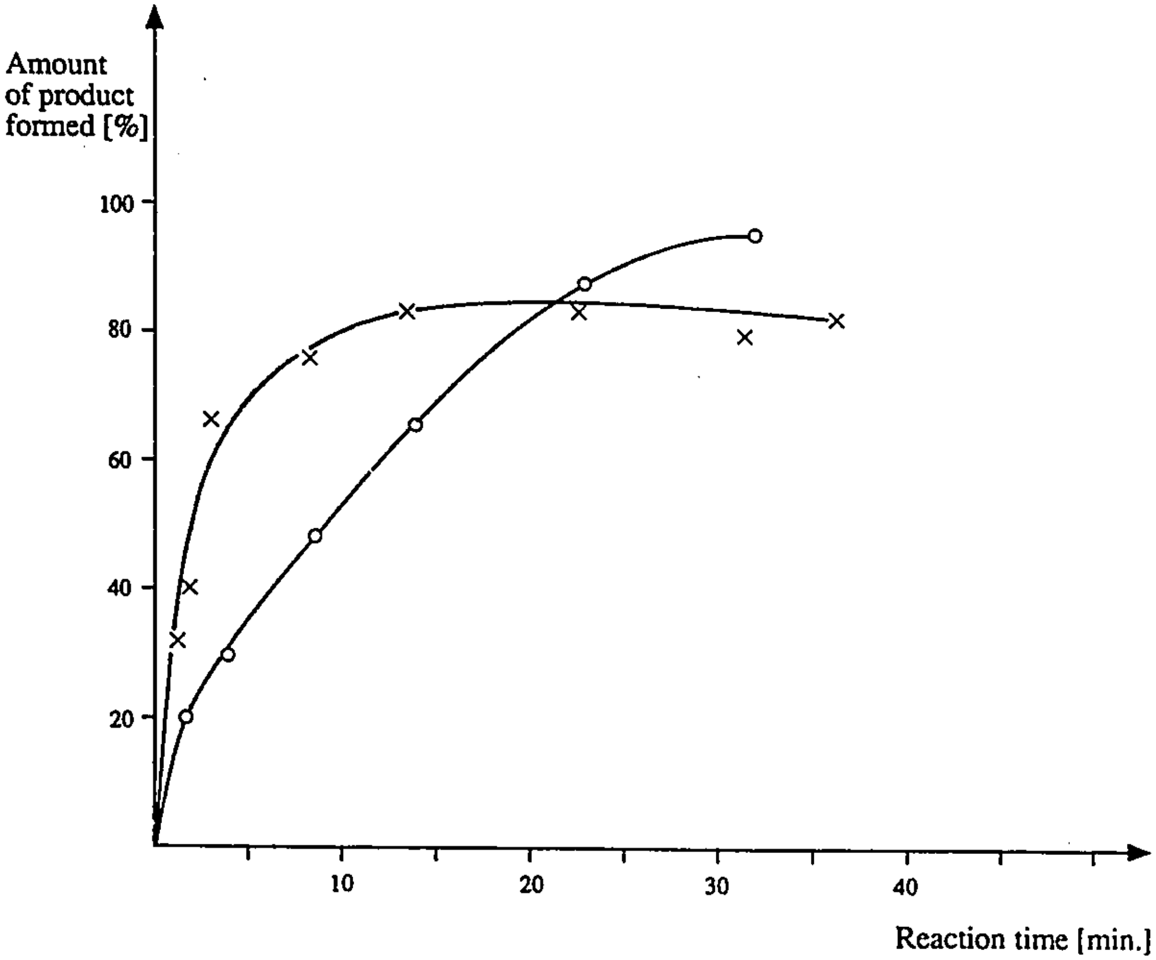
(*i*) electron transfer between the *in situ* generated **39** and nitroarene results in nitroaromatic radical anion formation which initiates a multi-step process of reduction;

(*ii*) direct hydride transfer occurs in the initial step;

(*iii*) high oxophilicity of vanadium results in complexation of the vanadium center by the nitro group and the formation of an intermediate able to interact with water producing the amine.

Figure 1

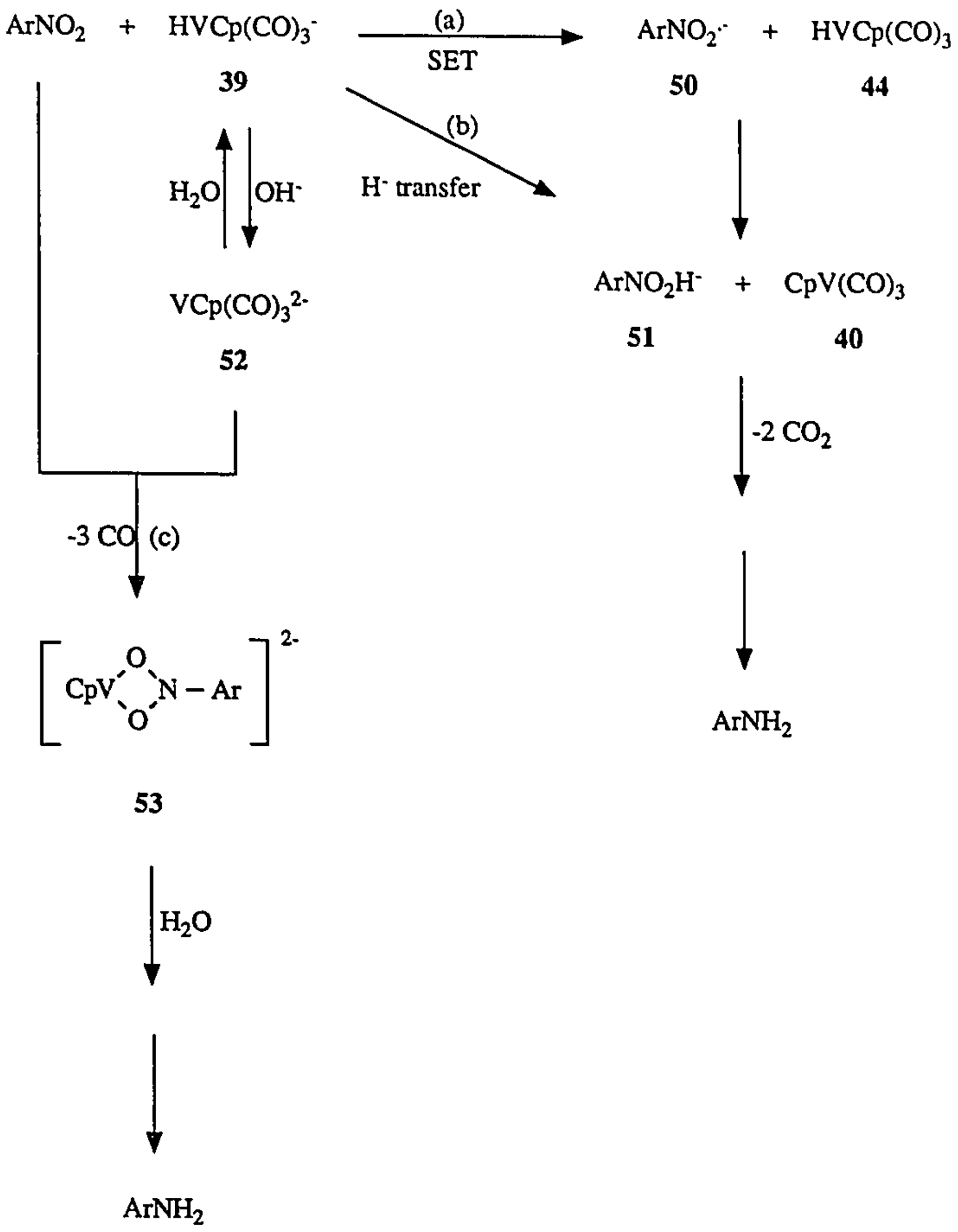
Plot of the Percent Yield of Amines as a Function of Time During CpV(CO)$_4$ Reduction of p-Nitrotoluene (×) and 2,6-Dimethylnitrobenzene (○)



Points connected for clarity

According to path a in Scheme 19, single electron transfer (SET) would result in the generation of radical anion **50** and 17-electron intermediate **44**. A subsequent hydrogen atom transfer could accomplish the first step of this reduction with formation of a protonated dianion of nitroaromatic compound **51** together with vanadium carbonyl **40**. Concurrently, the same result could be obtained by the formal S_N2 reaction between the nitroaromatic compound and **39** (envisaged by path **b**). In this event, the *ortho* substituents on the arene ring would make this process more difficult. The source of additional electrons from the total of 6 necessary for the reduction of nitro compound to the amine would be the carbon monoxide ligands of the vanadium complex **40** (formally, each carbon monoxide ligand can deliver two electrons, and in turn, be oxidized to carbon dioxide). While paths **a** and **b** are plausible, one cannot rule out the possibility of an interaction involving a nitro compound and an oxophilic vanadium complex **52**. The latter would be part of a possible equilibrium between **39** and **52** occurring in the aqueous, alkaline medium. Path **c** shows the formation of an intermediate complex **53** which would be cleaved by water affording the amine.

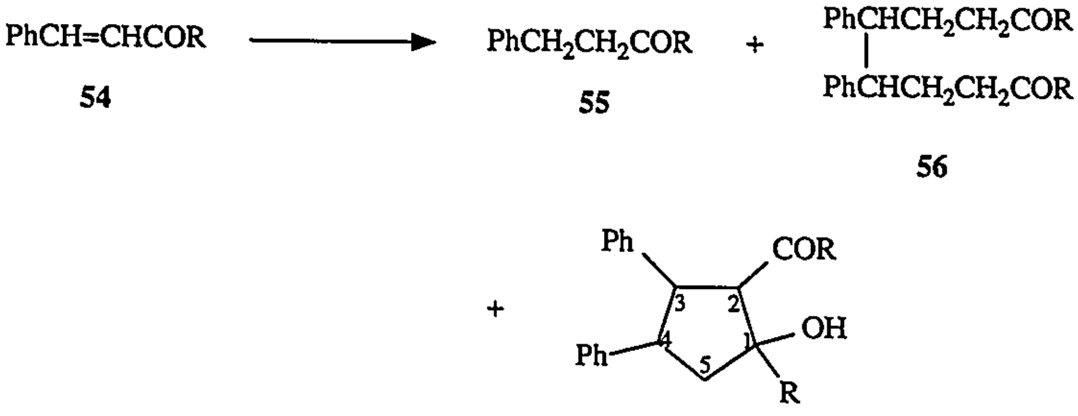
There are certainly more questions than answers concerning this reaction system. One of them, being fundamental in nature, addresses the role of a phase transfer agent in the redox reactions. A recent interesting theory, relative to this matter, will be presented in the last paragraph of the vanadium section (i.e., 2.1.2.4).


ArNO2 + HVCp(CO)3-
39
(a)
SET
ArNO2·- + HVCp(CO)3
50
44
(b)
H- transfer
H2O
OH-
VCp(CO)3 2-
52
ArNO2H- + CpV(CO)3
51
40
-2 CO2
ArNH2
-3 CO (c)
CpV O O N – Ar 2-
53
H2O
ArNH2

Scheme 19

2.1.2.3 Cyclodehydration and Reduction of α,β-Unsaturated Ketones

α,β-Unsaturated ketones are considered to be excellent one-electron acceptors which makes them especially suitable substrates in electrochemical reductions[112]. Benzylideneacetone (**54**, R = Me) and chalcone (**54**, R = Ph) represent examples of such compounds. The major products found during the process of their electrolysis are saturated ketone **55** and the dimer **56**[113]. Both products are believed to arise from the same free radical intermediate: PhCH·-CH=C(OH)R (**58**).

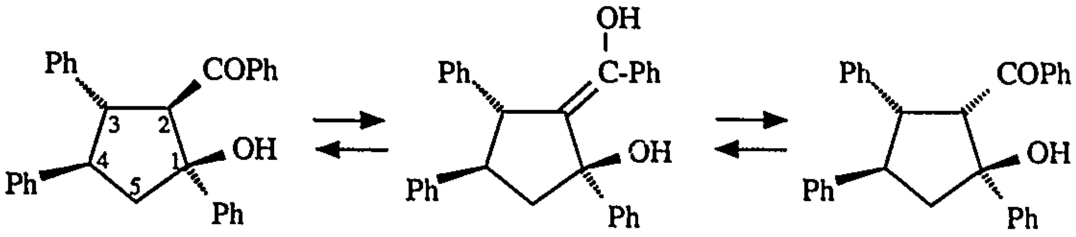


54 **55** **56** **57**

R = Me, Ph

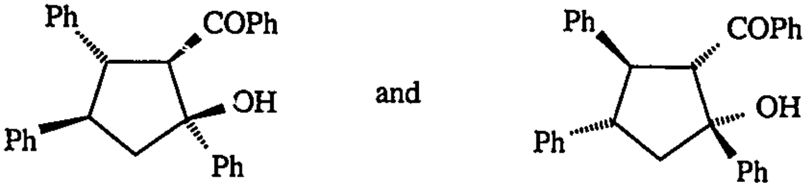
In addition to dimer **56**, the product of its self-cyclization **57** has been identified in a few cases[113b,c].

Electrolysis is not the only means of effecting such transformations. It was known as early as 1897[114] that zinc dust reduction of 1,3-diphenyl-2-propenone (chalcone) in acetic acid yields monomeric as well as dimeric products. While it has been accepted that one of the products was a diketone, 1,3,4,6-tetraphenylhexane-1,6-dione (**56**, R = Ph)[115], the unambiguous structural and stereochemical determination of a cyclic dimer was established in 1978 based on X-ray analysis[116]. The molecular structure of **59** obtained in zinc and acetic acid reduction of chalcone contains two phenyl substituents at C-3 and C-4 existing in a *trans* configuration. The 2-benzoyl and hydroxyl groups were found to be positioned *cis* to each other (see equation below). The latter configuration allows intramolecular hydrogen bonding between the hydrogen of a hydroxyl group and the carbonyl moiety. It is worthwhile noting that the stereochemistry at C-2 is interchangeable e.g.:



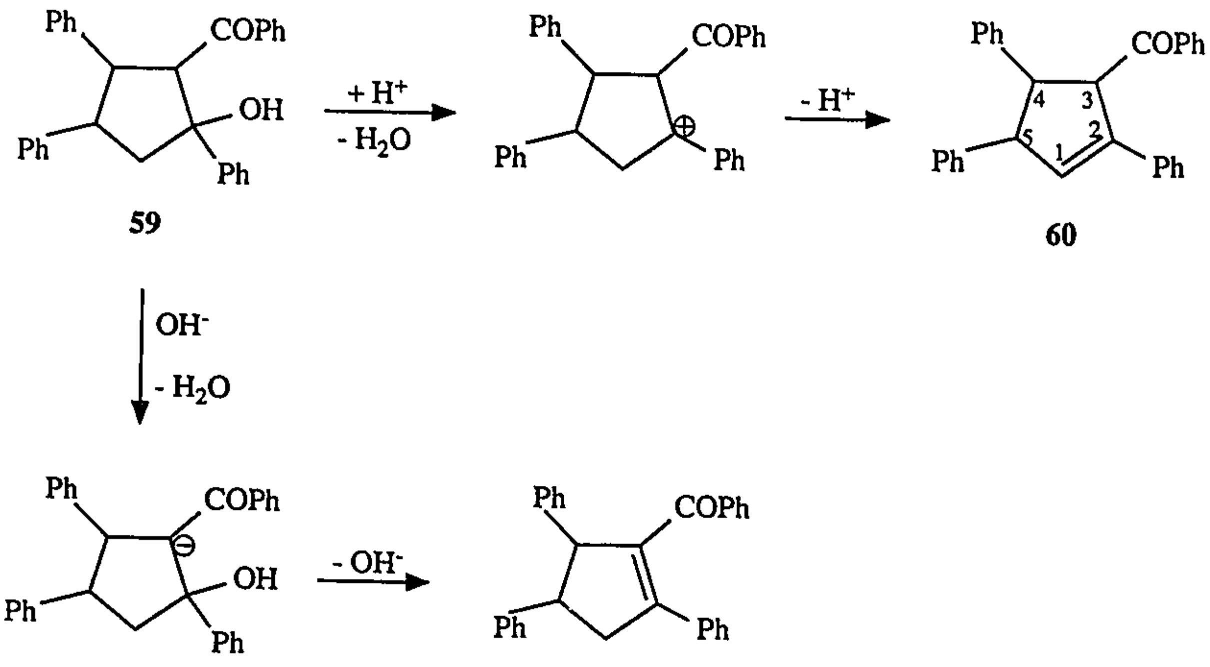
59

On the other hand, the relative configurations at C-3 and C-4 depend on the stereochemistry of an uncyclized diketone (i.e., **56**). The cyclization of *meso* **56** would lead to *cis* (C-3, C-4) isomer, while a *d,l* mixture of **56** would result in the formation of a *trans* analogue. In both cases, *cis* and *trans* stereoisomeric mixtures of cyclic products could be obtained. However for clarity, only one optical isomer is depicted here. E.g., **59** exists as a pair, which is depicted in Scheme 20.



Scheme 20

The ketol **59** has been found to undergo dehydration very easily, both in acidic and basic media[117]. Under the former conditions, the non-conjugated dehydration product **60** has been observed, while base treatment resulted in the formation of the conjugated product (**61**). The following scheme for the dehydration of **59** has been proposed[117].



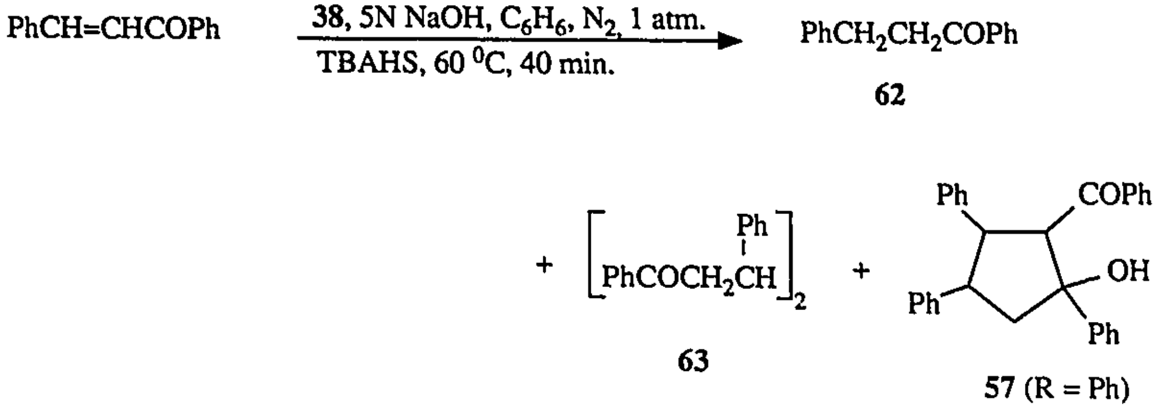
59 **60** **61**

Scheme 21

Among other non-electrochemical methods where the formation of dimers **56** or their cyclic analogues **57** have been reported are Ru(bpy)$_3^{2+}$ (bpy = 2,2′-bipyridine) photosensitised reactions involving an electron donor (1-benzyl-1,4-dihydronicotinamide) and benzylideneacetones[118], reactions of organomagnesium reagents with benzylideneacetophenones[119], or cyclodimerisation of benzylideneacetophenones by the use of triiron dodecacarbonyl[120]. While outer-sphere electron transfer has been proposed in the first example, the last two cases were believed to proceed according to a mechanism where initial coordination of the carbonyl compound took place, followed by electron transfer.

From the previous phase transfer experiment using 3-(p-nitrophenyl)-1-phenyl-2-propenone (3.4.14 in Table 4), where both nitro and the double bond functionalities were reduced, one could expect that vanadium hydride may be the active reagent towards the reduction of α,β-unsaturated ketones.

When 1,3-diphenyl-2-propenone (benzylideneacetophenone) was used as a substrate, under conditions indicated below, then the saturated ketone **62** was formed, but in 23% isolated yield. Two dimeric products accompanied its formation. The first was identified as 1,3,4,6-tetraphenylhexane-1,6-dione (**63**, 17% yield) and the second was cyclopentanol (**57**, R = Ph, 11% yield).



$$PhCH{=}CHCOPh \xrightarrow[\text{TBAHS, 60 }^0\text{C, 40 min.}]{\text{38, 5N NaOH, }C_6H_6\text{, }N_2\text{, 1 atm.}} PhCH_2CH_2COPh$$

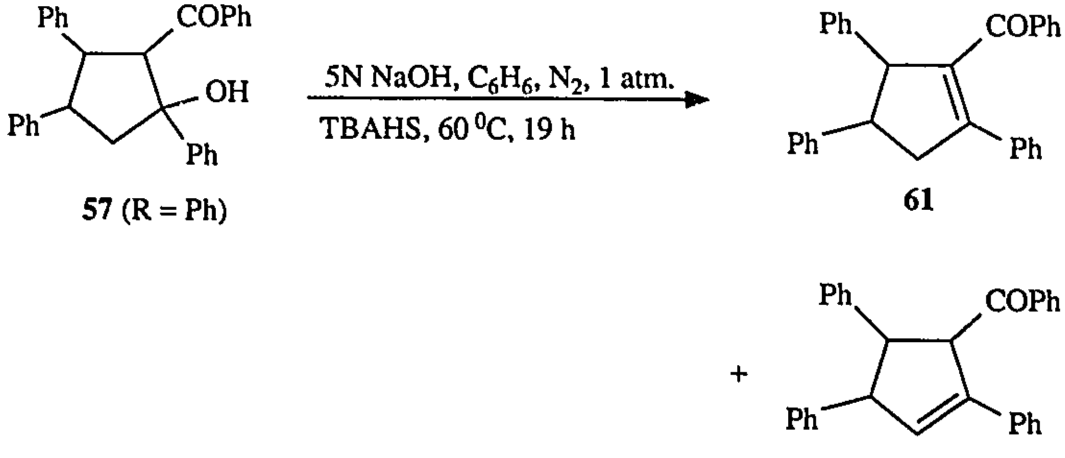
62

$$+ \left[PhCOCH_2\overset{\overset{\displaystyle Ph}{|}}{C}H \right]_2 +$$

63

57 (R = Ph)

The presence of the two dimeric products **63** and **57** (R = Ph) suggests that this reaction probably involves the intermediacy of benzylic radicals (i.e., analogue of **58**, R = Ph). When the cyclic ketol from the above reaction was left for 19 hours at 60 ^{0}C under phase transfer conditions, it resulted in dehydration affording cyclopentenone derivative (**61**). The proton NMR as well as IR of the latter were identical to those reported by Mirek et al.[117] indicating the same stereochemistry of the five-membered ring.



57 (R = Ph)

61

60

In addition to **61**, a small amount of its isomer **60** was also isolated, the ratio of **61** : **60** being 7.5 : 1. Noting that **59** was the precursor of **61** in Mirek's experiment[117], the implication is that **57** (R = Ph), obtained from chalcone and **38** under phase transfer conditions, is the same compound as **59**. The *trans* configuration of its phenyl substituents at C-3 and C-4 positions was therefore expected. On the other hand, **57** (R = Ph) obtained through electrochemical means by Fournier[113b], and again by Berthelot[113c] (**57**, R = $CH_3OC_6H_4$), has been reported to have the C-3, C-4 phenyl substituents in a *cis* configuration. However, the comparison of ^1H NMR spectra of Fournier[113b] and that of ours for compound **57** (R = Ph) indicated that in both circumstances the same geometric isomers were the subject of analysis. The chemical shifts and coupling constants were comparable in both cases. See columns (*i*) vs. (*ii*) in Table 6.

Table 6

Comparison of the Proton NMR Data of 57 (R = Ph) Obtained from 1,3-Diphenyl-2-propenone:

(*i*)[a] By Electroreduction[113b],

(*i i*)[b] Using Vanadium Carbonyl and Phase Transfer Conditions

Proton / Spectr. data	OH		H_2		H_3		H_4		H_5		$H_{5'}$	
	(*i*)	(*i i*)	(*i*)	(*i i*)	(*i*)	(*i i*)	(*i*)	(*i i*)	(*i*)	(*i i*)	(*i*)	(*i i*)
Chemical shift [ppm]	5.20 (s)	5.21 (d)	4.57 (d)	4.52 (d)	4.10 (q)	4.08 (dd)	3.79 (6 lines)	3.76 (6 lines)	3.0 (q)	2.56 (dd)	2.58 (q)	2.98 (8 lines)
Coupling const. [Hz]	—	$J_{OH\text{-}5'}=1.2$	$J_{2\text{-}3}=12$	$J_{2\text{-}3}=12.0$	$J_{3\text{-}2}=12$ $J_{3\text{-}4}=10.2$	$J_{3\text{-}2}=12.0$ $J_{3\text{-}4}=10.3$	$J_{4\text{-}3}=10.2$ $J_{4\text{-}5'}=11.4$ $J_{4\text{-}5}=5.7$	$J_{4\text{-}3}=10.3$ $J_{4\text{-}5'}=11.1$ $J_{4\text{-}5}=6.2$	$J_{5\text{-}5'}=14.3$ $J_{5\text{-}4}=5.7$	$J_{5\text{-}5'}=14.7$ $J_{5\text{-}4}=6.2$	$J_{5'\text{-}5}=14.3$ $J_{5'\text{-}4}=11.4$ —	$J_{5'\text{-}4}=14.7$ $J_{5'\text{-}4}=11.1$ $J_{5'\text{-}OH}=1.2$

[a] 250 MHz, ^1H ($CDCl_3$, TMS). [b] 300 MHz, ^1H ($CDCl_3$, TMS)

It should be noted that Fournier did not observe coupling across a σ-bond involving aliphatic OH[121] which, on the other hand, was reported by him and Berthelot[113c] for another isomer of **57** (R =$CH_3OC_6H_6$). The observed $J_{OH\text{-}H5'}$ coupling had a value of 1.22 Hz as indicated in Table 4. The geometry of both proposed structures of A and **B** (Scheme 22), differs only at C-3.

Structure of **57** (R = Ph) proposed by Fournier et al[113b]:

A

Proposed structure of **57** (R = Ph):

B

Scheme 22

What apparently led Fournier et al., to their final assignment of structure A was the attribution of large and small coupling constants to *cis* and *trans* configurations respectively. However, the use of vicinal proton couplings is not always a reliable method for the five-membered ring substituted derivatives[122].

Nuclear Overhauser Enhancement (NOE) experiments were carried-out to solve the structural assignment controversy. The peaks were irradiated prior to acquisition using the decoupler offset cycling (DOCYCL) method of Kinns and Sanders[123]. The results obtained (Table 7) fully support the proposed structure **B** (equivalent of **59**) implying that the structural assignments of Fournier[113b] (structure A in Scheme 22) and Berthelot[113c] were incorrect.

Table 7

NOE Analysis of 57 (R = Ph)[a]

Proton irradiated	Proton observed	% NOE
H_2	H_3	0
	H_4	4.1
	H_5	0
	$H_{5'}$	0
	OH	0
H_3	H_2	0
	H_4	0
	H_5	1.9
	$H_{5'}$	0
	OH	11.6
H_4	H_2	3.1
	H_3	0
	H_5	0
	$H_{5'}$	6.3
	OH	0
H_5	H_2	0
	H_3	2.6
	H_4	0
	$H_{5'}$	25.8
	OH	3.0
$H_{5'}$	H_2	2.6
	H_3	0
	H_4	11.9
	H_5	30.0
	OH	0

[a] Refer to the proposed structure B in Scheme 22

The same NOE technique was also applied to compound **61** which is the major alkaline dehydration product of the previously investigated cyclic ketol **59**. The results (Table 8) confirm *trans* stereochemistry at C-4 and C-5 positions.

Table 8

NOE Analysis of 61[a]

Proton(s) irradiated	Proton(s) observed	% NOE
H_5	$H_4 + H_3$	2.9
$H_4 + H_3$	H_5	3.3
	$H_{3'}$	35.6
$H_{3'}$	$H_4 + H_3$	18.1
	H_5	0

[a] Refer to the proposed structure of **61** in Scheme 23.

However, another inconsistency in the literature has been encountered. The ^1H NMR spectrum of **61** disclosed by Mirek and co-workers[117] contains proton assignments. The authors assigned the up-field signals (i.e., 3.25 ppm) to the H_4 proton attributing the multiplet at 3.90 ppm to both methylenic H_3 and $H_{3'}$ (see Table 9 and Scheme 23).

Table 9

Comparison of Proton NMR Chemical Shift Assignments of 61 Obtained from Dehydration of 57 (equivalent of 59):

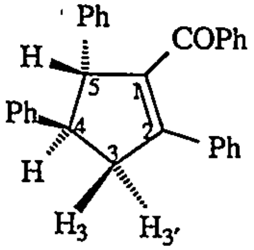
(*i*)[a] Refluxing in EtONa / EtOH[117],

(*ii*)[b] Under Phase Transfer Conditions (5N NaOH, C_6H_6, TBAHS, 60 °C, N_2)

Proton	H_5		H_4		H_3		$H_{3'}$	
	(*i*)	(*ii*)	(*i*)	(*ii*)	(*i*)	(*ii*)	(*i*)	(*ii*)
Chemical shift [ppm]	4.60 (m)	4.62 (m)	3.25 (m)	3.67 (m)	3.90 (m)	3.67 (m)	3.90 (m)	3.17 (m)

[a]80 MHz, ^1H ($CDCl_3$, TMS). [b]300 MHz, ^1H ($CDCl_3$, TMS).

Proposed structure of **61**

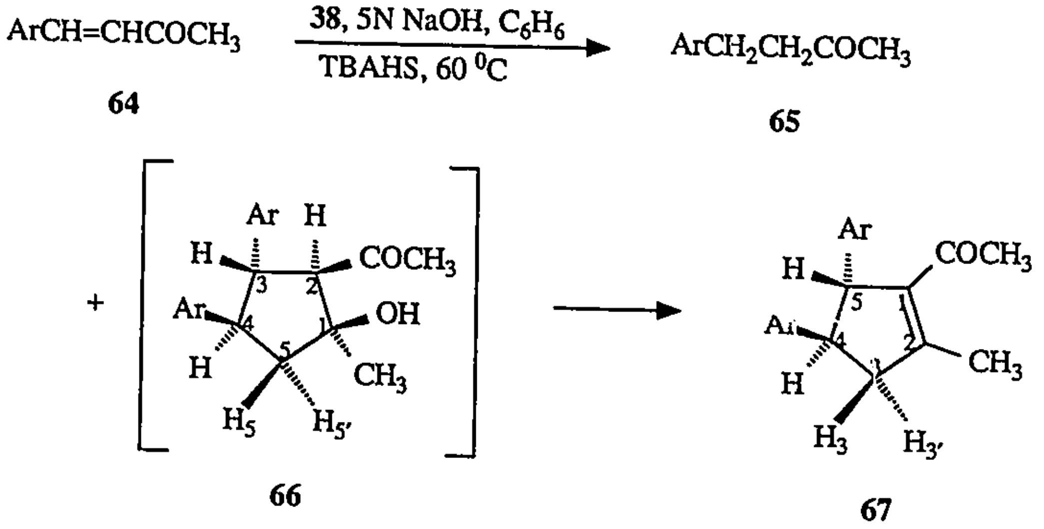


Scheme 23

What the current analysis revealed, and the Heteronuclear Correlation (HETCOR) experiment confirmed, is that the C-3 carbon contains two protons resonating around 3.20 and between 3.61 to 3.73 ppm respectively, thus implying that the multiplet between 3.61 and 3.73 ppm is a result of the overlaping signals from H_4 and H_3.

If one assumes that **59** and its dehydration product **61** arise via cyclization of **63** (i.e., **38** is required for forming **62** and **63** only, not involving the cyclization process) then the substitution of the benzoyl unit of the reactant by acyl should facilitate cyclic ketol (**57**) formation and/or its dehydrated analogues.

When **64** was applied as a substrate (Ar = Ph), 1-acetyl-2-methyl-*trans*-4,5-diphenylcyclopentene (**67**, Ar = Ph) was isolated in 70% yield together with 21% of the saturated ketone **65** (Ar = Ph).



The presence of both **38** and a phase transfer agent were necessary in order to achieve this transformation. This was fully demonstrated by appropriate control experiments conducted either without the phase transfer agent or in the absence of vanadium carbonyl **38**. In the former case, only traces of products were detected while the latter resulted in the complete retardation of the above reaction. The replacement of nitrogen for the carbon monoxide atmosphere had very little influence on the final product yield. Running the reaction at room temperature instead of 60 ^{0}C resulted in a significantly reduced reaction rate. It is worthwhile noting that the analogue of ketol **59** (i.e., **66**, Ar = Ph) has been isolated from the reaction mixture when the reaction was conducted using benzylideneacetone and a four-fold excess of the organic phase (i.e., lower effective base concentration).

trans-Diarylcyclopentenes **67** were isolated as major products from the reaction of a series of unsaturated ketones of structural type **64**, in which the arene ring contained an electron-donating or-withdrawing functionality (see Table 10 for results).

Table 10

Synthesis of 65 and 67 from 64 and 38 using Phase Transfer Conditions

Reference #	$ArCH=CHCOCH_3$ Ar =	Ratio of **64 : 38**	Reactn. time, h	Yield of products, % **65**	**67**
3.5.3	Ph	3.3	0.16	21	70
3.5.5	Ph	2.9	20.5[a]	5	44
3.5.6	Ph	2.9	0.25[b]	18	74
3.5.7	$p-ClC_6H_4$	4.7	1.0	9	71
3.5.8	$p-CH_3OC_6H_4$	4.3	1.0	32	68
3.5.9	$p-CH_3C_6H_4$	6.3	2.0	13	68
3.5.10	$p-CH_3C_6H_4$	8.6	2.0[b]	13	87
3.5.11	$2,4-(CH_3)_2C_6H_3$	4.1	2.0	25	34

[a] Room temperature. [b] CO atmosphere.

The stereochemistry of **67** was established on the basis of several spectral techniques. The infrared spectra of **67** displayed an intense carbonyl stretching band arround 1670 cm^{-1}. The NMR spectra were in accord with assigned structures. For example, the proton spectra displayed characteristic resonances and coupling constants for the appropriately substituted cyclopentene ring. The mass spectra also showed correct molecular ion peaks. The final support came from the X-ray analysis of **67** (Ar = 2,4-$(CH_3)_2C_6H_3$) showing all the spatial arrangements and distances of the cyclopentene ring (Figure 2 and Table 11).

Figure 2

ORTEP Diagram of 67 (Ar = 2,4-$(CH_3)_2C_6H_3$)

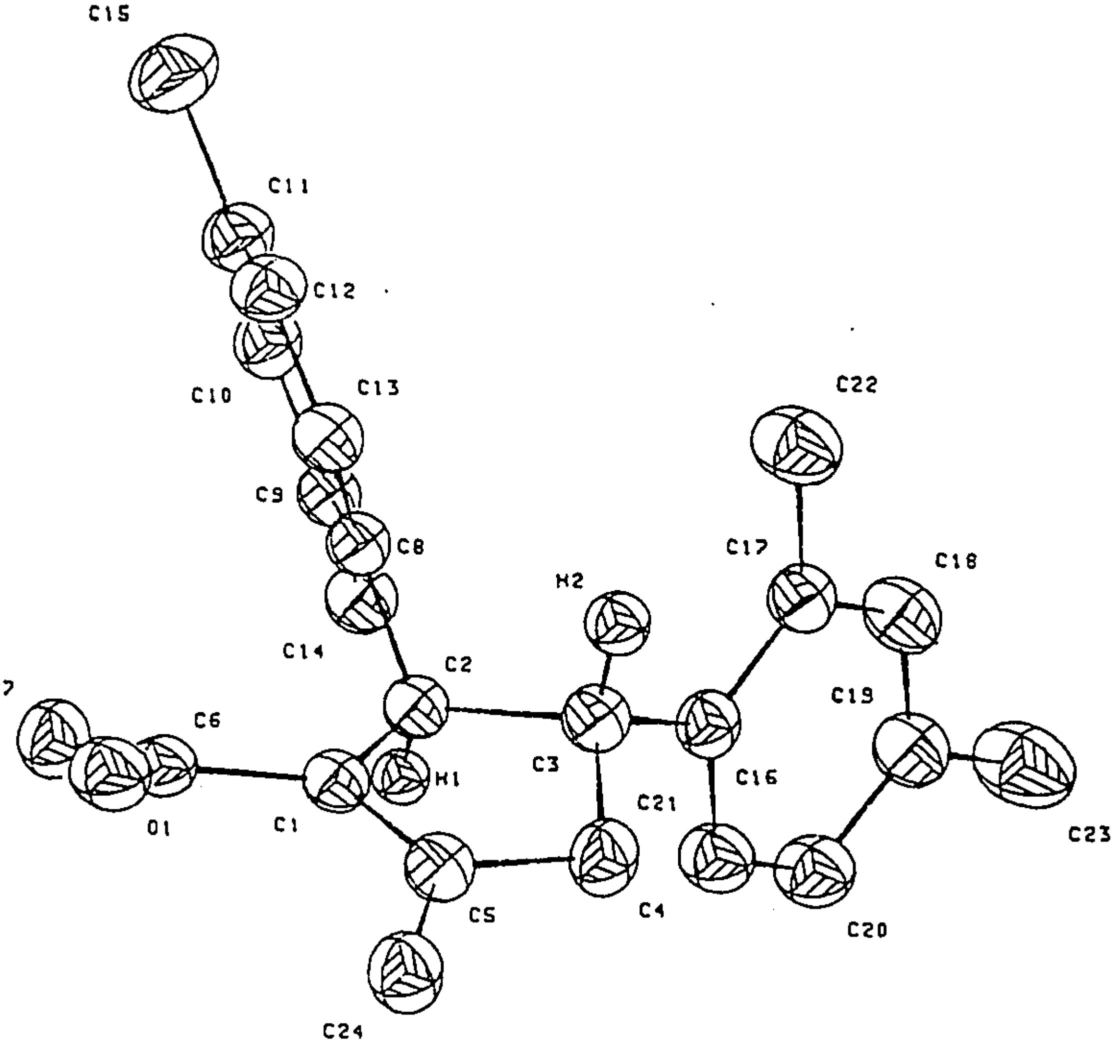


Table 11

Selected Interatomic Distances for 67 (Ar = 2,4-$(CH_3)_2C_6H_3$)

Bond	Length, Å[a]
C(1) - C(2)	1.521
C(1) - C(5)	1.340
C(1) - C(6)	1.483
C(2) - C(3)	1.560
C(2) - C(8)	1.513
C(3) - C(4)	1.538
C(3) - C(16)	1.514
C(4) - C(5)	1.498
C(5) - C(24)	1.496
C(6) - C(7)	1.493
C(6) - O(1)	1.222
C(8) - C(9)	1.397
C(8) - C(13)	1.399
C(9) - C(10)	1.392
C(9) - C(14)	1.508
C(10) - C(11)	1.389
C(11) - C(12)	1.383
C(11) - C(15)	1.509
C(12) - C(13)	1.379
C(16) - C(17)	1.402
C(16) - C(21)	1.394
C(17) - C(18)	1.396
C(17) - C(22)	1.505
C(18) - C(19)	1.388
C(19) - C(20)	1.386
C(19) - C(23)	1.506
C(20) - C(21)	1.376

[a] The e.s.d's range between 0.002 - 0.003Å.

The important difference between these reductive cyclization reactions and previously described dehalogenations or reductions of nitroarenes is that the former were semicatalytic, while the latter were stoichiometric. The substrate ratios (**64** to **38**) were as high as 8.6 : 1.0 (Table 10).

The stoichiometries of these reactions, as well as the product distribution, changed markedly when the methyl substituent was present on the double bond of **64**.

$$\underset{\mathbf{68}}{PhCR^1{=}CR^2COCH_3} \xrightarrow[\text{TBAHS, 60 }^0\text{C, N}_2\text{, 1 atm.}]{\mathbf{38}\text{, 5N NaOH, C}_6\text{H}_6} \underset{\mathbf{69}}{PhCHR^1\text{-}CHR^2COCH_3}$$

No cyclic derivatives were detected in this case, as the only isolated product was the saturated ketone **69** (Table 12).

Table 12

Synthesis of 69 from 68 and 38 using Phase Transfer Conditions

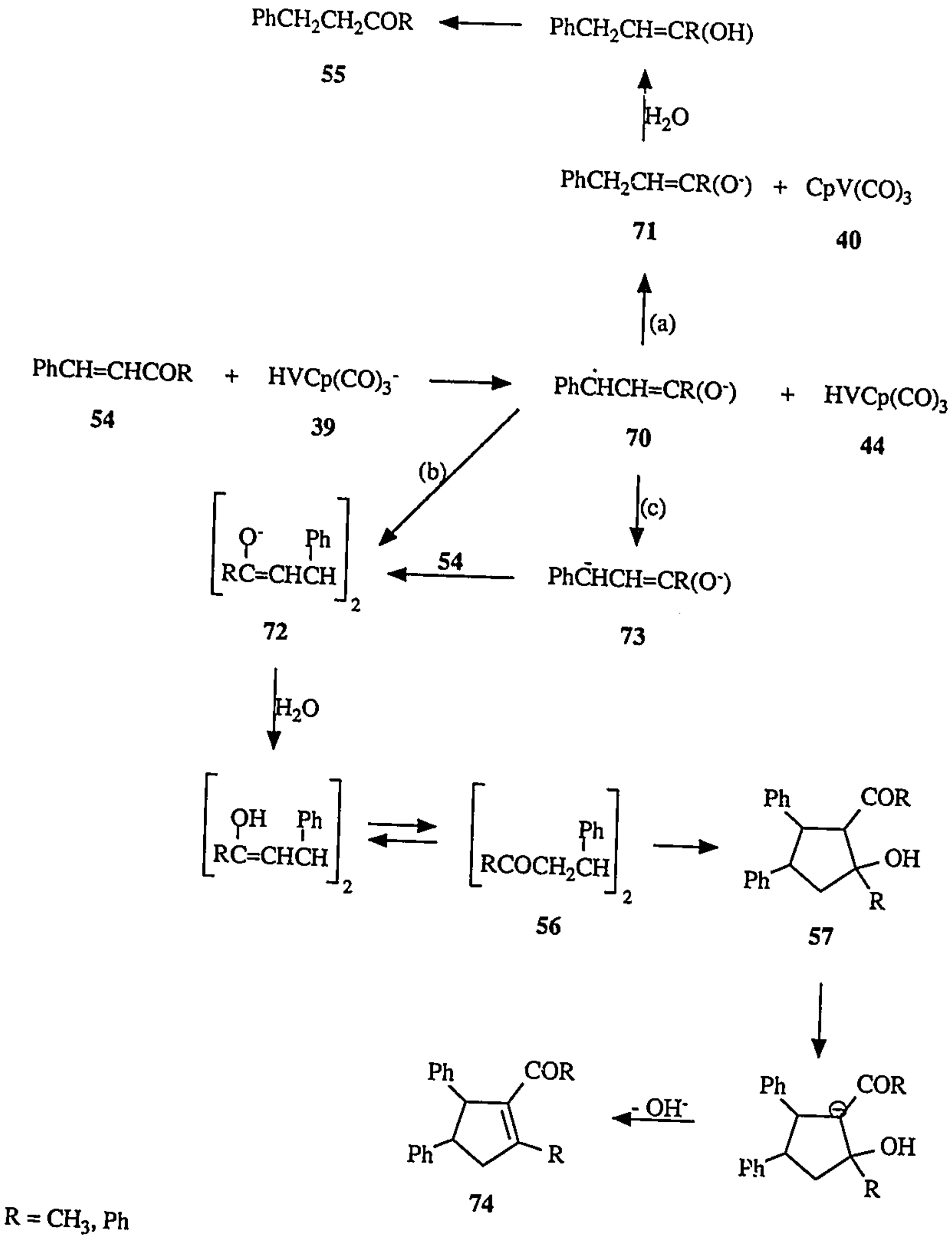
Reference #	$PhCR^1{=}CR^2COCH_3$		Ratio of **68 : 38**	Reactn. time, h	Yield of **69**, %
	R^1 =	R^2 =			
3.5.12	CH_3	H	1.0	5.0	71
3.5.13	H	CH_3	1.0	5.0	86

These results compare favorably with the phase transfer hydrogenation system involving hydridocobaltate anion[50], where among analogs of **68**, only compounds having a substituent at an α-carbon gave reaction, while cases involving α,β-unsaturated ketones where the β-position was substituted reacted sluggishly, if at all.

The unsuccessful attempt using 2-cyclohexenone was the only example involving an α,β-unsaturated ketone in homogeneous vanadium hydride reactions[99a]. When 2-cyclohexenone was treated with an equimolar amount of cyclopentadienylvanadium tetracarbonyl (**38**) under phase transfer conditions (5N NaOH, C_6H_6, TBAHS, 60 ^{0}C, 1 atm., N_2) reduction of the double bond occurred and cyclohexanone was formed in 82% yield. Similar reduction took place when 2-cyclopentenone was used as a starting material, affording cyclopentanone in 80% yield.

As previously mentioned, a possible mechanism for the reaction of α,β-unsaturated ketones (e.g., **54**) with *in situ* generated **39**, may involve the intermediacy of a radical species. Scheme 24 outlines this possibility.

The single electron transfer from hydride **39** to **54** would generate the benzyl radical enolate **70** and **44**. Path **a** envisages the hydrogen atom transfer leading to **71**, the protonation of which results in saturated ketone **55** formation. Alternatively, the dimerization of **70** may afford **72** (path **b**), which is the precursor of isolated **66** (R = Ph), and cyclic products **57** and **74**. Path **c** represents an electrochemically known[113d] second electron transfer to **70** affording dianion **73** which can undergo Michael addition to the substrate **54**, also giving **72**.


PhCH₂CH₂COR
55
PhCH₂CH=CR(OH)
H₂O
PhCH₂CH=CR(O⁻)
+
CpV(CO)₃
71
40
(a)
PhCH=CHCOR
+
HVCp(CO)₃⁻
54
39
PhĊHCH=CR(O⁻)
+
HVCp(CO)₃
70
44
(b)
(c)
O⁻
Ph
RC=CHCH
2
72
54
PhC̄HCH=CR(O⁻)
73
H₂O
OH
Ph
RC=CHCH
2
Ph
RCOCH₂CH
2
56
Ph
COR
OH
Ph
R
57
Ph
COR
Ph
R
74
- OH⁻
Ph
COR
OH
Ph
R
R = CH₃, Ph

Scheme 24

The processes described in this section affect the generation of $HVCp(CO)_3^-$ under remarkably simple and mild conditions. The use of a biphasic methodology avoids the requirements for anhydrous, inert-atmosphere conditions or the use of several-step processes involving amalgam or dispersion techniques. In addition, this research has demonstrated the utility of the *in situ* generated hydride for dehalogenation reactions, the very efficient reduction of sterically encumbered nitro compounds, and the stereospecific, semicatalytic, cyclodehydration of α,β-unsaturated ketones. Moreover, the described reactions represent the first examples of the use of phase transfer catalysis in the area of the early-transition-metal chemistry.

2.1.2.4 The Role of Phase Transfer Catalysts in Two Phase Redox Reactions

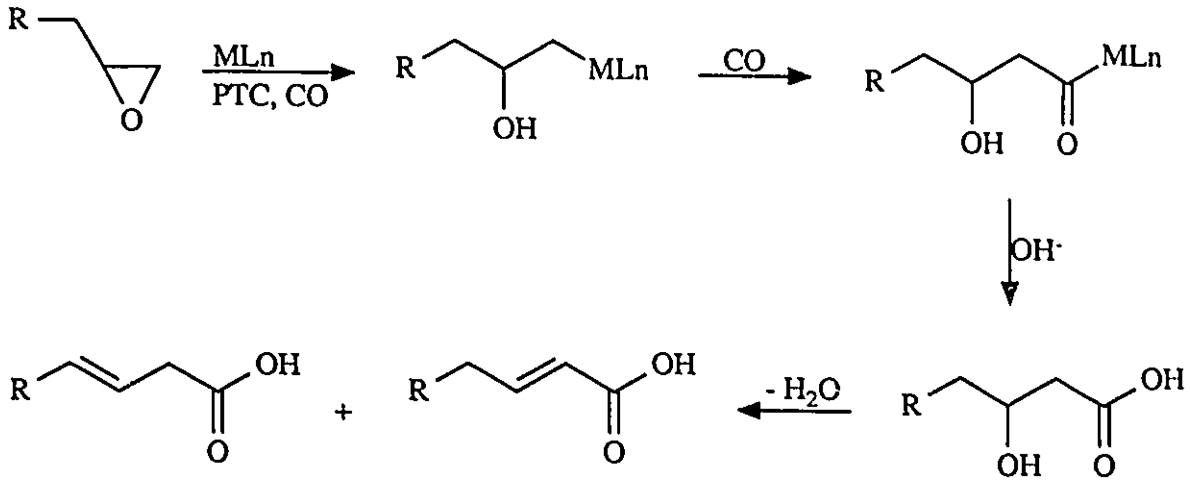
Traditionally, in phase transfer redox reactions, it has been considered that the role of the phase transfer agent is to transfer the aqueous redox species to the organic phase. It is also believed that such species, being in the form of ion pairs with lipophilic cations, assure good contact between corresponding anions and an organic substrate. Such contact is often difficult to achieve in polar solvents due to the high degree of aggressiveness of redox anions. On the other hand, the phase transfer methodology not only enables reactions to occur, which were impractical under homogeneous conditions, but often (which was also shown for vanadium hydride 39), improves results with respect to yields and the selectivity of the final product. In addition to the examples already given in the introductory chapter, it is worthwhile to mention permanganate[124] and hypochlorite[125] as oxidants or BH_4^- anions[126] as reducing agents. The scope of application of these reagents in organic synthesis have been considerably expanded by the use of PTC.

Evem as the number of applications grows there is very little information available about the mechanism of such processes. In a recent report, Schiffrin and co-workers[127] questioned the traditionally accepted view of mass transfer in PTC, proposing a mechanism based on heterogeneous electron transfer between redox centres occurring across immiscible phases. In Schiffrin's opinion, the quaternary ammonium cation plays the role of partitioning ion, fixing the interfacial Galvani potential difference, thereby enabling heterogeneous electron transfer to take place. He also argues that oxidizing ions, such as permanganate, have relatively small standard Gibbs energies of transfer $\Delta^{o}{}_{w}G^{0}{}_{t,i}$ (o = organic and w = aqueous, respectively), and that makes them naturally more abundant in the organic phase. This does not necessarily mean that it is a prerequisite for the redox reaction to occur. Although voltammetric experiments confirmed the main idea of electron transfer between two phases, this has only been described for organic solvents having high dielectric constants (e.g., >9). For the general application of this concept, additional clarification is needed. Nevertheless, it has been shown that the homogeneous mechanism is not necessarily the only possible reaction pathway for two phase redox reactions.

2.2 Two-Phase System and $Ni(CO)_3(CN)^-$ Catalyzed Rearrangement and Carbonylation of Vinyl Epoxides

The objective of the second project was to effect the carbonylation of epoxides by the use of a catalytic-two-phase system. The anticipated β-hydroxy acids constitute an important class of intermediates[128].

Recently, it has been found that *in situ* generated nickel cyanotricarbonyl anion (Scheme 5) is an efficient catalyst for carbonylation of allylic halides[33], allylic alcohols[38] and benzyl chlorides[101] under biphasic or phase transfer conditions. In cases where allylic halides or alcohols were used as starting materials, isomeric (*cis/trans*) mixtures of unsaturated acids were the isolated products. It seemed conceivable that the above mentioned acids could also be obtained using suitable epoxides, via the β-hydroxy acid intermediate **75** (Scheme 25).



75

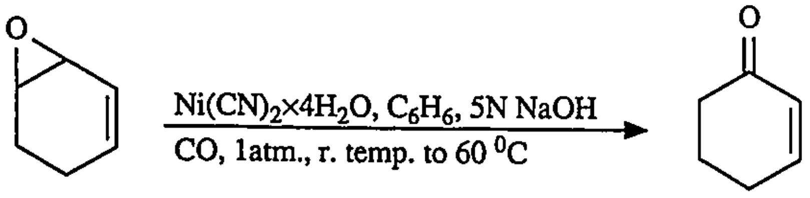
R = Alkyl group

MLn = Transition metal complex

Scheme 25

On the other hand, it is known[40] that cobalt carbonyl anion, generated under the PTC conditions, can effect the synthesis of β-hydroxy acids from vinyl epoxides, albeit in modest yields. The putative behaviour of previously mentioned nickel cyanide, under two-phase system conditions, was a stimulant towards its application for the carbonylation of epoxides.

Contrary to the unfunctionalized epoxides, the monoepoxide of 1,3-cyclohexadiene reacted in a facile and clean manner affording rearrangement product (2-cyclohexenone) instead of the hydroxy acid.



The presence of a phase transfer agent was not required in this reaction. On the contrary, it was found that the yield of 2-cyclohexenone decreased when CTAB or TBAHS were added to the reaction mixture (3.6.3, 3.6.4 and 3.6.6, 3.6.7 in Table 13). Other findings were that the presence of nickel(II) salt, cyanide ions, carbon monoxide atmosphere and the alkaline aqueous medium were all essential components in this process. The absence of any of these ingredients resulted in the complete lack of reaction (3.6.10 - 3.6.13). The yield of the final product could be increased by conducting the reaction at elevated temperatures (3.6.1, 3.6.2, 3.6.5 and Figure 3) and by using an increased proportion of nickel catalyst to starting material. For example a 25:1 ratio of starting material to catalyst afforded 2-cyclohexenone in 80% yield, while a 5:1 ratio resulted in a yield of 86% (3.6.8 and 3.6.2 respectively).

It was found that in order to achieve high conversion in this process, the presence of carbon monoxide was necessary throughout the reaction (i.e., not only for generation of the active species, but evidently also for its re-generation). This was demonstrated by conducting the following experiment: The reaction system was exposed to the carbon monoxide atmosphere during the initial 40-50 min. of the induction period. Then, just prior to addition of the starting material, the gas valves were switched, in order to replace carbon monoxide by nitrogen. Progress of this reaction was monitored by gas chromatography and the results are shown in Figure 4.

The amount of product formed was conveniently expressed in precent yield units, indicating the actual yield of 2-cyclohexenone at a given time. For the reaction initiated using CO, and then conducted under nitrogen atmosphere, the process of isomerization, most probably, continued until the dissolved carbon monoxide which was present in the system was consumed (the complete lack of CO gas renders this reaction impossible - 3.6.12 in Table 13). The yield of 2-cyclohexenone was only 33% in this case. On the other hand, when the same reaction was repeated under carbon monoxide, the yield of isomerization product increased to 86%.

Table 13

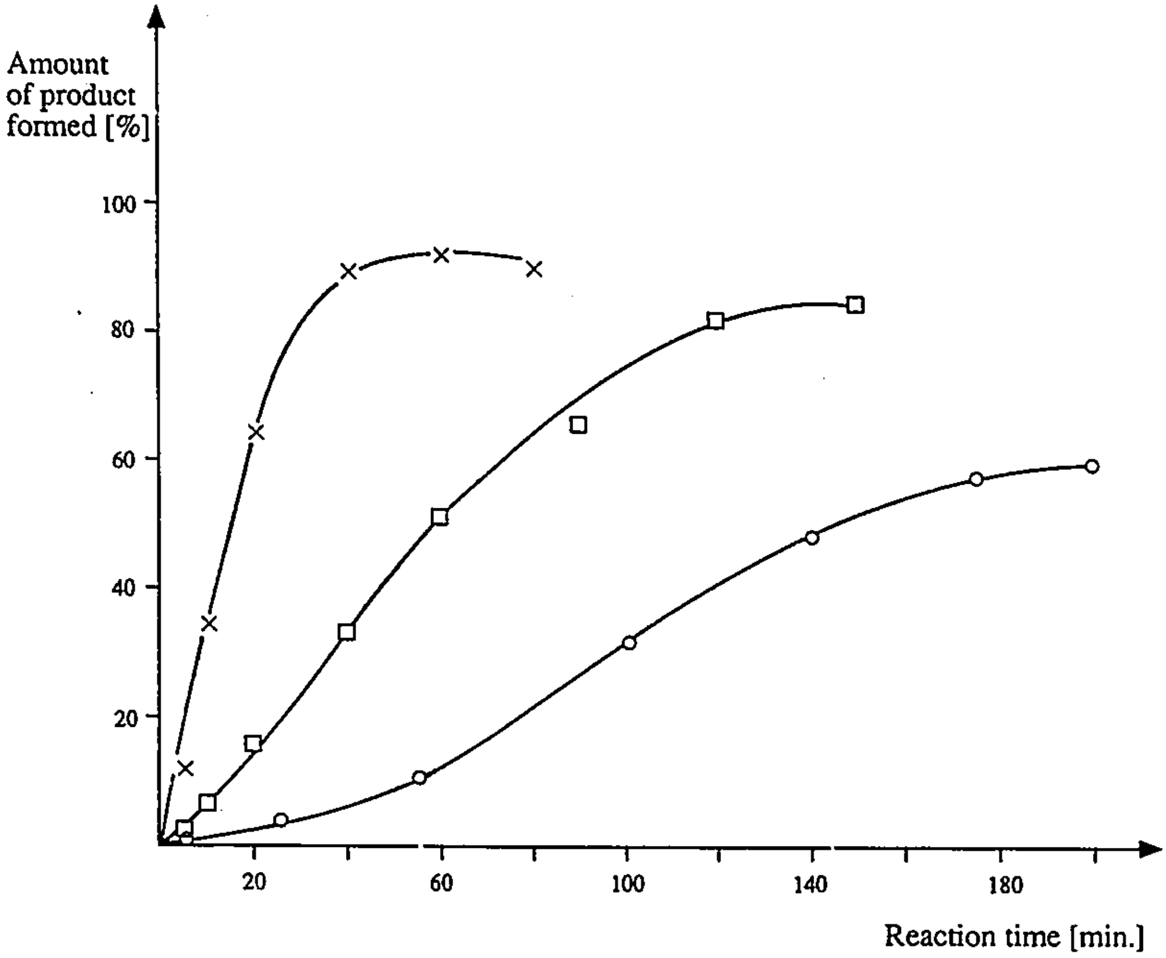
Influence of Reaction Conditions on the Nickel Catalyzed Isomerization of 3,4-Epoxycyclohexene[a]

Reference #	Reactn. time, h	Yield of 2-cyclohexenone, %
3.6.1	1.0	93[b]
3.6.2	2.5	86
3.6.3	1.5	66[c]
3.6.4	2.0	73[d]
3.6.5	3.5	63[e]
3.6.6	5.0	30[c,e]
3.6.7	5.0	39[d,e]
3.6.8	2.0	80[f]
3.6.9	2.0	44[g]
3.6.10	no reaction[h]	-
3.6.11	no reaction[i]	-
3.6.12	no reaction[j]	-
3.6.13	no reaction[k]	-
3.6.14	1.5	71[k,l]

[a] Only changes to the following reaction conditions: substrate/$\mathrm{Ni(CN)_2}$ = 5:1, C_6H_6, 5N NaOH, CO, 1 atm., 60 °C, are indicated. [b] Reaction at 69 °C. [c] CTAB added. [d] TBAHS added. [e] Room temperature (23 °C). [f] Substrate/$\mathrm{Ni(CN)_2}$ = 25:1. [g] 0.5 N NaOH. [h] $H_2O_{(dist.)}$ used as aqueous phase. [i] No Ni salt used. [j] Nitrogen atmosphere. [k] $\mathrm{NiBr_2}$ used as Ni salt. [l] KCN added.

Figure 3

Effect of Temperature on the Formation of 2-Cyclohexenone During Nickel Cyanide and Carbon Monoxide Catalyzed Isomerization of 3,4-Epoxycyclohexene under Biphasic Conditions



○ Reaction conducted at 23 ^{0}C,

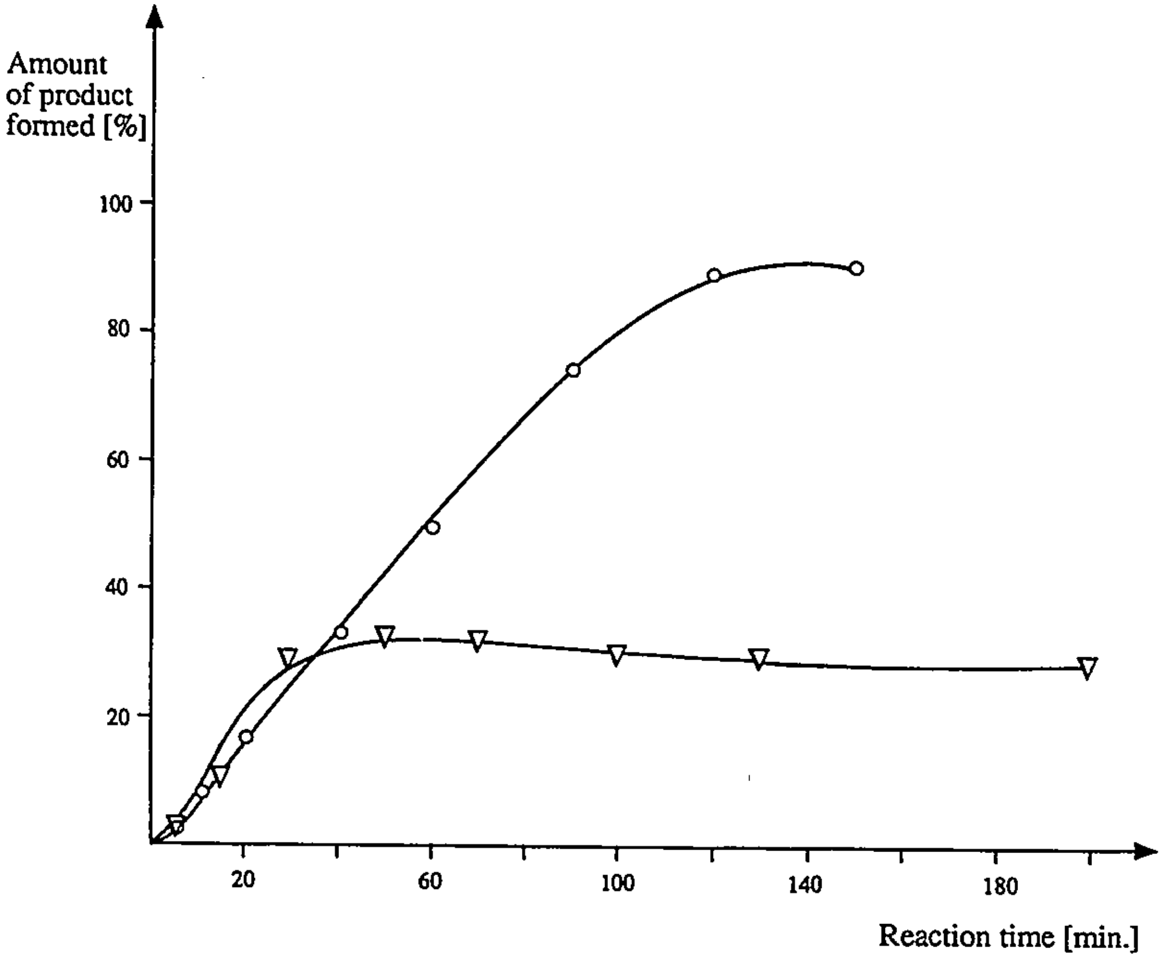
☐ Reaction conducted at 57 ^{0}C,

× Reaction conducted at 69 ^{0}C

Points connected for clarity

Figure 4

Plots of the Product Formation vs. Time during Nickel Catalyzed Isomerization of 3,4-Epoxycyclohexene - Effect of Carbon Monoxide

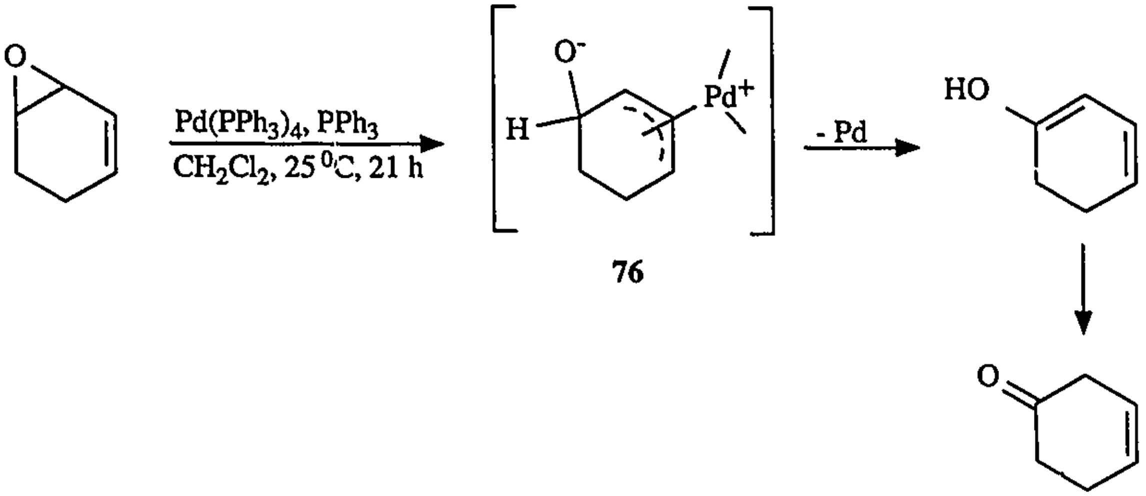


○ Reaction conducted under standard conditions (i.e., footnote (a) in Table 14),

▽ First 40 min. of induction period under carbon monoxide, then nitrogen atmosphere

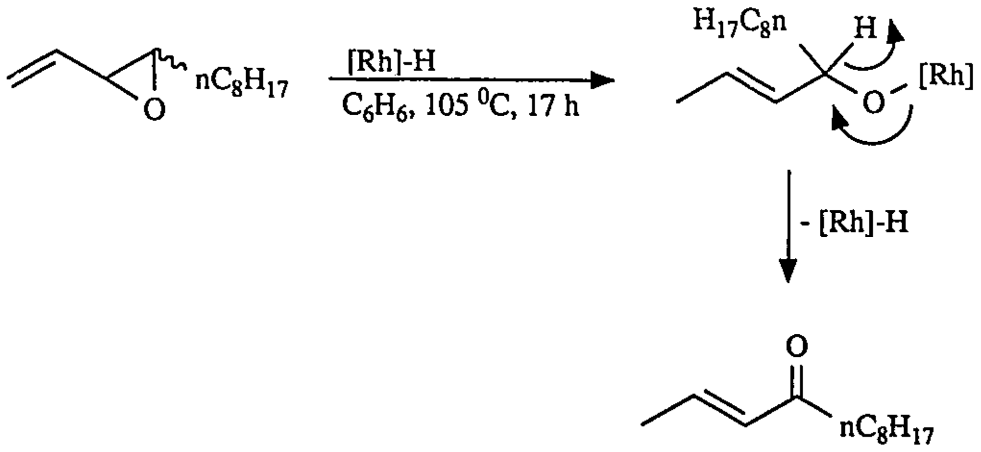
Points connected for clarity

The observed rearrangement of vinyl epoxide to the unsaturated carbonyl compound represents one of a few known examples[129-132], where a transition metal catalyst affects a similar reaction. None of these reports, however, are based on a catalytic-two-phase-system which was utilized here. For example, Noyori[131] used tetrakis(triphenylphosphine)palladium under homogeneous conditions and the β,γ-unsaturated carbonyl compounds were among the isolated rearrangement products.



The palladium π-allyl complex **76** was proposed as a reaction intermediate.

On the other hand, conjugated carbonyl compounds resulted when $HRh(PPh_3)_4$ was used as a catalyst toward isomerization of vinyl epoxides[132].

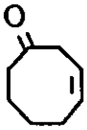
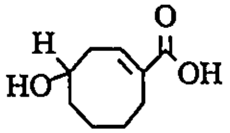
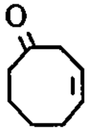
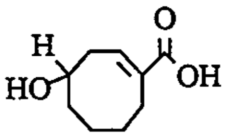
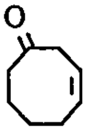
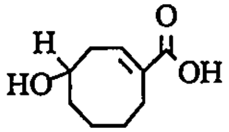


In this case Matsuda[132] proposed that Michael type addition took place and the subsequent elimination of rhodium hydride was responsible for the observed reaction. While other open chain vinyl epoxides also gave isomerization products in good yields, the corresponding cyclic derivatives did not react at all under similar reaction condition. Those findings contrasted strikingly with results obtained by Noyori, where cyclic vinyl oxiranes were found to be the most reactive compounds.

In the light of the above results it was interesting to learn how the reactivity of cyclic vinyl epoxides could be affected by the size of the ring in the nickel catalysed reaction. The five-membered ring epoxide was found to be the most reactive, as the isomerization process could be conducted at room temperature and required only 25 minutes for its completion. Very interesting results were obtained when larger ring cyclooctadiene epoxide was applied as a substrate. Two products resulted from this reaction: The first one, isolated from the organic phase, was the isomerization product, possessing unsaturation at the β,γ-position, while the second and the major one, was obtained after acidification of the aqueous layer. Its spectral characteristics clearly showed that it was a carbonylation product - the unsaturated δ-hydroxy acid (unsaturation at the α,β-position). Interestingly, the presence of TBAHS, as the phase transfer agent, favored the carbonylation reaction. Those and other results, using cyclic vinyl oxiranes, are collected in Table 14.

Table 14

Reactions of Cyclic Vinyl Epoxides Catalyzed by Nickel Cyanide and Carbon Monoxide under Biphasic or Phase Transfer Conditions[a]

Reference #	Vinyl epoxide	Reactn. time, h	Product(s)	Yield, %
3.6.16	3,4-epoxycyclopentene	0.4[b]	2-cyclopentenone	65
3.6.1	3,4-epoxycyclohexene	1.0[c]	2-cyclohexenone	93
3.6.17	3,4-epoxy-5,5-dimethylcyclohexene	5.5	6,6-dimethyl-2-cyclohexenone	67
3.6.18	3,4-epoxy-3,4-dimethylcyclohexene	(22)	o-xylene	(5)
			3,4-dimethylcyclohexa-1,3-diene	(8)
3.6.19	3,4-epoxycyclooctene	22		24
				60
3.6.20	3,4-epoxycyclooctene	15.5[d]		55
				20.5
3.6.21	3,4-epoxycyclooctene	(46)		(10)
				(74)

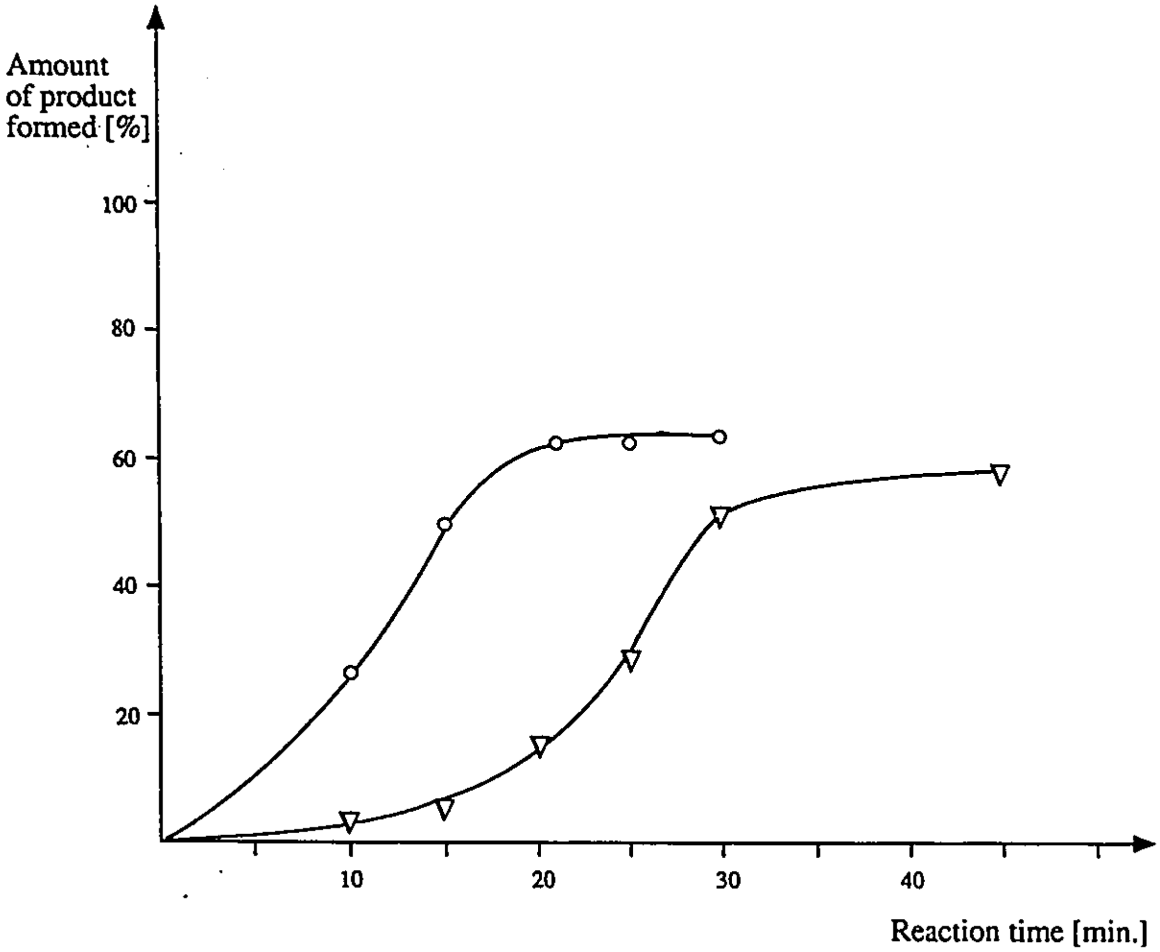
[a] Reaction conditions as described in Table 13, except where noted otherwise; numbers in parentheses refer to the reaction conditions when TBAHS was added as phase transfer agent. [b] Room temperature. [c] 69 °C. [d] Reaction scale was doubled.

From these experiments, only the use of cyclooctadiene epoxide led to the isolation of the hydroxy acid product. As previously stated, the yield of hydroxy acid increases when a phase transfer agent, such as TBAHS, is added to the reaction mixture; this increase, however, takes place at the expense of a longer reaction time. Interestingly, doubling the reaction scale shortens the reaction time as well as reversing the product distribution (3.6.20 in Table 14). In this situation, the rearrangement product becomes the dominant one, probably as a result of decreased effectiveness in mixing. It was expected that using substituted cyclic vinyl epoxides, such as 3,4-epoxy-3,4-dimethylcyclohexene (3.6.18), would hinder the isomerization process and more hydroxy acid product could be formed. However, contrary to these expectations, the reaction was sluggish and only small amounts of o-xylene and 3,4-dimethylcyclohexa-1,3-diene were isolated as products. The usual isomerization products were formed when substituents were present on the six-membered ring, but not at the epoxide carbons (i.e., 3.6.17).

All reactions had an induction period of 40-50 minutes, the importance of which was demonstrated by the use of 3,4-epoxycyclopentene, both with and without the applied induction period (Figure 5).

Figure 5

Influence of Induction Period on the Reactivity of 3,4-Epoxycyclopentene during Rearrangement under Biphasic Conditions[a]



○ 40 min. of induction period applied,

∇ No induction period applied

[a]Reaction conditions as described in Table 14

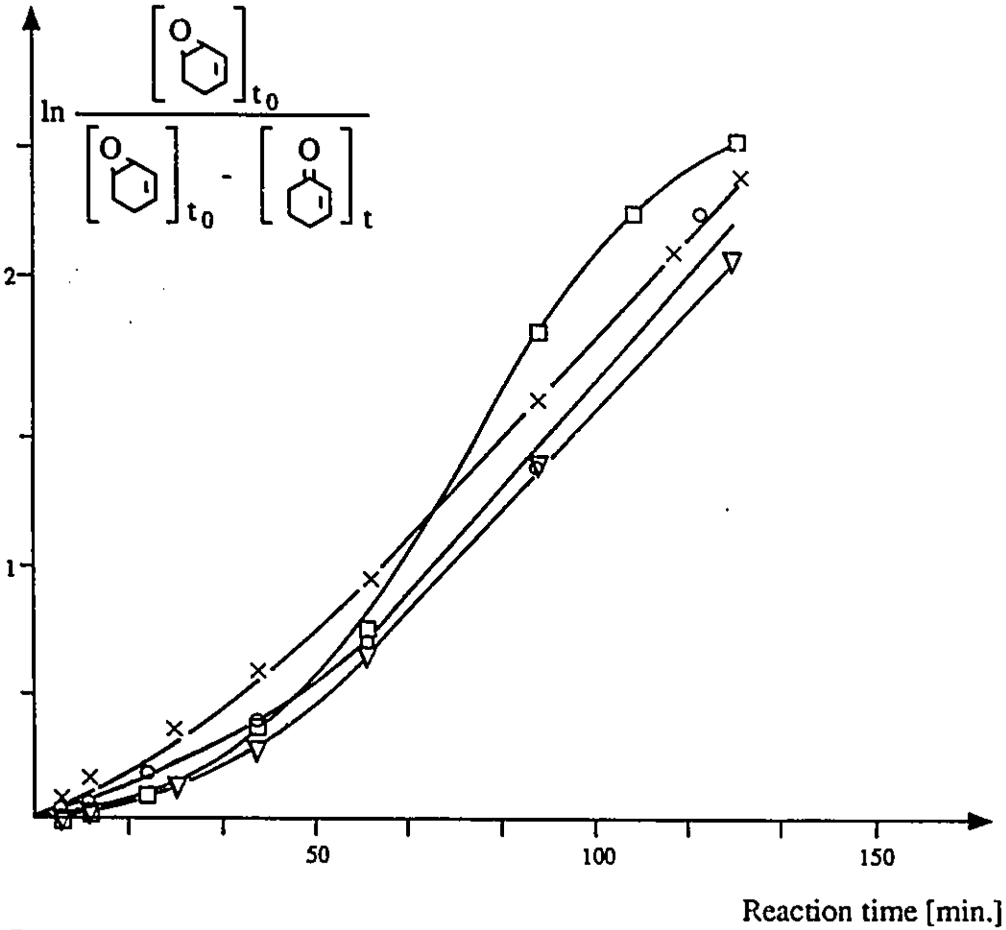
Points connected for clarity

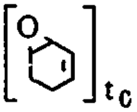
As can be seen from the plots in Figure 5, the reaction performed without an induction period required a longer time and afforded the product in lower yields.

As stated previously, monitoring of the reaction rate as a function of the stirring speed could provide insight into the two-phase system reaction mechanism (i.e., extraction vs. interfacial). According to the generally accepted view, biphasic reactions, including isomerization of a vinyl epoxide, should show some rate dependence on the stirring speed. This was indeed the case when a series of experiments were conducted using 3,4-epoxycyclohexene as a model reactant. The results shown in Figure 6 were plotted assuming the reaction was first order and the conversion of the vinyl epoxide to the corresponding rearrangement product was quantitative. The expected dependence is best seen in the initial forty to fifty minutes of reaction time. After that time departure from linearity occurs (the most pronounced corresponding to the reaction performed at 450 RPM). The reactivity of the system also depends on the stirring speed during the induction period (compare cases: induction period at 450 RPM and reaction at 1000 RPM vs. induction period at 700 RPM and reaction at 1000 RPM).

Figure 6

Dependence of the Pseudo First Order Kinetics on the Stirring Rate in the Isomerization of 3,4-Epoxycyclohexene



 = Initial concentration of 3,4-epoxycyclohexene,

 = Concentration of 2-cyclohexenone at time t

□ Induction period at 700 RPM, reaction at 450 RPM,

○ Induction period at 700 RPM, reaction at 700 RPM,

× Induction period at 700 RPM, reaction at 1000 RPM,

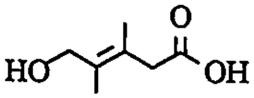
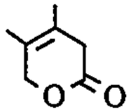
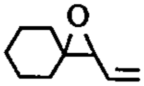
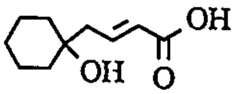
∇ Induction period at 450 RPM, reaction at 1000 RPM

Points connected for clarity

Generally, lower yields of the final products resulted when acyclic vinyl oxiranes were employed as substrates (Table 15).

Table 15

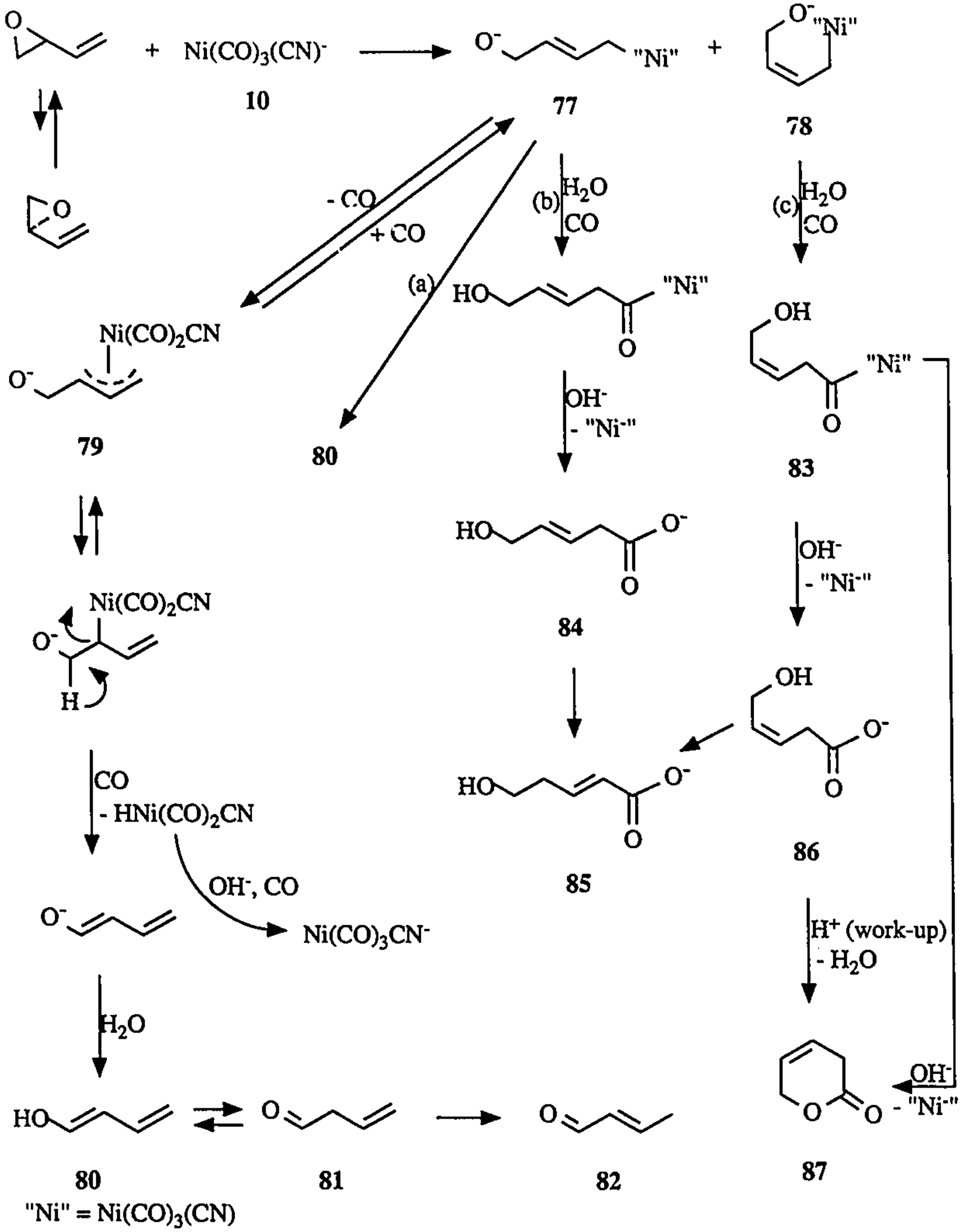
Reactions of Acyclic Vinyl Epoxides Catalyzed by Nickel Cyanide and Carbon Monoxide under Biphasic or Phase Transfer Conditions[a]

Reference #	Vinyl epoxide	Reactn. time, h	Product(s)	Yield, %
3.6.24	3,4-epoxy-pentene	4.0	E-2-pentenal	18
3.6.25	3,4-epoxy-3-methyl-butene	2.5	E-2-methyl-2-butenal	45
3.6.26	3,4-epoxy-3-ethyl-butene	5.0	E-2-ethyl-2-butenal	12
3.6.27	3,4-epoxy-2,3-dimethyl-butene	14	polymer-like tar	0
3.6.28	3,4-epoxy-2,3-dimethyl-butene	(14)		(19)
				(39)
3.6.29		(22)		(40)

[a] Reaction conditions as described in Table 13; numbers in parentheses refer to reaction conducted in the presence of TBAHS.

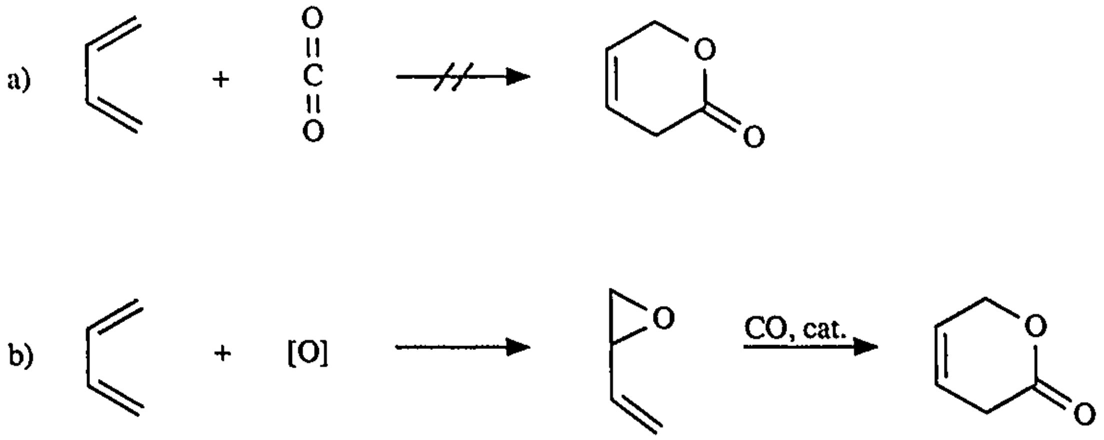
While pentadiene epoxide, isoprene oxide, and its ethyl analogue, 3,4-epoxy-3-ethyl-butene (3.6.24, 3.6.25 and 3.6.26 in Table 15, respectively), rearranged to the corresponding aldehydes, 3,4-epoxy-2,3-dimethylbutene polymerized under the same reaction conditions (3.6.27). The course of this reaction markedly changed when a PTC agent was added. Although there were no products in the organic phase, the acidification of the aqueous layer afforded two compounds. One was the hydroxy acid derivative (19% yield) and the second appeared to be a six-membered ring lactone (39% yield - 3.6.28). Using 3′-vinylcyclohexanespiro-2′-oxirane as the substrate afforded a single, carbonylated product, albeit in 40% yield (3.6.29). The identity of the all products (listed in both Tables 14 and 15), were unambiguously established based on spectral results and by elemental analyses in some cases. In addition, the structure of 4-hydroxy-1-cyclooctenyl carboxylic acid was confirmed using the Relayed Coherence Transfer-COSY (RCT-COSY) spectroscopy[133] (see attached spectra).

The fact that δ-hydroxy acids were among the isolated products of the vinyl epoxide and nickel catalysed reactions suggests that the unsaturated functionality of the latter was attacked by the *in situ* generated catalyst **10** (e.g., via Michael type addition). A mechanism, consistent with this possibility, has been proposed in order to explain the isomerization and/or carbonylation of vinyl epoxides. Although the type and number of substituents on the vinyl epoxide seem to determine the final outcome of its reaction with **10**, for clarity reasons the vinyl epoxide depicted in Scheme 26 does not carry any substituents (the generation of **10** was previously described in Scheme 5).


+
Ni(CO)3(CN)-
10
O-
"Ni"
+
O-
"Ni"
77
78
- CO
+ CO
(a)
(b) H2O
CO
(c) H2O
CO
Ni(CO)2CN
O-
79
80
HO
"Ni"
O
OH
"Ni"
O
83
OH-
- "Ni-"
HO
O-
O
84
OH-
- "Ni-"
OH
O-
O
86
HO
O-
O
85
Ni(CO)2CN
O-
H
CO
- HNi(CO)2CN
OH-, CO
Ni(CO)3CN-
O-
H2O
H+ (work-up)
- H2O
OH-
- "Ni-"
O
O
87
HO
O
O
80
81
82
"Ni" = Ni(CO)3(CN)

Scheme 26

The initial Michael type attack of **10** on both conformers of the vinyl epoxide may produce a mixture of isomeric (*cis/trans*) σ-allyl intermediates **77** and **78**. Under a CO atmosphere, each of these intermediates can exist in equillibrium with its corresponding π-allyl derivative. For example, **77** loses a carbonyl ligand to produce **79**, which in turn can be a source of either **77** or **78** via π-allyl to σ-allyl interchange and rotation about the C3-C4 bond. In this manner, certain equilibria between **77** and **78** may develop. Similar equilibria involving vinyl epoxides and iron pentacarbonyl have been described in the literature[134]. If there is an interaction between an oxygen and a nickel centre within complex **78**, its stabilizing effect may determine the dominance of this structure over **77**. The intermediate **79** and/or its σ-allyl derivative can eliminate catalyst **10** (under CO) producing the rearrangement product **80**, which tautomerizes to its keto form **81**. Under alkaline, aqueous conditions this β,γ-unsaturated carbonyl compound can rearrange to the corresponding conjugated derivative, **82**. The possibility also exists that either **77** or **78** could eliminate **10** and thus also generate the rearrangement product (path **a** envisages such a process involving **77**). On the other hand, as represented by the parallel paths **b** and **c**, such σ-allyl complexes can undergo carbon monoxide insertion forming the carboxylate derivatives **84** and **86** having *trans* and *cis* double bond geometries, respectively. Unlike the rearrangement product **81** which resides in the organic phase, these carbonylation products would be present in the aqueous layer. Both **84** and **86** would also be subject to the analogous **81-82** rearrangement, which may lead to **85** in either case. During acidic work-up, the *cis* isomer **86** may cyclize, affording the unsaturated δ-lactone **87**. Another plausible route to this lactone would be the intramolecular cyclization of **83**, which is competitive with nucleophilic attack of hydroxide ions[135]. However, should this be the case, then the unsaturated δ-lactone thus formed could be hydrolyzed by base to the carboxylate **86** and stay in this form until further acidic work-up regenerates the lactone. It is worthwhile noting that in 1979 the vinyl oxirane approach to the unsaturated δ-lactone formation was independently studied by Aumann[134] and Ley[136]. Their goal was to achieve a transformation equivalent to a formal [4+2]-cycloaddition of 1,3-diene and carbon dioxide[137] (path **a** in Scheme 27).



Scheme 27

In both reports, however, an excess of iron carbonyl was required to prepare the complex and drastic conditions (200 bar, 75 °C)[134] or UV irradiation[136] were necessary in the carbonylation step.

Seemingly trivial, the β,γ to α,β isomerization of carbonyl compounds, such as **81** to **82** or **84** to **85**, requires separate attention.

In most of the cases which are listed in Tables 14 and 15, the α,β-unsaturated carbonyl compounds constitute the isolated products. Exceptions include 3-cyclooctenone as the rearrangement product of 3,4-epoxy-cyclooctene (3.6.19 - 3.6.21 in Table 14) and both carbonylation products obtained from 3,4-epoxy-2,3-dimethylbutene (3.6.28 in Table 15). The lack of β,γ to α,β isomerization in the first mentioned case could be explained knowing that in the medium (7 - 10 carbon) size ring cycloalkenones, the effectiveness of conjugation between the carbonyl and the olefin decreases with increasing ring size[138]. Because of this effect, 2-cyclooctenone would be destabilized relative to the 3-cyclooctenone. In the second, noted exception, the carbonylation products contained non-conjugated double bonds substituted at both the β and γ positions which made them stable to isomerization. The experimental results suggest that β,γ-unsaturated carbonyl compounds are the kinetic products of the nickel catalysed reactions of vinyl epoxides under phase transfer or biphasic conditions. Although there is a distinct possibility that β,γ to α,β isomerization of the double bond could be mediated by the metal complex[130] (i.e., **10**), the same process has been well documented to occur under both biphasic and phase transfer conditions, promoted by base[33,37,38]. Moreover, when non-conjugated 3-cyclohexenone was submitted to the reaction conditions described in Table 13, but in the absence of the nickel salt, and stirred for five minutes, it resulted in the complete isomerization of the reactant to the corresponding 2-cyclohexenone (evidenced by IR and ^1H NMR spectroscopies).

As previously noted, and also shown in Tables 14 and 15, the presence of a phase transfer catalyst changes the distribution of rearrangement and carbonylation products. A possible explanation of this phenomenon could be that the lipophilic quarternary ammonium salt helps remove the carboxylate anion from the organic phase (or the interphase) once it is formed there, and thus shifts the equilibrium towards the CO insertion product[28].

In conclusion, the catalytic processes described in Chapter 2.2 convert vinyl epoxides to unsaturated ketones and/or unsaturated δ-hydroxy acids and their cyclic esters in yields ranging from 12 to 93%. The biphasic or phase transfer systems applied offer mild conditions and ease of final product separation. These results represent the first examples of the use of transition metals and the catalytic-two-phase system in the area of isomerization of vinyl epoxides. To this author's knowledge, the formation of unsaturated δ-hydroxy acids has not been observed previously, either under biphasic or phase transfer conditions.

2.3 Metal and Phase Transfer Catalyzed Reactions Invoiving Nitric Oxide

In recent years, there has been significant interest in the study of transition metal nitrosyls and reactions involving coordinated nitric oxide[103,104,139]. The reasons for this are, to some extent, due to a better understanding of the way NO binds to transition metals, which apart from having some similarities, is distinctively different to that of CO (NO having an additional electron can function as an electron donor, giving NO^+, or an electron acceptor, giving NO^-)[140]. Another stimulus to investigating NO chemistry comes from the area of pollution control[139a] (e.g., diminishing NO emission from combustion engines). However, what seems to be particularly exciting for the organic chemist is the developement of synthetic methods for the production of organo-nitrogen compounds from nitric oxide in reactions assisted by transition metal catalysts.

Transition metal anions play a central role in the formation of metal-carbon bonds[141]. If metal-carbon bond arrangement is envisaged to be preceding ligand migratory insertion (i.e., coordinated NO)[103], then the formation of a C-N linkage seems possible. Another way of achieving C-N bond formation could be realized by addition of alkyl halide to the NO moiety of the nitrosyl complex[139b].

Phase transfer catalysis is a widely used technique in organic synthesis for the generation of metal containing anions under exceptionally mild conditions. As already described (section 1.2.1), one of the most valuable applications of this type of chemistry is in carbonylation processes. It seemed conceivable, therefore, that use of nitric oxide instead of carbon monoxide would result in novel and useful chemistry.

When nitric oxide was bubbled through a solution of t-pentyl alcohol containing benzyl bromide **88** (Ar = Ph), tetrakis(triphenylphosphine)palladium(0), 3N aqueous sodium hydroxide, and TBAHS as the phase transfer agent, for 17 hours at room temperature, the O-benzyl oxime ether **89** (Ar = Ph) was isolated in 38% yield (3.7.5 in Table 16).

$$\underset{\mathbf{88}}{\mathrm{ArCH_2Br}} \quad + \quad \mathrm{NO} \quad \xrightarrow[\text{3N NaOH, t-pentyl alcohol, r. temp.}]{\mathrm{Pd(PPh_3)_4,\ PPh_3,\ TBAHS}} \quad \underset{\mathbf{89}}{\mathrm{ArCH{=}NOCH_2Ar}}$$

Oxime ether formation, however, was accompanied by several by-products, among which dibenzyl ether and benzyl alcohol were most abundant. Small amounts of benzaldehyde were also identified in this reaction. The reactions conducted using equimolar amount of phosphine relative to $Pd(PPh_3)_4$ afforded less dibenzyl ether as the by-product. Tri-n-butylphosphine appeared to be almost as useful as triphenylphosphine (3.7.6 vs. 3.7.5 in Table 16). Use of benzyltriethylammonium chloride as the phase transfer agent also gave less dibenzyl ether (3.7.1 - 3.7.3); however, the amounts of oxime ether were also reduced. The latter was not formed in the absence of the quaternary ammonium salt (3.7.7) and it was detected only in trace amounts when toluene was used as the organic solvent (3.7.2). Its yield was also significantly lower using methylene chloride as the organic phase (3.7.3). The absence of palladium catalyst and triphenylphosphine gave oxime ether, but only in 8% yield (3.7.10). Several other metal catalysts were found to be useful in promoting the conversion of benzyl bromide into oxime ether. These are listed in Table 17 and include: bis(dibenzylideneacetone)palladium(0) [$Pd(dba)_2$], dichlorotris(triphenylphosphine)-ruthenium, dinitrosylbis(triphenylphosphine)ruthenium and the dimer of chloro(hexa-1,5-diene)rhodium(I) [$Rh(hd)Cl]_2$.

Table 16

Influence of Reaction Conditions of the Palladium Catalyzed Reaction on Benzyl Bromide with Nitric Oxide[a]

Reference #	Reactn. time, h	PPh_3	Yield of **89** (Ar = Ph), %[b]	Yield of other products, %[b] $(PhCH_2)_2$	$PhCH_2OH$
3.7.1	45	NO	20[c]	1	n. d.[d]
3.7.2	18	NO	Trace[c,e]	Trace	37
3.7.3	18	NO	14[c,f]	Trace	Trace
3.7.4	17	NO	23	25	26
3.7.5	17	YES	38	4	30
3.7.6	17	YES	36[g]	3	n. d.[d]
3.7.7	17[h]	YES	-	Trace	Trace
3.7.8	17	YES	Trace[i]	Trace	37
3.7.9	17	YES	27[j]	4	22
3.7.10	17	NO	8[k]	13	35

[a] Only changes to the following reaction conditions: substrate/$Pd(PPh_3)_4$/PPh_3/TBAHS = 25:1:1:2, 3N NaOH, t-pentyl alcohol, room temperature, are indicated. [b] Yields determined by GC. [c] TEBACl as phase transfer agent. [d] Yield not determined. [e] Toluene as the organic solvent, 55 ^{0}C. [f] CH_2Cl_2 as the organic solvent. [g] PBu_3 as the phosphine. [h] No phase transfer agent added. [i] 1N NaOH. [j] 5N NaOH. [k] No $Pd(PPh_3)_4$ used.

Table 17

Metal Complex and Phase Transfer Catalyzed Reactions of Benzyl Bromide with Nitric Oxide[a]

Reference #	MLn	PPh_3	Yield of **89** (Ar = Ph), %[b]	Yield of $(ArCH_2)_2O$, %[b]
3.7.11	$Pd(dba)_2$	NO	30[c]	6
3.7.12	$RuCl_2(PPh_3)_3$	NO	31	5
3.7.13	$RuCl_2(PPh_3)_3$	YES	29[d]	16
3.7.14	$Ru(NO)_2(PPh_3)_2$	YES	32[d]	5
3.7.15	$[1,5\text{-HDRhCl}]_2$	NO	26[c]	12

[a] Using 3N NaOH, t-pentyl alcohol, room temperature, 25:1:2 = substrate/MLn/TBAHS ratio, for 17 hours. [b] Yields determined by GC. [c] 42 hours reaction. [d] PPh_3 added in equimolar amount to MLn.

It is interesting to note that the reactions catalyzed by ruthenium complexes were not affected by the presence of added triphenylphosphine (3.7.12 - 3.7.15 in Table 17).

Oxime ethers were isolated in 25 - 40% yields from a variety of benzylic bromides using tetrakis(triphenylphosphine)palladium and triphenylphosphine as the metal catalyst system, and tetrabutylammonium hydrogen sulphate as the phase transfer agent (Table 18).

Table 18

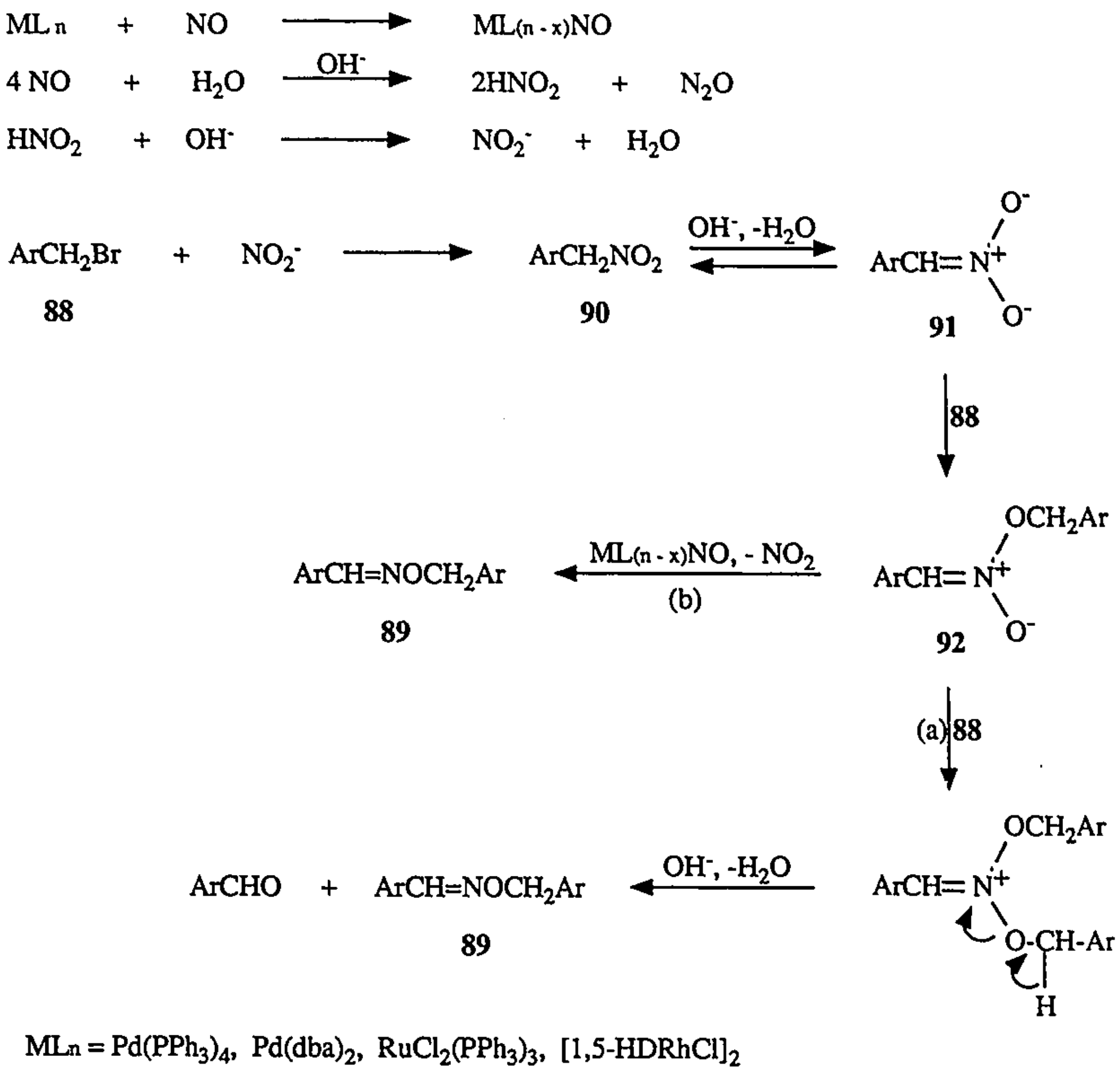
Palladium and Phase Transfer Catalyzed Reactions of Benzylic Bromides with Nitric Oxide[a]

Reference #	Ar in 88	Yield of 89, %	Yield of $(ArCH_2)_2O$, %
3.7.16	Ph[b]	4[c]	n. d.[d]
3.7.17	$p\text{-}CH_3C_6H_4$	33	6
3.7.18	$m\text{-}CH_3C_6H_4$	40	19
3.7.19	$o\text{-}CH_3C_6H_4$	25	9
3.7.20	$p\text{-}FC_6H_4$	34	7
3.7.21	$2\text{-}C_{10}H_7$	40	n. d.[d]

[a] Reaction conditions are indicated in Table 16. [b] $PhCH_2Cl$. [c] 42 hours reaction. [d] Yield not determined.

Only 4% yield of oxime ether resulted when benzyl chloride was used as a starting material (3.7.16 in Table 18), while 1-bromonaphthalene and bromocyclohexane were inert under the same reaction conditions.

It seems reasonable to suggest that these reactions proceed by base catalysed tautomerism of the nitrosoarylmethane[142]. The benzylic oxime thus formed could then be O-alkylated under PTC conditions[143]. The above mentioned nitrosoarylmethane might arise from the *in situ* generated metal nitrosyl complex which then oxidatively adds benzyl bromide, followed by migratory insertion of NO ligand. However, the fact that even traces of a free oxime were not detected during these reactions may suggest that an alternative pathway was at work. Such a mechanism, not involving a free oxime, is outlined in Scheme 28.



Scheme 28

Although nitric oxide could be coordinated to the transition metal forming the corresponding metal nitrosyl complex ($ML_{n-x}NO$), some NO may undergo base promoted disproportionation to form nitrite ion[144]. This was verified by conducting an experiment in which 3N NaOH solution was left overnight at room temperature and nitric oxide atmosphere (no PT agent was used). Subsequent addition of PPNCl allowed isolation of $PPN^+NO_2^-$, which was positively identified by mp (223 - 226 ^{0}C, lit.[145] 225 - 226 ^{0}C) and fast atom bombardment mass spectrometry (3.7.24). Reaction of **89** with nitrite ion, under phase transfer conditions would give arylnitromethane **90** and/or its aci-form **91**. The nitronic ester **92** could be formed via alkylation under phase transfer conditions. At this point **92** could be deoxygenated by metal nitrosyl to the oxime ether **89** (path **b**) or alkylated again by another benzyl bromide molecule to afford **93**, which then could collapse to oxime ether **89** and benzylic aldehyde[146] (path **a**). The above scheme implies that nitrite ion alone (i.e., without metal complex and NO gas) can effect the same transformation as nitric oxide. It was found that sodium nitrite under phase transfer conditions could afford oxime ether in 16% yield (3.7.25), which increased to 29% when the same reaction was repeated in the presence of $Pd(PPh_3)_4$ (3.7.26). This yield was lower than the 38% obtained using NO under similar conditions (3.7.5 in Table 16) and may suggest that some nitric oxide, in addition to being converted to NO_2^-, can contribute to the conversion of the halide into oxime ether.

Despite the fact that the product yields are rather modest, the described reaction system represents the first examples of the successful application of nitric oxide in phase transfer catalysis. Furthermore, this is the first example of a catalytic reaction of halides with free or co-ordinated nitric oxide (and nitrite).

CHAPTER 3

Experimental Data

3.1 General Comments

Infrared spectra were recorded on either a Perkin Elmer 783 spectrometer calibrated with external polystyrene standard or a Nicolet MX-1, FT spectrometer. NMR (^{1}H and ^{13}C) spectra were recorded on EM 360A, Varian T-60, Gemini 200, or Varian XL-300 spectrometers. Chemical shifts were reported relative to TMS. Gas chromatography was performed on Varian Vista 6000, Varian 3300, and Varian 3400 chromatographs, each equipped with a flame ionization detector and a Varian 4270 integrator. The columns used for the analyses included a DB-1 megabore column and a number of glass packed columns with the following packing materials: 3% OV-17 on Chromosorb W, HP; OV-101 on Chromosorb W; 5% Carbowax 20 M on Chromosorb G, AW DMCS; 3% SP-2300 on 100/120 Supelcoport. Mass spectra were obtained on a VG 707 E mass spectrometer. A Fisher-Johns apparatus was used for melting point determinations. MHW Laboratories (Phoenix, Arizona) or Guelph Chemical Laboratories (Guelph, Ontario) performed the elemental analyses, while the single crystal X-ray analysis was obtained from Simon Fraser University, Burnaby, British Columbia.

Some of the organic reactants, such as benzylidene acetone derivatives[148] or vinyl epoxides[136], were prepared by literature methods or were purchased from commercial sources: Aldrich Chemical Co., Fairfield Chemical Co., Lancaster Synthesis Ltd., and Wiley Organics. Cyclopentadienylvanadium tetracarbonyl was either synthesized following a literature procedure[147] or purchased from Strem Chemical Co. Hydrated nickel cyanide was purchased from Fisher Scientific Co., and dichlorotris(triphenylphosphine)ruthenium was supplied by Aldrich Chemical Co. The dinitrosylbis(triphenylphosphine)ruthenium[149], the dimer of chloro(hexa-1,5-diene)rhodium(I)[150], bis(dibenzylideneacetone)palladium(0)[151] and tetrakis(triphenylphosphine)palladium(0)[152] were prepared by literature procedures. Phase transfer catalysts were purchased from commercial sources and were used as received. Carbon monoxide and nitric oxide were supplied by Air Products Co. and Matheson Co., respectively. Thin-layer chromatographic plates (silica gel) were purchased from Terochem Co., or were hand-made using 60 PF-254 silica gel containing $CaSO_4$ supplied by BDH Inc. Organic solvents were purified by standard methods. All the deuterated solvents were purchased from MSD Isotopes.

3.2 Synthesis of $HVCp(CO)_3^-$ under Biphasic Conditions

3.2.1 Synthesis of $[HVCp(CO)_3]^-[(C_4H_9)_4N]^+$

A mixture of benzene (10ml) and 5N NaOH (10ml) was deoxygenated using a nitrogen stream. Cyclopentadienylvanadium tetracarbonyl (0.228g, 1.0 mmol) was then added, followed by tetrabutylammonium hydrogen sulfate (0.363g, 1.10 mmol) and the reaction mixture was stirred overnight at room temperature. The organic phase was concentrated without separation from the aqueous phase, and the resulting mixture was filtered using Schlenk techniques to afford a yellow solid. The latter was washed with water (3 × 10 ml) and cold ether, and then vacuum dried to give bright yellow $HVCp(CO)_3^-(C_4H_9)_4N^+$ in 87% yield. IR (CH_3CN): ν_{CO} 1887, 1776 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.68 (s; 5H, C_5H_5), - 6.28 (s, broad; 1H, HV).

3.2.2 Synthesis of $[HVCp(CO)_3]^-[(Ph_3P)_2N]^+$

A mixture of 0.228g (1.0 mmol) of cyclopentadienylvanadium tetracarbonyl in benzene (10 ml) and 5N NaOH (10ml) was heated at 60 ^{0}C for 2 hours under nitrogen. The resulting mixture consisted of a light yellow organic phase and an intense red-orange aqueous phase. Addition of 0.574g (1.0 mmol) of bis(triphenylphosphine)nitrogen(1+) chloride resulted in a dark brown suspension. After cooling to room temperature, both phases were filtered in a Schlenk tube under nitrogen and the resulting solid was washed first with 5% NaOH (3 × 10 ml) and then with a cold diethyl ether (2 × 5 ml). Drying under vacuum gave 0.502g (68%, based on $CpV(CO)_4$) of orange $[HVCp(CO)_3]^-[(Ph_3P)_2N]^+$. IR (THF): ν_{CO} 1890, 1780 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.44 (s; 5H, C_5H_5), -6.23 (s, broad; 1H, HV).

3.3 Vanadium and Phase Transfer Catalyzed Dehalogenation of RX

General Procedure

The following general procedure was used. Nitrogen was bubbled for 15 minutes through a mixture of benzene (10 ml) and 5N NaOH (10 ml) containing tetrabutylammonium hydrogen sulfate (0.85g, 0.25 mmol) in a 50 ml, three necked, round bottom flask. Cyclopentadienylvanadium tetracarbonyl (0.228g, 1.0 mmol) was then added and the temperature of the stirred mixture was gradually increased to 60 ^{0}C. The halide (1.0 mmol) was added and the reaction mixture was stirred for the period indicated in Tables 2 or 3. As the reaction proceeded, the colour of the organic phase turned from orange to pale yellow. After being cooled to room temperature, the phases were separated. The organic phase was washed with brine and dried (Na_2SO_4). Quantitative analysis was accomplished either by GC (vs. p-xylene, butylbenzene or mesitylene as the internal standard) or by direct isolation of the final product. The crude material from the rotary evaporator was purified by preparative thin-layer chromatography (silica gel) or by distillation. The following subsections provide relevant details for each experiment; the results of all these reactions have been tabulated: Table 2 (page 48) and Table 3 (page 50).

3.3.1 2-Methylnaphthalene

Dehalogenation of 2-bromomethylnaphthalene afforded 2-methylnaphthalene in 76% yield. ^{1}H NMR ($CDCl_3$): δ 2.47 (s; 3H, CH_3), 7.19-7.90 (m; 7H, aromatic protons); MS: m/e 142 $[M]^+$.

3.3.2 2-Methylnaphthalene

When the dehalogenation of 2-bromomethylnaphthalene was carried out as described in 3.3 except that the halide to cyclopentadienylvanadium tetracarbonyl ratio was 1:0.8, 2-methylnaphthalene was obtained in 66% yield.

3.3.3 2-Methylnaphthalene

When the dehalogenation of 2-bromomethylnaphthalene was performed as described in 3.3 except that the halide to cyclopentadienylvanadium tetracarbonyl ratio was 1:0.3, 2-methylnaphthalene was obtained in 32% yield.

3.3.4 2-Methylnaphthalene

The absence of cyclopentadienylvanadium tetracarbonyl during dehalogenation of 2-bromomethylnaphthalene when carried out as described in 3.3 suppressed the yield of 2-methylnaphthalene to nil.

3.3.5 2-Methylnaphthalene

Repetition of the experiment (3.3.1) using dimethyldodecylethylammonium bromide as the phase transfer catalyst afforded 2-methylnaphthalene in 69% yield.

3.3.6 2-Methylnaphthalene

Repetition of experiment (3.3.1) using TEBACl as the phase transfer catalyst afforded 2-methylnaphthalene in 22% yield.

3.3.7 2-Methylnaphthalene

Repetition of experiment (3.3.1) using PEG-400 as the phase transfer catalyst reduced the yield of 2-methylnaphthalene to nil.

3.3.8 2-Methylnaphthalene

Repetition of experiment (3.3.1) except that no phase transfer catalyst was used gave 2-methylnaphthalene in 7% yield.

3.3.9 2-Methylnaphthalene

Carrying out the same experiment as described in 3.3.1 except for the use of 2N NaOH afforded 2-methylnaphthalene in 14% yield.

3.3.10 2-Methylnaphthalene

Repetition of experiment (3.3.1) except for the use of 8N NaOH gave 2-methylnaphthalene in 72% yield.

3.3.11 2-Methylnaphthalene

Repetition of experiment (3.3.1) at room temperature produced 2-methylnaphthalene in 60% yield.

3.3.12 2-Methylnaphthalene

Dehalogenation of 2-bromomethylnaphthalene was carried out as described in (3.3.1) except that carbon monoxide was used instead of nitrogen, affording 2-methylnaphthalene in 92% yield.

3.3.13 2-Methylnaphthalene

Repetition of experiment (3.3.12) using a 1 : 0.5 ratio of halide to cyclopentadienylvanadium tetracarbonyl gave 2-methylnaphthalene in 50% yield.

3.3.14 1-Methylnaphthalene

Dehalogenation of 1-(chloromethyl)naphthalene afforded 1-methylnaphthalene in 74% yield. ^{1}H NMR ($CDCl_3$): δ 2.63 (s; 3H, CH_3), 7.16-7.95 (m; 7H, aromatic protons); MS: m/e 142$[M]^+$.

3.3.15 Diphenylmethane

Dehalogenation of bromodiphenylmethane gave diphenylmethane in 62% yield. ^{1}H NMR ($CDCl_3$): δ 3.99 (s; 2H, CH_2), 7.23 (m; 10H, aromatic protons); MS: m/e 168 $[M]^+$.

3.3.16 p-Chlorotoluene

Dehalogenation of p-chlorobenzyl chloride gave p-chlorotoluene in 44% yield. ^{1}H NMR ($CDCl_3$): δ 2.32 (s; 3H, CH_3), 7.02-7.35 (m; 4H, aromatic protons); MS: m/e 126 $[M]^+$, 91 $[M-Cl]^+$.

3.3.17 p-Methylanisole

Dehalogenation of p-methoxybenzyl chloride afforded p-methylanisole in 50% yield. ^{1}H NMR ($CDCl_3$): δ 2.24 (s; 3H, CH_3), 3.68 (s; 3H, OCH_3), 6.63-7.06 (m; 4H, aromatic protons). In addition, analysis of the product was carried out by gas chromatography including direct comparison of mixtures to which autentic material had been added.

3.3.18 o-Xylene

Dehalogenation of o-methylbenzyl chloride afforded o-xylene in 47% yield. ^{1}H NMR ($CDCl_3$): δ 2.25 (s; 6H, CH_3's), 7.05 (s; 4H, aromatic protons); MS: m/e 106 $[M]^+$. In addition, analysis of the product was carried out by gas chromatography aided by "spiking" with authentic material.

3.3.19 Methyl phenyl sulfone

Dehalogenation of chloromethyl phenyl sulfone was carried out at room temperature as described in 3.3 and resulted in the formation of methyl phenyl sulfone in 76% yield. MS: m/e 156 $[M]^+$, 141 $[M-CH_3]^+$. GC analysis of the product indicated an identical retention time to that of the authentic material.

3.3.20 Acetophenone

Dehalogenation of o-chloroacetophenone afforded acetophenone in 39% yield. ^1H NMR ($CDCl_3$): δ 2.62 (s; 3H, $COCH_3$), 7.25-8.06 (m; 5H, aromatic protons).

3.3.21 Acetophenone

Dehalogenation of o-bromoacetophenone gave acetophenone in 54% yield.

3.3.22 Styrene

Dehalogenation of β-bromostyrene gave styrene in 88% yield. Analysis of the product was carried out by gas chromatography aided by "spiking" with authentic material and by GC/MS. ^1H NMR ($CDCl_3$): δ 5.05-5.70 (m; 2H, olefinic CH_2), 6.65 (dd; 1H, olefinic CH), 7.10-7.40 (m; 5H, aromatic protons); MS: m/e 104 $[M]^+$, 78 $[M-C_2H_2]^+$.

3.3.23 Naphthalene

Dehalogenation of 2-bromonaphthalene afforded naphthalene in 72% yield. ^1H NMR ($CDCl_3$): δ 7.15-7.80 (m; aromatic protons); MS: m/e 128 $[M]^+$. In addition, analysis of the product was carried out by gas chromatography aided by "spiking" with authentic material.

3.3.24 Cyclohexane

Dehalogenation of bromocyclohexane afforded cyclohexane in 66% yield. Analysis of the product was carried out by gas chromatography aided by "spiking" with authentic material, and also by GC/MS spectrometry. MS: m/e 84 $[M]^+$.

3.3.25 Octane

Dehalogenation of 1-bromooctane gave octane in 60% yield. Analysis of the product was carried out by gas chromatography aided by "spiking" with authentic material and by GC/MS. MS: m/e 114 $[M]^+$

3.4 Vanadium and Phase Transfer Catalyzed Reduction of Nitroarenes General Procedure

Except for the use of the nitro reactant instead of halide, the procedure was identical to that described for the dehalogenation reactions (i.e., 3.3). The yields of products were determined by gas chromatography, except where noted otherwise. Table 4 (page 53) and Table 5 (page 54) list the results of the experiments which detailed describtion is provided in the following subsections.

3.4.1 Aniline

Reduction of nitrobenzene afforded aniline in 75% yield. Analysis of the product was carried out by gas chromatography aided by "spiking" with autentic material, as well as by GC/MS. MS: m/e 93 $[M]^+$.

3.4.2 Aniline

Reduction of nitrobenzene was performed as described in 3.4 except that the reaction was carried out at room temperature. Aniline was obtained in 68% yield.

3.4.3 o-Toluidine

Reduction of o-nitrotoluene afforded o-toluidine in 83% yield. ^1H NMR ($CDCl_3$): δ 2.13 (s; 3H, CH_3), 3.45 (s, broad; 2H, NH_2), 6.45-7.10 (m; 4H, aromatic protons); MS: m/e 107 $[M]^+$.

3.4.4 m-Toluidine

Reduction of m-nitrotoluene afforded m-toluidine in 82% yield. ^1H NMR ($CDCl_3$): δ 2.29 (s; 3H, CH_3), 3.45 (s, broad; 2H, NH_2), 6.35-7.15 (m; 4H, aromatic protons); MS: m/e 107 $[M]^+$.

3.4.5 p-Toluidine

Reduction of p-nitrotoluene gave p-toluidine in 88% yield. ^1H NMR ($CDCl_3$): δ 2.22 (s; 3H, CH_3), 3.36 (s, broad; 2H, NH_2), 6.45-7.00 (m; 4H, aromatic protons); MS: m/e 107 $[M]^+$.

3.4.6 o-Anisidine

Reduction of o-nitroanisole afforded o-anisidine in 85% yield. ^1H NMR ($CDCl_3$): δ 3.70 (s, broad; 2H, NH_2), 3.80 (s; 3H, OCH_3), 6.60-6.75 (m; 4H, aromatic protons); MS: m/e 123 $[M]^+$.

3.4.7 m-Anisidine

Reduction of m-nitroanisole gave m-anisidine in 85% yield. ^1H NMR ($CDCl_3$): δ

3.50 (s, broad; 2H, NH_2), 3.70 (s; 3H, OCH_3), 6.10-7.15 (m; 4H, aromatic protons); MS: m/e 123 $[M]^+$.

3.4.8 p-Anisidine

Reduction of p-nitroanisole afforded p-anisidine in 74% yield. ^1H NMR ($CDCl_3$): δ 3.30 (s, broad; 2H, NH_2), 3.72 (s; 3H, OCH_3), 6.60-6.70 (m; 4H, aromatic protons); MS: m/e 123 $[M]^+$.

3.4.9 o-Isopropylaniline

Reduction of o-isopropylnitrobenzene afforded o-isopropylaniline in 99% yield. The isolated yield was 82%. IR (neat): ν_{NH} 3370, 3460 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.25 (d; 6H, CH_3's, J = 6.8 Hz), 2.89 (5 lines; 1H, CH, J = 6.8 Hz), 3.6 (s, broad; 2H, NH_2), 6.65-7.14 (m; 4H, aromatic protons); MS: m/e 135 $[M]^+$, 120 $[M-CH_3]^+$.

3.4.10 o-Aminobiphenyl

Reduction of o-nitrobiphenyl gave o-aminobiphenyl in 94% yield (80% of isolated yield). IR (KBr): ν_{NH} 3370, 3470 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.6 (s, broad; 2H, NH_2), 6.40-7.35 (m; 9H, aromatic protons); MS: m/e 169 $[M]^+$.

3.4.11 m-Aminobiphenyl

Reduction of m-nitrobiphenyl afforded m-aminobiphenyl in 87% yield (68% of isolated yield). MS: m/e 169 $[M]^+$.

3.4.12 2,6-Dimethylaniline

Reduction of 2,6-dimethylnitrobenzene afforded 2,6-dimethylaniline in 98% yield. IR (neat): ν_{NH} cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.15 (s; 6H, CH_3's), 6.40-6.95 (m; 3H, aromatic protons); MS: m/e 121 $[M]^+$.

3.4.13 p-Aminostilbene

Reduction of p-nitrostilbene gave p-aminostilbene in 76% of isolated yield. MS: m/e 195$[M]^+$.

3.4.14 4-$NH_2C_6H_4CH_2CH_2COPh$

Reduction of was performed as described in 3.4 except that a 2 : 1 ratio of 4-$NO_2C_6H_4CH_2CH_2COPh$ to cyclopentadienylvanadium tetracarbonyl was used. 4-$NH_2C_6H_4CH_2CH_2COPh$ was obtained in 66% yield. IR (KBr): ν_{NH} 3360, 3445 cm^{-1}, ν_{CO} 1685 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.94 (t; 2H, CH_2), 3.23 (m; 2H, CH_2), 3.6 (s, broad; 2H, NH_2), 6.60-7.95 (m; 9H, aromatic protons); MS: m/e 225 $[M]^+$.

3.4.15 Competition Experiments

Competition experiments were performed as described in 3.4 using 1:1:1 mixtures of cyclopentadienylvanadium tetracarbonyl and investigated nitroarenes. The results are listed in Table 19.

Table 19

Competition Experiments

entry	competing nitroarenes	reaction time, min.	remaining materials, (%)[a]
1	nitrobenzene vs 2,6-dimethylnitrobenzene	30	aniline (72) 2,6-dimethylnitrobenzene (100)
2	nitrobenzene vs o-isopropylnitrobenzene	60	aniline (60) nitrobenzene (6) o-isopropylaniline (25)

[a] Quantitative analyses was performed by gas chromatography.

3.4.16 p-Toluidine

p-Nitrotoluene was converted to p-toluidine by the method described in 3.4 except that tetrabutylammonium bromide used in place of tetrabutylammonium hydrogen sulfate as the phase transfer agent. p-Toluidine was obtained in 82% yield.

3.4.17 p-Toluidine

p-Nitrotoluene afforded p-toluidine in 14% yield by using method described in 3.4 except that benzyltriethylammonium chloride was applied as the phase transfer catalyst.

3.4.18 Attempted Reduction of p-Nitrotoluene under Solid/Liquid Phase Transfer Conditions

In a 50 ml three necked round bottom flask was placed 0.28g (5.0 mmol) of powdered KOH, 0.228g (1.0 mmol) of cyclopentadienylvanadium tetracarbonyl, 0.080g (0.30 mmol) of

18-crown-6, and dry benzene (25 ml) under nitrogen. The mixture was stirred for 40 minutes at room temperature, p-nitrotoluene (0.137g, 1.0 mmol) was added and the solution was then stirred for 3 hours. During that time aliquats were withdrawn for gas chromatographic analyses. The analysed samples did not show presence of any reduced material, even when the temperature was raised to 60 ^{0}C and the reaction mixture was allowed to stir for an additional 3 hours.

3.4.19 p-Toluidine

The use of PEG-400 as the phase transfer catalyst in an attempted reduction on p-nitrotoluene as described in 3.4 was unsuccessful.

3.4.20 p-Toluidine

Reduction of p-nitrotoluene as described in 3.4 except that no phase transfer agent was used afforded p-toluidine in 11% yield (180 min. reaction).

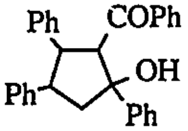
3.4.21 Comparison of the Reactivities of p-Nitrotoluene and 2,6-Dimethylnitrobenzene

The procedure described in 3.4 was followed for the reduction of p-nitrotoluene and 2,6-dimethylnitrobenzene. The two reactions were independently carried out by being placed in a common oil bath in order to minimize the effects of the temperature variations.

3.5 General Procedure for the Reaction of α,β-Unsaturated Ketones with $CpV(CO)_4$ under Phase Transfer Conditions

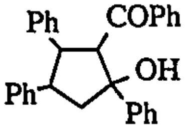
The procedure described in (3.3) for the halide reaction was followed with the following modifications: 1.0 mmol of the α,β-unsaturated ketone was used instead of halide, and less than 1.0 mmol of cyclopentadienylvanadium tetracarbonyl was used. The reagents were stirred for the period indicated in Tables 10 and 12, unless stated otherwise. A gas chromatographic analyses aided in the yield determination of the final products, except cyclic ketols, which are reported as isolated yields. The isolation of these compounds was accomplished using a Harrison 7924 chromatotron and 5:1 hexane/ethyl acetate as the developing solvent system. The following subsections provide experimental detailes of the reactions which have been tabulated: Table 10 (page 71) and Table 12 (page 74).

3.5.1 Reduction of 1,3-Diphenyl-2-propenone

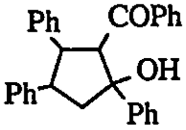
Reduction of 1,3-diphenyl-2-propenone (chalcone) afforded 1,3-diphenylpropan-1-one in 23% yield. ^1H NMR ($CDCl_3$): δ 3.06 (t; 2H, CH_2), 3.30 (m; 2H, CH_2), 7.19-7.96 (m; 5H, aromatic protons); MS: m/e 210 $[M]^+$. Appreciable quantities of two dimeric derivatives were also isolated from this reaction: 1,3,4,6-tetraphenylhexane-1,6-dione was formed in 17% yield: IR (KBr): ν_{CO} 1679 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.37 (m; 4H, CH_2's), 3.85 (m; 2H, CH's), 6.94-7.84 (m; 20H, aromatic protons); ^{13}C NMR ($CDCl_3$): δ 42.27, 42.31 (both broad, CH_2's), 45.55 (CH), 126.40, 127.79, 127.93, 128.43, 128.91, 132.87 (aromatic CH's), 136.98, 141.37 (aromatic quaternary carbons), 198.48 (CO); MS (CI/Ether): m/e 419 $[M+1]^+$. Cyclopentanol:  was isolated in 11% yield (for the stereochemistry of substitution see structure **57**(R=Ph) in Scheme 22). IR (KBr): ν_{OH} 3438 cm^{-1}, ν_{CO} 1642 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.56 (dd; 1H, H_5, $J_{H5\text{-}H5'} = 14.65$ Hz,

$J_{H5\text{-}H4}$ = 6.16 Hz), 2.98 (8 lines; 1H, $H_{5'}$, $J_{H5'\text{-}H5}$ = 14.65 Hz, $J_{H5'\text{-}H4}$ = 11.07 Hz, $J_{H5'\text{-}OH}$ = 1.22 Hz), 3.76 (6 lines; 1H, H_4, $J_{H4\text{-}H3}$ = 10.25 Hz, $J_{H4\text{-}H5'}$ = 11.07 Hz, $J_{H4\text{-}H5}$ = 6.16 Hz), 4.08 (dd; 1H, H_3, $J_{H3\text{-}H2}$ = 12.01 Hz, $J_{H3\text{-}H4}$ = 10.25 Hz), 4.51 (d; 1H, H_2, $J_{H2\text{-}H3}$ = 12.01 Hz), 5.21 (d; 1H, OH, $J_{OH\text{-}H5'}$ = 1.22 Hz), 7.02-7.57 (m; 20H, aromatic protons); ^{13}C NMR ($CDCl_3$): δ 51.45 (CH_2), 59.59 (CH), 63.63 (CH), 84.28 (C_1 of the cyclopentane ring), 124.81, 126.28, 126.85, 126.94, 127.55, 127.84, 128.02, 128.08, 128.27, 128.32, 128.37, 133.19, (aromatic CH's), 137.50, 139.77, 143.87, 145.18 (aromatic quaternary carbons), 204.77 (CO); MS: m/e 400 $[M\text{-}H_2O]^+$; MS (CI/Ether): m/e 419 $[M+1]^+$.

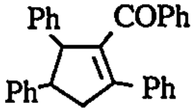
3.5.2 Dehydration of



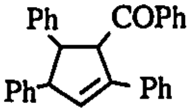
Dehydration reaction was carried out under phase transfer conditions. The reaction system consisted of benzene as the organic phase (10 ml), 5N NaOH (10 ml) as the aqueous phase and tetrabutylammonium hydrogen sulfate: (0.085g, 0.25 mmol) as the phase transfer catalyst. Addition of



and stirring for 19 hours at 60 ^{0}C, resulted in the formation of the cyclopentene derivative:

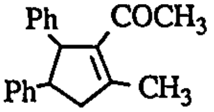


isolated in 65% yield (for the stereochemistry of substitution see structure **61** in Scheme 23). IR (KBr): ν_{CO} 1635 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.17 (m; 1H, $H_{3'}$), 3.67 (m; 2H, H_4 and H_3), 4.62 (m; 1H, H_5), 7.07-7.68 (m; 20H, aromatic protons); ^{13}C NMR ($CDCl_3$): δ 45.22 (CH_2), 53.12 (CH), 64.55 (CH), 126.52, 126.58, 127.25, 127.65, 127.95, 128.06, 128.23, 128.37, 128.52, 129.20, 132.45 (aromatic CH's), 135.42, 136.84, 139.38, 142.29, 143.88, 146.17 (olefinic and aromatic quarternary carbons), 196.51 (CO); MS: m/e 400$[M]^+$. The by-product of this reaction,

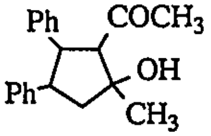


was characterized by the following data (the stereochemistry of substitution similar to structure **61** mentioned above). IR (KBr): ν_{CO} 1680 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 3.38 (t; 1H, H$_4$), 4.21 (m; 1H, H$_5$), 5.16 (m; 1H, H$_3$), 6.49 (dd; 1H, H$_1$), 7.16-7.69 (m; 20H, aromatic protons); MS: m/e 400[M]$^+$.

3.5.3 Reduction of 4-Phenyl-3-buten-2-one

Reduction of 4-phenyl-3-buten-2-one afforded 1-acyl-2-methyl-*trans*-4,5-diphenylcyclopentene:  in 70% yield (for the stereochemistry of substitution see structure **67**). IR (KBr): ν_{CO} 1680 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.83 (s; 3H, COCH$_3$), 2.18 (m; 3H, CH$_3$), 2.66 (dd; 1H, H$_3$), 3.03 (dd; 1H, H$_{3'}$), 3.16 (m; 1H, H$_4$), 4.19 (m; 1H, H$_5$), 7.00-7.30 (m; 10H, aromatic protons); MS: m/e 276 [M]$^+$, 261 [M-CH$_3$]$^+$, 233 [M-COCH$_3$]$^+$. 4-Phenylbutan-2-one was also isolated from this reaction in 21% yield. IR (neat): ν_{CO} 1720 cm^{-1}; MS: m/e 148 [M]$^+$, 133 [M-CH$_3$]$^+$.

3.5.4 Reduction of 4-Phenyl-3-buten-2-one

Reduction of 4-phenyl-3-buten-2-one was performed by a variation of the general procedure described in 3.5. In this reaction the volume of the organic solvent was increased to 100 ml. Chromatographic purification afforded ketol  in 13% yield (for the stereochemistry of substitution see structure **66**). IR (nujol mull): ν_{OH} 3440 cm^{-1}, ν_{CO} 1705 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 2.16 (dd; 1H, H$_5$, $J_{H5\text{-}H5'} = 13.95$ Hz, $J_{H5\text{-}H4} = 7.33$ Hz), 2.38 (8 lines; 1H, H$_{5'}$, $J_{H5'\text{-}H5} = 13.95$ Hz, $J_{H5'\text{-}H4} = 10.31$ Hz, $J_{H5'\text{-}OH} = 1.01$ Hz), 3.15 (d; 1H, H$_2$, $J_{H2\text{-}H3} = 11.97$ Hz), 3.28 (6 lines; 1H, H$_4$, $J_{H4\text{-}H3} = 10.45$ Hz, $J_{H4\text{-}H5'} = 10.31$ Hz, $J_{H4\text{-}H5} = 7.33$ Hz), 3.62 (dd; 1H, H$_3$, $J_{H3\text{-}H2} = 11.97$ Hz, $J_{H3\text{-}H4} = 10.45$ Hz), 3.89 (d; 1H, OH, $J_{OH\text{-}H5'} = 1.01$ Hz); MS: m/e 294 [M]$^+$, 276 [M-H$_2$O]$^+$; MS (CI/Ether): m/e 295 [M+1]$^+$.

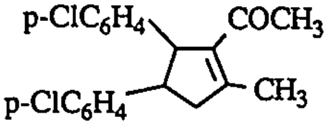
3.5.5 Reduction of 4-Phenyl-3-buten-2-one

Reduction of 4-phenyl-3-buten-2-one was performed as described in 3.5 except that the reaction was carried out at room temperature. 1-Acetyl-2-methyl-*trans*-4,5-diphenylcyclopentene was obtained in 44% yield while 4-phenylbutan-2-one was formed in 5% yield.

3.5.6 Reduction of 4-Phenyl-3-buten-2-one

Reduction of 4-phenyl-3-buten-2-one was performed as described in 3.5 except that the reaction was carried out under carbon monoxide atmosphere. 1-Acetyl-2-methyl-*trans*-4,5-diphenylcyclopentene was obtained in 74% yield together with 4-phenylbutan-2-one, which was formed in 18% yield.

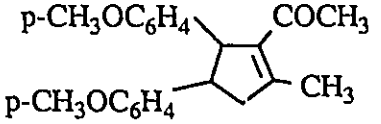
3.5.7 Reduction of 4-(p-Chlorophenyl)-3-buten-2-one

Reduction of 4-(p-chlorophenyl)-3-buten-2-one afforded cyclopentene derivative: 

in 71% yield (the stereochemistry of substitution similar to that in structure **67**). IR (neat): ν_{CO} 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.89 (s; 3H, $COCH_3$), 2.27 (m; 3H, CH_3), 2.59-3.13 (m; 3H, H_4, H_3 and $H_{3'}$), 6.93-7.26 (m; 8H, aromatic protons); MS: m/e 344[M]$^+$. 4-(p-Chlorophenyl)butan-2-one was obtained in 9% yield. IR (neat): ν_{CO} 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.05 (s; 3H, CH_3), 2.75 (m; 4H, CH_2's), 6.90-7.30 (m; 4H, aromatic protons); MS: m/e 182[M]$^+$.

3.5.8 Reduction of 4-(p-Methoxyphenyl)-3-buten-2-one

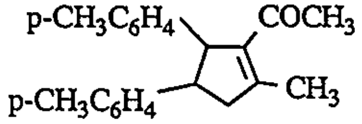
Reduction of 4-(p-methoxyphenyl)-3-buten-2-one gave cyclopentene derivative:



in 68% yield (the stereochemistry of substitution similar to that in structure **67**). IR (KBr): ν_{CO} 1675 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.87 (s; 3H, COCH$_3$), 2.17 (m; 3H, CH$_3$), 2.59 (dd; 1H, H$_3$), 2.96 (dd; 1H, H$_{3'}$), 3.08 (m; 1H, H$_4$), 3.76 (s; 3H, OCH$_3$), 4.07 (m; 1H, H$_5$), 6.74-7.05 (m; 8H, aromatic protons); ^{13}C NMR (CDCl$_3$): δ 16.62 (CH$_3$), 30.03 (COCH$_3$), 47.19 (CH$_2$), 52.56 (CH), 57.17, 55.22 (OCH$_3$), 61.50 (CH), 113.85, 114.04, 127.96, 128.19, 136.48, 136.83, 138.11, 152.78, 158.14, 158.23, (olefinic and aromatic carbons), 199.39 (CO); MS: m/e 336 [M]$^+$. 4-(p-Methoxyphenyl)butan-2-one was obtained in 32% yield.

3.5.9 Reduction of 4-(p-Tolyl)-3-buten-2-one

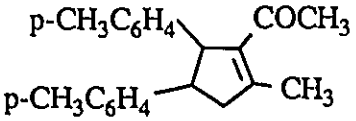
Reduction of 4-(p-tolyl)-3-buten-2-one afforded cyclopentene derivative:



in 68% yield (the stereochemistry of substitution similar to that in structure **67**). IR (neat): ν_{CO} 1675 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.86 (s; 3H, COCH$_3$), 2.26, 2.29, 2.38 (s, each; 9H, CH$_3$'s), 2.59 (dd; 1H, H$_3$), 2.99 (dd; 1H, H$_{3'}$), 3.11 (m; 1H, H$_4$), 4.11 (m; 1H, H$_5$), 6.89-7.09 (m; 8H, aromatic protons), ^{13}C NMR (CDCl$_3$): δ 16.63 (olefinic CH$_3$), 20.97, 21.02 (aromatic CH$_3$'s), 30.08 (COCH$_3$), 47.36 (CH$_2$), 52.67 (CH), 61.79 (CH), 126.86, 126.95, 129.22, 129.39, 135.92, 136.05, 137.93, 141.42, 142.03, 153.10 (olefinic and aromatic carbons), 199.26 (CO); MS: m/e 304 [M]$^+$. 4-(p-Tolyl)butan-2-one was obtained in 13% yield.

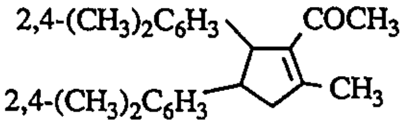
3.5.10 Reduction of 4-(p-tolyl)-3-buten-2-one

Reduction of 4-(p-tolyl)-3-buten-2-one was performed as described in 3.5.9 except that the reaction was carried out under carbon monoxide atmosphere. The cyclopentene derivative: was obtained in 87% yield. 4 -(p-Tolyl)butan-2-one was formed in 13% yield.



3.5.11 Reduction of 4-(2,4-dimethylphenyl)-3-buten-2-one

Reduction of 4-(2,4-dimethylphenyl)-3-buten-2-one gave the cyclopentene derivative: in 34% yield (the stereochemistry of substitution was similar to that of **67**, also shown in Figure 2). IR (KBr): ν_{CO} 1675 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.87 (s; 3H, COCH$_3$), 2.18 (m; 3H, CH$_3$), 2.17, 2.19, 2.23, 2.26, (s, each; 12H, CH$_3$ on aromatic rings), 2.50 (dd; 1H, H$_3$), 3.01 (dd; 1H, H$_{3'}$), 3.34 (m; 1H, H$_4$), 4.26 (m; 1H, H$_5$), 6.85-7.26 (m; 6H, aromatic protons); ^{13}C NMR (CDCl$_3$): δ 16.75 (olefinic CH$_3$), 19.42, 19.60, 20.86, 20.92, (aromatic methyls), 29.76 (COCH$_3$), 47.32 (CH$_2$), 56.91 (CH), 125.61, 125.91, 127.09, 127.23, 130.98, 131.18, 135.23, 135.28, 135.46, 135.64, 138.32, 139.97, 140.82, 153.20, (olefinic and aromatic carbons), 199.02 (CO); MS: m/e 332 [M]$^+$. The saturated ketone, 4-(2,4-dimethylphenyl)butan-2-one was obtained in 25% yield. MS: m/e 176 [M]$^+$.



3.5.12 4-Phenylpentan-2-one

Reduction of 4-phenyl-3-penten-2-one afforded 4-phenylpentan-2-one in 71% yield. IR (neat): ν_{CO} 1715 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.25 (d; 3H, CH$_3$), 2.05 (s; 3H, COCH$_3$), 2.69 (8 lines; 2H, CH$_2$), 3.29 (6 lines; 1H, CH), 7.17-7.36 (m; 5H, aromatic protons); MS: m/e 162 [M]$^+$, 147 [M-CH$_3$]$^+$.

3.5.13 3-Methyl-4-phenylbutan-2-one

Reduction of 3-methyl-4 phenyl-3-buten-2-one gave 3-Methyl-4-phenylbutan-2-one in 86% yield. MS: m/e 162 $[M]^+$, 147 $[M-CH_3]^+$.

3.5.14 Cyclohexanone

Reduction of 2-cyclohexenone afforded cyclohexanone in 82% yield (15 minutes reaction). IR (neat): ν_{CO} 1710 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.80-2.45 (m; aliphatic protons); MS: m/e 96 $[M]^+$.

3.5.15 Cyclopentanone

Reduction of 2-cyclopentenone afforded cyclopentanone in 80% yield (15 minutes reaction). IR (neat): ν_{CO} 1735 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.85-2.25 (m; aliphatic protons); MS: m/e 82 $[M]^+$

3.6 Two-Phase System and $Ni(CO)_3(CN)^-$ Catalyzed Rearrangement and Carbonylation of Vinyl Epoxides

General Procedure

The following general procedure was used: a mixture of benzene (20 ml) and 5N NaOH (15 ml) was degassed by purging nitrogen through a reaction vessel (100 ml three necked flask equipped with condenser) for 15 minutes. After having replaced nitrogen by carbon monoxide, a $Ni(CN)_2{\bullet}4H_2O$ (0.183g, 1.0 mmol) was added. The resulting solution was stirred under carbon monoxide for 40-50 minutes while the temperature was gradually raised to 60 ^{0}C. The vinyl epoxide (5.0 mmol) was added and the reaction mixture was stirred for the period of time indicated in Tables 13-15. The formation of a rearrangement product as well as the disappearance of a starting material were followed by gas chromatography. After reaction was complete, the reaction mixture was cooled to room temperature, and purged with nitrogen for 5 minutes. Work-up was affected by separation of the two phases; the organic phase was washed with brine, dried (Na_2SO_4) and rotary evaporated to afford a crude rearrangement product, while the aqueous layer was carefully acidified with 10% HCl (**caution: HCN evolution !**), extracted with ethyl acetate (3 × 20 ml), dried (Na_2SO_4) and concentrated (rotary evaporator) to give the crude carbonylation product. The rearrangement product was purified by preparative thin-layer chromatography using 8:2 hexane/diethyl ether as the eluant or quantitatively analyzed by gas chromatography. The hydroxy acid product was purified by recrystallization (the crude mixture was dissolved in the minimum amount of acetone, diluted with hexane and left in a freezer for overnight) or by preparative thin-layer chromatography (7:3 hexane/ethyl acetate as the developing solvent system). The following subsections provide experimental details for the reactions which have been tabulated: Table 13 (page 81), Table 14 (page 86) and Table 15 (page 91).

3.6.1 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that the reaction was carried out at 69 ^{0}C. 2-Cyclohexenone was the only isolated product, obtained in 93% yield. IR (neat): ν_{CO} 1685 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.96-2.09 (m; 2H, CH_2), 2.28-2.44 (m; 4H, CH_2's), 5.98-6.03 (m; 1H, olefinic CH), 6.95-6.99 (m; 1H, olefinic CH); MS: m/e 96 $[M]^+$.

3.6.2 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene afforded 2-cyclohexenone in 86% yield.

3.6.3 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that the reaction was carried out in the presence of cetyltrimethylammonium bromide as the phase transfer catalyst. 2-Cyclohexenone was the only product, obtained in 66% yield.

3.6.4 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-Epoxycyclohexene was performed as described in 3.6 except that reaction was carried out using tetrabutylammonium hydrogen sulfate as phase transfer agent. 2-Cyclohexenone was isolated in 73% yield.

3.6.5 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that reaction was carried out at room temperature. 2-Cyclohexenone was isolated in 63% yield as the only product.

3.6.6 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that reaction was carried out at room temperature and in the presence of cetyltrimethylammonium bromide as the phase transfer agent. 2-Cyclohexenone was isolated in 30% yield as the only product.

3.6.7 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that the reaction was carried out at room temperature, and in the presence of tetrabutylammonium hydrogen sulfate as the phase transfer agent. 2-Cyclohexenone was obtained in 39% yield.

3.6.8 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that 25:1 ratio of substrate to nickel catalyst was used. 2-Cyclohexenone was isolated in 80% yield.

3.6.9 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that the reaction was carried out using 0.5N NaOH as the aqueous phase. 2-Cyclohexenone was obtained in 44% yield.

3.6.10 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that reaction was carried out using distilled water as the aqueous phase. 3,4-Epoxycyclohexene was recovered unchanged.

3.6.11 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that the reaction was carried out in the absence of a nickel salt. 2-Cyclohexenone was not detected even when reaction was run overnight.

3.6.12 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that, instead of carbon monoxide, nitrogen gas was used as the reaction atmosphere. There was no 2-cyclohexenone formation even when reaction was run overnight.

3.6.13 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that, instead of $Ni(CN)_2 \cdot 4H_2O$, $NiBr_2$ was used as the nickel salt. 2-Cyclohexenone was not formed even when reaction was run overnight.

3.6.14 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6.13 except that in addition to $NiBr_2$, KCN (0.130g, 2.0 mmol) was added. 2-Cyclohexenone was formed in 71% yield.

3.6.15 Isomerization of 3,4-Epoxycyclohexene

Isomerization of 3,4-epoxycyclohexene was performed as described in 3.6 except that after 40 minutes of induction period under carbon monoxide, the gas valves were switched and the reaction was carried out under nitrogen atmosphere. 2-Cyclohexenone was isolated as the only product in 33% yield.

3.6.16 Isomerization of 3,4-Epoxycyclopentene

Isomerization of 3,4-Epoxycyclopentene was performed as described in 3.6 except that the reaction was carried out at room temperature. 2-Cyclopentenone was the only product formed in 65% yield. Analysis of the product was carried out by gas chromatography aided by "spiking" with authentic material, as well as by GC/MS spectrometry.

3.6.17 Isomerization of 3,4-epoxy-5,5-dimethylcyclohexene

Isomerization of 3,4-epoxy-5,5-dimethylcyclohexene afforded 6,6-dimethyl-2-cyclohexenone in 67% yield. ^1H NMR ($CDCl_3$): δ 1.06 (s; 6H, CH_3's), 1.78 (t; 2H, CH_2), 2.33 (10 lines; 2H, CH_2), 5.87 (dt; 1H, H_1), 6.83 (dt; 1H, H_3); ^{13}C NMR ($CDCl_3$): δ 23.15 (CH_2), 23.84(CH_3's), 35.99 (CH_2), 41.19 (quarternary carbon), 198.34 (CO); MS: m/e 124 $[M]^+$.

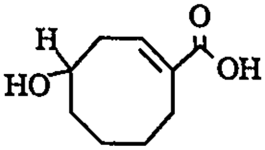
3.6.18 Attempted Carbonylation of 3,4-Epoxy-3,4-dimethylcyclohexene

Attempted carbonylation of 3,4-epoxy-3,4-dimethylcyclohexene, as described in 3.6 except that reaction was carried out in the presence of 0.25 mmol of tetrabutylammonium hydrogen sulfate as phase transfer catalyst, afforded 5% of o-xylene: MS: m/e 106 $[M]^+$, 91 $[M\text{-}CH_3]^+$ (also analysed by gas chromatography aided by "spiking" with authentic material), and 8% of 3,4-dimethylcyclohexa-1,3-diene: ^1H NMR ($CDCl_3$): δ 1.68, 1.71 (s, each; 6H,

CH_3's), 2.06 (m; 4H, CH_2's), 5.66-6.76 (m; 2H, olefinic protons); ^{13}C NMR ($CDCl_3$): δ 17.13, 19.04 (CH_3's), 22.97, 29.46 (CH_2's), 123.32, 129.93 (olefinic CH's).

3.6.19 Reaction of 3,4-Epoxycyclooctene

3,4-Epoxycyclooctene was converted to 2-cyclooctenone in 24% yield: IR (neat): ν_{CO} 1700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.50 (m; 2H, CH_2), 1.73 (m; 2H, CH_2), 1.96 (m; 2H, CH_2), 2.34 (m; 2H, CH_2), 2.99 (d; 2H, CH_2), 5.42-5.63 (m; 2H, olefinic protons); ^{13}C NMR ($CDCl_3$): δ 24.27, 25.33, 26.74, 41.88, 43.92 (CH_2's), 124.04, 131.34 (olefinic carbons), 213.96 (CO), and 4-hydroxy-1-cyclooctenyl carboxylic acid in 60% yield:



: IR (KBr): ν_{OH} 3390 cm^{-1}, ν_{CO} 1683 cm^{-1}; ^1H NMR (acetone-d_6): δ 2.24-1.80 (m; 6H, CH_2's), 2.49 (m; 4H, CH_2's), 2.9 (s, broad; 1H, OH), 3.81 (m; 1H, CH), 6.99 (t; 1H, olefinic proton), 10.5 (s, v.broad; COOH); ^{13}C NMR (acetone-d_6): δ 21.80, 25.48, 29.25, 36.09, 36.41 (CH_2's), 71.93 (CH), 135.35, 140.09 (olefinic carbons), 168.97 (COOH);

m. p. = 127.0-128.5 ^0C; Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.13; H, 8.36.

3.6.20 Reaction of 3,4-Epoxycyclooctene

3,4-Epoxycyclooctene was converted to 55% of 3-cyclooctenone and 20.5% of 4-hydroxy-1-cyclooctenyl carboxylic acid when the scale of reaction 3.6.19 was doubled.

3.6.21 Reaction of 3,4-Epoxycyclooctene

Reaction of 3,4-epoxycyclooctene was performed as described in 3.6 except that process was carried out in the presence of 0.25 mmol of tetrabutylammonium hydrogen sulfate as phase transfer agent. 3-Cyclooctenone was obtained in 10% yield, while 4-hydroxy-1-cyclooctenylcarboxylic acid was formed in 74% yield.

3.6.22 Isomerization of 3,4-Epoxycyclopentene

Isomerization of 3,4-epoxycyclopentene was performed as described in 3.6.16, except that reaction was carried out without an induction period. 2-Cyclopentenone was obtained in 58% yield.

3.6.23 Dependence of the Pseudo First Order Kinetics on the Stirring Rate in the Isomerization of 3,4-Epoxycyclohexene

The kinetic measurements were carried out using 3,4-epoxycyclohexene as a model reactant and the reaction procedure described in 3.6. The stirring speed was controlled by the use of the IKAMAG-RET-G stirrer. The temperature durring all experiments was maintained at 60 ^{0}C ± 0.5 ^{0}C. The concentration of the rearrangement product formed was calculated based on the GC area vs. internal standard.

3.6.24 Isomerization of 3,4-Epoxypentene

Isomerization of 3,4-epoxy-pentene afforded E-2-pentenal in 18% yield. Analysis of the product was carried out by gas chromatography aided by "spiking" with authentic material, as well as by GC/MS spectrometry. MS: m/e 84 $[M]^+$.

3.6.25 Isomerization of 3,4-Epoxy-3-methylbutene

Isomerization of 3,4-epoxy-3-methylbutene afforded E-2-methyl-2-butenal in 45% yield: IR (neat): ν_{CO} 1680 cm^{-1}.

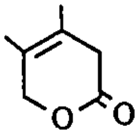
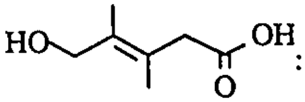
3.6.26 Isomerization of 3,4-Epoxy-3-ethylbutene

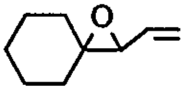
Isomerization of 3,4-epoxy-3-ethylbutene afforded E-2-ethyl-2-butenal in 12% yield. ^{1}H NMR (CDCl$_3$): δ 0.93 (t; 3H, CH$_3$), 1.95 (d; 3H, olefinic CH$_3$), 2.24 (q; 2H, CH$_2$), 6.51 (q; 1H, olefinic CH), 9.33 (s; 1H, CHO). In addition, analysis of the product was carried out by gas chromatography aided by "spiking" with authentic material.

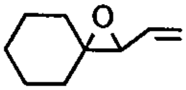
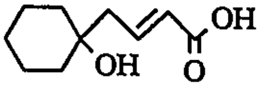
3.6.27 Reaction of 3,4-Epoxy-2,3-dimethylbutene

Reaction of 3,4-epoxy-2,3-dimethylbutene performed according to procedure described in 3.6 resulted in a polymer-like tar formation.

3.6.28 Reaction of 3,4-Epoxy-2,3-dimethylbutene

Reaction of 3,4-epoxy-2,3-dimethylbutene was performed as described in 3.6 except that it was carried out in the presence of 0.25 mmol of tetrabutylammonium hydrogen sulfate as the phase transfer agent. After acidification and subsequent extraction, 39% of 3,6-dihydro-4,5-dimethyl-2H-pyran-2-one was isolated:  : IR (neat): ν_{CO} 1740 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.65, 1.69 (m, each; 6H, CH$_3$'s), 2.95 (m; 2H, CH$_2$), 4.67 (m; 2H, CH$_2$); MS: m/e 126 [M]$^+$, as well as 19% of E-3,4-dimethyl-5-hydroxy-3-pentenoic acid:  : IR (nujol mull): ν_{OH} 3299 cm^{-1}, ν_{CO} 1675 cm^{-1}; ^{1}H NMR (acetone-d_6): δ 1.72 (s; 6H, CH_3's), 3.02 (s; 2H, CH_2), 4.04 (s; 2H, CH_2), 9.9 (s, v.broad; COOH); ^{13}C NMR (acetone-d_6): δ 16.39, 18.63 (CH_3's), 40.34, 63.17 (CH_2's), 125.12, 133.48 (olefinic quarternary carbons), 173.12 (COOH); MS: m/e 144 $[M]^+$, were isolated from the aqueous phase. No products were detected in the organic phase.

3.6.29 Carbonylation of 

Carbonylation of 2-ethenyl-1-oxaspiro[2.5]octane :  was performed as described in 3.6 except that reaction was carried out in the presence of 0.25 mmol of tetrabutylammonium hydrogen sulfate as the phase transfer catalyst. 4(1-Hydroxy-cyclohexyl)-2-butenoic acid:  was isolated in 40% yield from the aqueous phase. IR (KBr): ν_{OH} 3235 cm^{-1}, ν_{CO} 1695 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.23-1.63 (m; 10H, cyclohexyl CH_2's), 2.37 (dd; 2H, -CH_2-C=C, $J_{H4\text{-}H3} = J_{H4'\text{-}H3} = 7.7$ Hz), 2.6 (s, v.broad; OH), 5.87 (d; 1H, H_2, $J_{H2\text{-}H3} = 15.4$ Hz), 7.14 (5 lines; 1H, H_3, $J_{H3\text{-}H4} = J_{H3\text{-}H4'} = 7.7$ Hz, $J_{H3\text{-}H2} = 15.4$ Hz); ^{13}C NMR (acetone-d_6): δ 22.62, 26.38, 38.19 (cyclohexyl CH_2's), 45.98 (-$\underline{C}H_2$-C=C), 71.26 (cyclohexyl quarternary carbon), 124.41 (CH), 147.29 (CH), 167.98 (COOH); MS: m/e 166 $[M\text{-}H_2O]^+$, 99 $[C_6H_{11}OH]^+$; m. p. = 131.5-132.5 °C; Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.86; H, 8.78.

3.7 Metal Complex and Phase Transfer Catalysed Nitric Oxide Reactions General Procedure

The following general procedure was used: To a three necked round bottomed flask equipped with a condenser and a dropping funnel was placed tetrabutylammonium hydrogen sulfate (0.4 mmol), 12.5 ml of 3N NaOH and 10 ml of t-pentyl alcohol. The reaction system was degassed by bubbling nitrogen through the solution for 15 minutes. The metal complex (0.20 mmol, also 0.20 mmol of PPh_3 if applied) was added and nitrogen was replaced by nitric oxide, which was slowly bubbled through the reaction mixture. The benzylic bromide (5.0 mmol) in t-pentyl alcohol (2.5 ml) was then introduced, drop-by-drop (for the period of ca. 30 minutes). The resulting solution was stirred overnight at room temperature (reaction times indicated in Tables 16 and 17). The layers were separated, and the organic layer was washed with aqueous NaCl, dried ($MgSO_4$), and concentrated. Pure oxime ether was obtained by silica gel thin-layer or column chromatography using 8:2 hexane/ethyl acetate as the eluant. The following subsections provide relevant details for each experiment; the results for most of these reactions have been included in Table 16 (page 99), Table 17 (page 100) and Table 18 (page 101).

3.7.1 Reaction of Benzyl Bromide

Reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine was added), except that the process was carried out in the presence of 0.40 mmol of benzyltriethylammonium chloride as the phase transfer catalyst. $PhCH{=}NOCH_2Ph$ was isolated in 20% yield. ^1H NMR ($CDCl_3$): δ 5.15 (s; 2H, CH_2), 7.31-7.52 (m; 10H, aromatic protons), 8.08 (s; 1H, CH=NO); ^{13}C NMR ($CDCl_3$): δ 76.37 (CH_2), 127.05, 127.93, 128.38, 128.41, 128.63, 129.79 (aromatic CH's), 132.17, 137.46 (aromatic quarternary carbons), 148.99 (CH=NO); MS: m/e 211 $[M]^+$, 181 $[M-NO]^+$; MS (CI/Ether): m/e 212 $[M]^+$. Among the by-products, 1% of dibenzyl ether: $(C_6H_5CH_2)_2O$ was formed. ^1H NMR ($CDCl_3$): δ 4.50 (s; 4H, CH_2's), 7.70 (m; 10H, aromatic protons); MS: m/e 107 $[C_6H_5CH_2O]^+$.

3.7.2 Reaction of Benzyl Bromide

Reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine added), except that in this case the process was carried out in the presence of 0.40 mmol of benzyltriethylammonium chloride as the phase transfer catalyst, and toluene was used as the organic solvent. $PhCH{=}NOCH_2Ph$ was formed in trace amounts (witnessed by GC/MS) as the benzyl alcohol was the major product (37% yield). NMR ($CDCl_3$): δ 1.80 (s; 1H, OH), 4.70 (s; 2H, CH_2), 7.34 (m; 5H, aromatic protons); MS: m/e $[M]^+$. Dibenzyl ether was formed only in trace amounts (identified by GC/MS).

3.7.3 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine added), except that in this case the process was carried out in the presence of 0.40 mmol of benzyltriethylammonium chloride as the phase transfer catalyst, with methylene chloride used as the organic solvent. $PhCH{=}NOCH_2Ph$ was formed in 14% yield, while dibenzyl ether and benzyl alcohol were detected in trace amounts.

3.7.4 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine added). $PhCH{=}NOCH_2Ph$ was formed in 23% yield, while dibenzyl ether and benzyl alcohol were detected in 25% and 26% yield, respectively.

3.7.5 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (with added triphenylphosphine). $PhCH=NOCH_2Ph$ was formed in 38% yield, while dibenzyl ether and benzyl alcohol were formed in 4% and 30% yield, respectively.

3.7.6 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7, except that in this case process was carried out in the presence of 0.20 mmol of tributhylphosphine. $PhCH=NOCH_2Ph$ was formed in 36% yield, while dibenzyl ether was obtained in 3% yield.

3.7.7 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (with added triphenylphosphine), except without a phase transfer agent. There was no formation of an oxime ether in this reaction, while dibenzyl ether and benzyl alcohol, the usual by-products, were present in only trace amounts (identified by GC/MS).

3.7.8 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (with added triphenylphosphine), except that in this case 1N NaOH was used as an aqueous phase. $PhCH=NOCH_2Ph$ was formed in trace amount (identified by GC/MS), while dibenzyl ether and benzyl alcohol were present in trace amounts and 37% yield, respectively.

3.7.9 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (with added triphenylphosphine), except that in this case 5N NaOH was used as an aqueous phase.

$PhCH=NOCH_2Ph$ was formed in 27% yield, while dibenzyl ether and benzyl alcohol were obtained in 4% and 22% yield, respectively.

3.7.10 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine added), with the exception that a transition metal catalyst was not used. $PhCH=NOCH_2Ph$ was formed in 8% yield, while dibenzyl ether and benzyl alcohol were obtained in 13% and 35% yield, respectively.

3.7.11 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine added), with the exception that 0.20 mmol of bis(dibenzylideneacetone)-palladium(0) was used as the transition metal catalyst. $PhCH=NOCH_2Ph$ was obtained in 30% yield, while dibenzyl ether was formed in 6% yield.

3.7.12 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine added), with the exception that 0.20 mmol of dichlorotris(triphenylphosphine)-ruthenium was used as the transition metal catalyst. $PhCH=NOCH_2Ph$ was obtained in 31% yield, while dibenzyl ether was formed in 5% yield.

3.7.13 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7.12 (with added triphenylphosphine). $PhCH=NOCH_2Ph$ was obtained in 29% yield, while dibenzyl ether was formed in 16% yield.

3.7.14 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine added), with the exception that 0.20 mmol of dinitrosylbis(triphenylphosphine)-ruthenium was used as the transition metal catalyst. $PhCH=NOCH_2Ph$ was obtained in 32% yield, while dibenzyl ether was formed in 5% yield.

3.7.15 Reaction of Benzyl Bromide

The reaction of benzyl bromide was performed as described in 3.7 (no triphenylphosphine added), with the exception that 0.20 mmol of the dimer of chloro(hexa-1,5-diene)rhodium(I) was used as the transition metal catalyst. $PhCH=NOCH_2Ph$ was obtained in 26% yield, while dibenzyl ether was formed in 12% yield.

3.7.16 Reaction of Benzyl Chloride

The reaction of benzyl chloride was performed as described in 3.7 (with added triphenylphosphine). An oxime ether: $PhCH=NOCH_2Ph$ was obtained in 4% yield.

3.7.17 Reaction of p-Methylbenzyl Bromide

The reaction of p-methylbenzyl bromide was performed as described in 3.7 (with added triphenylphosphine). An oxime ether: p-$MeC_6H_4CH=NOCH_2$(p-MeC_6H_4), was obtained in 33% yield. ^1H NMR ($CDCl_3$): δ 1.33, 1.34 (s, each; 6H, CH_3's on aromatic rings), 5.13 (s; 2H, CH_2), 7.13-7.46 (m; 8H, aromatic protons), 8.07 (s; 1H, CH=NO); MS: m/e 239 $[M]^+$, 209 $[M-NO]^+$. A by-product of this reaction was the dibenzylic ether: $(p\text{-}MeC_6H_4CH_2)_2O$, which was formed in 6% yield. MS: m/e 121 $[CH_3C_6H_4CH_2O]^+$, 105 $[CH_3C_6H_4CH_2]^+$.

3.7.18 Reaction of m-Methylbenzyl Bromide

The reaction of m-methylbenzyl bromide was performed as described in 3.7 (with added triphenylphosphine). An oxime ether: $m\text{-}MeC_6H_4CH{=}NOCH_2(m\text{-}MeC_6H_4)$ was obtained in 40% yield. A by-product of this reaction was the dibenzylic ether, $(m\text{-}MeC_6H_4CH_2)_2O$, which was formed in 19% yield.

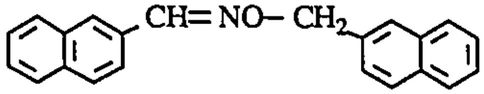
3.7.19 Reaction of o-Methylbenzyl Bromide

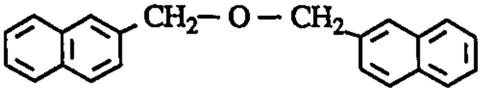
The reaction of o-methylbenzyl bromide was performed as described in 3.7 (with added triphenylphosphine). An oxime ether: $o\text{-}MeC_6H_4CH{=}NOCH_2(o\text{-}MeC_6H_4)$ was obtained in 25% yield. MS: m/e 239 $[M]^+$, 209 $[M-NO]^+$. A by-product of this reaction was the dibenzylic ether, $(p\text{-}MeC_6H_4CH_2)_2O$, formed in 9% yield.

3.7.20 Reaction of p-Fluorobenzyl Bromide

The reaction of p-fluorobenzyl bromide was performed as described in 3.7 (with added triphenylphosphine). An oxime ether: $p\text{-}FC_6H_4CH{=}NOCH_2(p\text{-}FC_6H_4)$ was obtained in 34% yield. ^1H NMR ($CDCl_3$): δ 5.13 (s; 2H, CH_2), 7.00-7.57 (m; 8H, aromatic protons), 8.07 (s; 1H, CH=NO); MS: m/e 247 $[M]^+$, 217 $[M-NO]^+$. A by-product of this reaction was the dibenzylic ether, $(p\text{-}FC_6H_4CH_2)_2O$, formed in 7% yield.

3.7.21 Reaction of 2-(Bromomethyl)naphthalene

The reaction of 2-(bromomethyl)naphthalene was performed as described in 3.7 (with added triphenylphosphine). An oxime ether: 

was obtained in 40% yield. ^{1}H NMR ($CDCl_3$): δ 5.25 (s; 2H, CH_2), 7.05-7.75 (m; 14H, aromatic protons), 8.10 (s; 1H, CH=NO). A by-product of this reaction was the dibenzylic ether: 

formed in 6% yield.

3.7.22 Attempted Reaction of 1-Bromonaphthalene

There was no reaction when 1-bromonaphthalene was submitted to the reaction conditions described in (3.7)

3.7.23 Attempted Reaction of Bromocyclohexane

There was no reaction when bromocyclohexane was submitted to the reaction conditions described in (3.7)

3.7.24 Formation of $[NO_2]^-[(Ph_3P)_2N]^+$

Nitric oxide was bubbled overnight through a solution of 3N NaOH (20 ml) at room temperature (no phase transfer or metal catalyst were added). PPNCl (10 mmol) was added and the reaction mixture was stirred for five hours. Extraction with methylene chloride (3 × 20 ml) and subsequent rotary evaporation afforded the crude product. Purification was accomplished by triple recrystallization from acetone/diethyl ether (1:1 mixture), affording colourless needles of $[NO_2]^-[PPN]^+$ which were dried over $CaCl_2$. M.p. = 223-226 ^{0}C;

MS(FAB/Glycerol), Positive Ion: m/e 538[Ph_3=N=PPh_3]$^+$; MS(FAB/Glycerol), Negative Ion: m/e 138[NO_2 + Glycerol]$^-$, 46[NO_2]$^-$.

3.7.25 Reaction of Benzyl Bromide

Repetition of experiment (3.7.10), using $NaNO_2$ (3.450g, 50 mmol) instead of nitric oxide, afforded the oxime ether, PhCH=$NOCH_2Ph$, in 16% yield.

3.7.26 Reaction of Benzyl Bromide

Repetition of experiment (3.7.5), using $NaNO_2$ (3.450g, 50 mmol) instead of nitric oxide, afforded the oxime ether, PhCH=$NOCH_2Ph$, in 29% yield.

REFERENCES

1. M.Mąkosza and B.Serafin. Rocz.Chem. **39**,1123(1965).
2. a) C.M.Starks and D.R.Napier. Ital.Pat. 823,967(1968),
   b) C.M.Starks. J.Am.Chem.Soc. **93**,195(1971).
3. A.Brändström and K.Gustavi. Acta Chem.Scand. **23**,1215(1969).
4 M.Mąkosza and M.Fedoryński. Adv.Catal. **35**,375(1987).
5. G.J.Soula. J.Org.Chem. **50**,3717(1985).
6. C.J.Thoman, T.D.Habeeb, M.Huhn, M.Korpusik and D.F.Slish. J.Org.Chem. **54**,4476(1989).
7. G.Barak and Y.Sasson. Bull.Soc.Chim.Fr. 584(1988).
8. a) M.Ellwood, J.Griffiths and P.Gregory. J.Chem.Soc., Chem.Commun. 181(1980).
   b) H.Iwamoto, T.Sonoda and H.Kabayashi. Tetrahedron Lett. **24**,4703(1983).
9. E.Angeletti, P.J.Tundo and P.Venturello. J.Chem.Soc. Perkin Trans. **1**,1137(1982).
10. P.J.Tundo. J.Org.Chem. **44**,2048(1979).
11. M.Rabinovitz, Y.Cohen and M.Halpern. Angew.Chem.Int.Ed.Engl. **25**,960(1986).
12. R.Neuman and Y.Sasson. J.Org.Chem. **49**,3448(1984).
13. F.Montanari, D.Landini and F.Rolla. Top.Curr.Chem. **101**,162(1982).
14. W.P.Weber and G.W.Gokel. "Phase Transfer Catalysis in Organic Synthesis", Springer-Verlag, New York, 1977.
15. C.M.Starks and C.Liotta. "Phase Transfer Catalysis. Principles and Techniques", Academic Press, New York, 1978.
16. E.V.Dehmlow and S.S.Dehmlow. "Phase Transfer Catalysis", Verlag Chemie, Weinheim, 2nd ed., 1983.
17. W.E.Keller. "Phase Transfer Reactions". Fluka-Compendium, vol.2, Georg Thieme Verlag, New York, 1987.

18. M.Mąkosza and M.Wawrzyniewicz. Tetrahedron Lett. 4659(1969).

19. M.Fedoryński and M.Mąkosza. J.Organomet.Chem. **51**,89(1973).

20. H.Alper and D.des Roches. J.Organomet.Chem. **117**,C44(1976).

21. H.Alper. Fundam.Res.Homogeneous Catal. **4**,79(1984).

22. H.Alper. Am.Chem.Soc., Symp.Ser. **326**,8(1987).

23. T.G.Southern. Polyhedron **8**,407(1989).

24. H.des Abbayes. Israel J.Chem. **26**,249(1985).

25. H.Alper. J.Organomet.Chem. **300**,1(1986).

26. a) I.Wender and P.Pino. "Organic Synthesis via Metal Carbonyls", vol.2, Wiley-Interscience, New York, 1977,

    b) J.Falbe. "New Synthesis with Carbon Monoxide", Springler-Verlag, Berlin, 1980.

27. a) H.Alper and H.des Abbayes. J.Organomet.Chem. **134**,C11(1977)

    b) L.Cassar and M.Foa. J.Organomet.Chem. **134**,C15(1977).

28. H.des Abbayes, J.C.Clement, P.Laurent, G.Tanguy, and N.Thilmont. Organometallics **7**,2293(1988).

29. a) B.Weinberger, G.Tanguy and H.des Abbayes. J.Organomet.Chem. **280**,C31(1985),

    b) H.des Abbayes, J.C.Clement, P.Laurent, J.J.Yaouanc, G.Tanguy, B.Weinberger. in press.

30. V.Galamb and H.Alper. Trans.Met.Chem. **8**,271(1983).

31. J.J.Brunet, C.Sidot and P.Caubere. J.Org.Chem. **48**,1166(1983).

32. I.Amer and H.Alper. J.Org.Chem. **53**,5147(1988).

33. F.Joo and H.Alper. Organometallics **4**,1775(1985).

34. a) J.F.Bunnet. Acc.Chem.Res. **11**,413(1978),

    b) R.A.Rossi. Acc.Chem.Res. **15**,164(1982).

35. J.J.Brunet and M.Taillefer. J.Organomet.Chem. **361**,C1(1989).

36. V.Galamb, M.Gopal and H.Alper. Organometallics **2**,801(1983).

37. M.Foa and L.Cassar. Gazz.Chim.Ital. **109**,619(1979).

38. H.Alper and I.Amer. J.Mol.Catal. **54**,L33(1989).

39. H.Alper, H.Arzoumanian, J.F.Petrignani, and M.S.Maldonado. J.Chem.Soc. Chem.Commun. 340(1985).

40. H.Alper and S.Calet. Tetrahedron Lett. **29**,1763(1988).

41. L.Cassar, M.Foa, M.Montanari and G.P.Marinelli. J.Organomet.Chem. **173**,335(1979).

42. K.Yamamura and S.I.Murahashi. Tetrahedron Lett. 4429(1977).

43. H.des Abbayes and M.A.Boudeville. J.Org.Chem. **42**,4104(1977).

44. A.Alemagna, C.Baldoli, P.del Buttero, E.Licandro and S.Maiorana. Gazz.Chim.Ital. **115**,555(1985).

45. H.des Abbayes and H.Alper. J.Am.Chem.Soc. **99**,98(1977).

46. G.P.Boldrini, A.Umani-Ronchi and M.Panunzio. J.Organomet.Chem. **171**,171(1979).

47. a) K.E.Hashem, J.F.Petrignani and H.Alper. J.Mol.Catal. **26**,285(1984),
b) F.Joo and H.Alper. Can.J.Chem. **63**,1157(1985).

48. L.Cassar. Ann.N.York Acad.Sci., 333(1980)208, see page 222.

49. a) F.Wada, R.Ishihara, Y.Kamohara and T.Matsuda. Bull.Chem.Soc.Jpn. **52**,2959(1979),
b) R.Bar and Y.Sasson. Tetrahedron Lett. **22**,1709(1981).

50. D.L.Reger, M.M.Habib and D.J.Fauth. J.Org.Chem. **45**,3860(1980).

51. K.R.Januszkiewicz and H.Alper. Organometallics. **2**,1055(1983).

52. J.Blum, I.Amer, A.Zoran and Y.Sasson. Tetrahedron Lett. **24**,4139(1983).

53. K.R.Januszkiewicz and H.Alper. Can.J.Chem. **62**,1031(1984).

54. J.Azran, O.Buchman, I.Amer and J.Blum. J.Mol.Catal. **34**,229(1986).

55. H.Alper, K.D.Logbo and H.des Abbayes. Tetrahedron Lett. 2861(1977).

56. R.Bar, Y.Sasson and J.Blum. J.Mol.Catal. **16**,175(1982).

57. H.Alper, F.Sibtain and J.Heveling. Tetrahedron Lett. **24**,5329(1983).

58. H.Alper and F.Sibtain. J.Organomet.Chem. **285**,225(1985).

59. a) C.M.Starks and P.H.Washecheck. U.S. Patent 3,547,962,(1970),

b) D.R.Napier and .M.Starks. U.S. Patent 3,992,432,(1976)

60. H.Alper, K.Januszkiewicz and D.J.H.Smith. Tetrahedron Lett. **26**,249(1985).

61. H.A.Zahalka, K.Januszkiewicz and H.Alper. J.Mol.Catal. **35**,249(1986).

62. J.Tsuji. Synthesis **5**,369(1984).

63. K.Januszkiewicz and H.Alper. Tetrahedron Lett. **24**,5159(1983).

64. D.M.Roundhill, M.M.Dickson and N.S.Dixit. J.Am.Chem.Soc. **102**,5538(1980).

65. K.Osowska-Pacewicka and H.Alper. J.Org.Chem. **53**,808(1988).

66. M.Quenard, V.Bonmarin and G.Gelbard. Tetrahedron Lett. **28**,2237(1987).

67. G.Barak and Y.Sasson. J.Org.Chem. **54**,3484(1989).

68. a) H.Alper and K.Hashem. J.Org.Chem. **45**,2269(1980),

b) Y.Sasson, A.Zoran and J.Blum. J.Mol.Catal. **11**,293(1981).

69. H.Alper and K.Hashem. Transition Met.Chem. **6**,219(1981).

70. V.V.Grushin, A.B.Vymenits and M.E.Vol'pin. J.Organomet.Chem. **382**,185(1990).

71. V.V.Grushin, I.S.Akhren and M.E.Vol'pin. J.Organomet.Chem. **371**,403(1989).

72. a) L.Cassar, M.Foa, M.Montanari and G.P.Marinelli. J.Organomet.Chem. **173**,335(1979),

b) M.Foa, R.Santi and F.Garavaglia. J.Organomet.Chem. **206**,C29(1981),

c) R.Noyori, I.Umeda and T.Ishigami. J.Org.Chem. **37**,1542(1972).

73. D.W.Armstrong and H.Kornahrens. Tetrahedron Lett. 4525(1979).

74. J.M.Rosenfeld and J.L.Cvocco. Analytical Chemistry **50**,701(1978).

75. a) J.Dockx. Synthesis 411(1973),

b) R.A.Jones. Aldrichim.Acta **9**,35(1976).

76. a) P.G.Potvin and J-M.Lehn. "Progress in Macrocyclic Chemistry", vol.3, Wiley, New York, 1987, pages 217-218,

b) A.W.Herriott and D.Picker. J.Am.Chem.Soc. **97**,2345(1975),

c) D.Landini, A.Maria and F.Montanari. J.Am.Chem.Soc. **100**,2796(1978).

77. a) A.J.Parker. Chem.Rev. **69**,1(1969),

    b) C.L.Liotta and J.P.Harris. J.Am.Chem.Soc. **96**,2250(1974),

    c) D.J.Sam and H.E.Simmons. J.Am.Chem.Soc. **96**,2257(1974).

78. a) A.Jończyk. Bull.Acad.Pol.Sci. Ser.Sci.Chim. **22**,849(1974),

    b) A.Jończyk, A.Kwast and M.Mąkosza. J.Chem.Soc. Chem.Comm. 902(1977),

    c) A.Jończyk, A.Kwast and M.Mąkosza. Tetrahedron Lett. 541(1979).

79. G.W.Parshall. "Homogeneous Catalysis", Wiley-Interscience, New York, 1980.

80. J.C.Bailar Jr. Cat.Rev.-Sci.Eng. **10**,17(1974).

81. Z.Michalska and D.E.Webster. Platinum Met.Rev. **18**,65(1974).

82. L.W.Gosser, K.H.Knoth and G.W.Parshall. J.Mol.Catal. **2**,253(1977).

83. D.L.Reger and M.M.Habib. J.Mol.Catal. **4**,315(1977).

84. D.D.M.Wayner and F.W.Hartstock. J.Mol.Catal. **48**,15(1988).

85. G.W.Parshall. J.Am.Chem.Soc. **94**,8716(1972).

86. Y.Dror and J.Manassen. J.Mol.Catal. **2**,219(1977).

87. F.Joo and Z.Toth. J.Mol.Catal. **8**,369(1980).

88. D.Sinou. Bull.Soc.Chim.Fr. 480(1987).

89. a) A.F.Borowski, D.J.Cale-Hamilton and G.Wilkinson. Nouv.J.Chem. **2**,137(1978),

    b) F.Joo, M.Somsak and M.T.Beck. J.Mol.Catal. **24**,71(1984),

    c) F.Joo and M.T.Beck. J.Mol.Catal. **24**,135(1984).

90. a) Z.Toth, F.Joo and M.T.Beck. Inorg.Chim.Acta **42**,153(1980),

    b) F.Joo and Z.Toth. J.Mol.Catal. **8**,369(1980).

91. C.Larpent and H.Patin. J.Mol.Catal. **44**,191(1988).

92. R.T.Smith, R.K.Ungar, L.J.Sanderson and M.C.Baird. Organometallics **2**,1138(1983).

93. B.R.James. "Homogeneous Hydrogenation", Wiley, New York, 1973, pages 209-213.

94. F.Alario, Y.Amrani, Y.Colleuille, T.P.Dang, J.Jenck, D.Morel and D.Sinou. J.Chem.Soc. Chem.Commun. 202(1986).

95. O.Bortalini, F.Di Furia, G.Modena and R.Sergalia. J.Org.Chem. **50**,2688(1985).

96. U.K.Pat.Appl. GB 2,085,874 to Johnson Matthey plc.

97. M.Y.Darensbourg and C.E.Ash. Adv.Organomet.Chem. **27**,1(1987).

98. a) M.D.Grillone and B.B.Kedzia. J.Organomet.Chem. **140**,161(1977),
b) H.A.Hadali, C.Arcus and D.F.Shriver. Inorg.Syn. **20**,218(1980),
c) D.J.Darensbourg, A.Rokicki and M.Y.Darensbourg. J.Am.Chem.Soc. **103**,3224(1981),
d) D.H.Gibson, F.U.Ahmed and K.R.Phillips. Organometallics **1**,679(1982).

99. a) R.J.Kinnes, W.D.Jones and R.G.Bergman. J.Am.Chem.Soc. **100**,7902(1978),
b) W.D.Jones, J.M.Huggins and R.G.Bergman. J.Am.Chem.Soc. **103**,4415(1981).

100. R.D.Wilson and R.Bau. J.Am.Chem.Soc. **96**,7601(1974).

101. I.Amer and H.Alper. J.Amer.Chem.Soc. **111**,927(1989).

102. J.P.Collman, L.S.Hegedus, J.R.Norton and R.G.Finke. "Principles and Applications of Organotransition Metal Chemistry", University Science Books, Mill Valley, CA, 1987, Chapter 6.1, pages 357-376.

103. a) W.P.Weiner, M.A.White and R.G.Bergman. J.Am.Chem.Soc. **105**,2922(1983),
b) M.D.Seidler and R.G.Bergman. J.Am.Chem.Soc. **106**,6110(1984).

104. a) P.Legzdins, B.Wassink, F.W.B.Einstein and A.C.Willis. J.Am.Chem.Soc. **108**,317(1986),
b) A.Goldhaber, K.P.C.Vollhardt, E.C.Walborsky and M.Wolfgruber. J.Am.Chem.Soc. **108**,516(1986).

105. U.Puttfarcken and D.Rehder. J.Organomet.Chem. **185**,219(1980).

106. E.C.Ashby. Acc.Chem.Res. **21**,414(1988).

107. a) H.Alper and S.Amaratunga. Tetrahedron Lett. **21**,2603(1980),
b) K.Januszkiewicz and H.Alper. J.Mol.Catal. **19**,139(1983).

108. P.Wardman. Life Chem.Rep. **3**,22(1985).

109. M.Meot-Ner and P.Neta. J.Phys.Chem. **90**,4648(1986).

110. P.Neta and D.Meisel. J.Phys.Chem. **80**,519(1976).

111. O.H.Wheeler. Can.J.Chem. **41**,192(1963).

112. M.M.Baizer and L.G.Feoktistov. "Organic Electrochemistry", Marcell Dekker, New York, 1983, page 359.

113. a) R.Pasternak. Helv.Chim.Acta **31**,753(1948),
b) F.Fournier, J.Berthelot and J.J.Basselier. Tetrahedron **41**,5667(1985),
c) J.Berthelot, C.Guette, F.Fournier and D.Davoust. Tetrahedron Lett. **28**,1881(1987),
d) D.A.Jaeger, D.Bolikal and B.Nath. J.Org.Chem. **52**,276(1987).

114. C.Harries and F.Hübner. Ann. **296**,294(1897).

115. A.Russel. J.Chem.Soc. 218(1934).

116. M.Gawęda, B.Kawałek, Ł.Lebioda, J.Mirek and M.Ciechanowicz-Rutkowska. Polish J.Chem. **52**,1747(1978).

117. J.Mirek, M.Gawęda and B.Kawałek. Polish J.Chem. **55**,987(1981).

118. C.Pac, Y.Miyauchi, O.Ishitani, M.Ihama, M.Yasuda and H.Sakurai. J.Org.Chem. **49**,26(1984).

119. M.Okubo, M.Yoshida, K.Horinauchi, H.Nishida and Y.Fukuyama. Bull.Chem.Soc.Jpn. **56**,1196(1983).

120. T.Ukeda and Y.Otsuji. Chemistry Lett. 1631(1986).

121. J.K.O'Loane, C.M.Combs and R.L.Griffith. J.Org.Chem. **29**,1730(1964).

122. G.Hunter, J.A.Miller, M.Moore and G.M.Ullah. Mag.Reson. **21**,275(1983).

123. M.Kinns and J.K.M.Sanders. J.Mag.Reson. **56**,518(1984).

124. a) D.J.Sam and H.E.Simmons. J.Am.Chem.Soc. **94**,4024(1972),
b) D.G.Lee, S.G.Lamb and V.S.Chang. Org.Synth. **60**,11(1981).

125. a) G.A.Lee and H.H.Freedman. Tetrahedron Lett. 1641(1976),
b) F.Ishi and K.Kishi. Synthesis 706(1980).

126. S.Colonna and R.Fornasier. Synthesis 531(1975).

127. V.J.Cunnane, D.J.Schiffrin, C.Beltran, B.Geblewicz and T.Salomon. J.Electroanal.Chem. **247**,203(1988).

128. U.Schmidt, M.Kroner and H.Griessner. Synthesis 832(1989).

129. G.Adamec, C.Bibby and R.Grigg. J.Chem.Soc. Chem.Commun. 491(1972).

130. H.Alper, D. des Roches, T.Durst and R.Legault. J.Org.Chem. **41**,3611(1976).

131. M.Suzuki, Y.Oda and R.Noyori. J.Am.Chem.Soc. **101**,1623(1979).

132. S.Sato, I.Matsuda and Y.Izumi. Tetrahedron Lett. **26**,1527(1985).

133. A.Bax and G.Drobny. J.Magn.Res. **61**,306(1985).

134. R.Aumann, H.Ring, C.Krüger and R.Goddard. Chem.Ber. **112**,3644(1979).

135. H.M.Colquhoun, J.Holton, D.J.Thompson and M.V.Twigg. "New Pathways for Organic Synthesis. Practical Applications of Transttion Metals", Plenum Press, New York, 1984, page 198.

136. G.D.Annis, S.V.Ley, C.R.Self and R.Sivaramakrishan. J.Chem.Soc. Perkin Trans. **1**,270(1981).

137. R.A.Ruden and R.B.Bonjouklian. J.Am.Chem.Soc. **97**,6892(1975).

138. R.C.Mease and J.A.Hirsch. J.Org.Chem. **49**,2925(1984).

139. a) K.K.Pandey. Coord.Chem.Rev. **51**,69(1983),

     b) J.A.McCleverty, C.W.Ninnes and I.Wołochowicz. J.Chem.Soc. Dalton Trans. 743(1986),

     c) T.Okamoto, K.Kobayashi, S.Oka and S.Tanimoto. J.Org.Chem. **52**,5089(1987).

140. a) J.H.Enemark and R.D.Feltham. Coord.Chem.Rev. **13**,339(1974),

     b) J.A.McCleverty. Chem.Rev. **79**,53(1979).

141. J.E.Ellis. J.Organomet.Chem. **86**,1(1975).

142. a) O.Touster. Org.Reactions **7**,327(1953),

     b) J.H.Boyer. "The Chemistry of the Nitro and Nitroso Groups", Part 1, ed. H.Feuer, Wiley, New York, 1969, pages 215 - 299.

143. S.Hiraku, Y.Noyuki and T.Moritaka. Chem.Lett. **7**,869(1980).

144. J.J.Lagowski. "Modern Inorganic Chemistry", Dekker, New York, 1973, page 403.

145. A.Martinsen and J.Songstad. Acta Chem.Scand. Ser. A **31**,645(1977).

146. E.Kaji, A.Igarashi and S.Zen. Bull.Chem.Soc.Jpn. **49**,3181(1976).

147. Vogel's Textbook of Practical Organic Chemistry, 4th ed., Longman Scientific & Technical, 1978, page 749.

148. R.B.King. Organomet.Synth. **1**,105(1965).

149. J.J.Levison and S.D.Robinson. J.Chem.Soc. A 2947(1970).

150. I.A.Zakharova, L.A.Leites and V.T.Aleksanyan. J.Organomet.Chem. **78**,283(1974).

151. Y.Ishii. Ann.N.Y.Acad.Sci. **239**,114(1974).

152. R.D.Coulson. Inorg.Synth. **13**,121.(1972)

CLAIMS TO ORIGINAL RESEARCH

1. Synthesis of (η^5-cyclopentadienyl)tricarbonylhydridovanadate anion from (η^5-cyclopentadienyl)vanadium tetracarbonyl under biphasic conditions.

2. Stoichiometric reduction of nitro aromatic compounds by (η^5-cyclopentadienyl)-vanadium tetracarbonyl under phase transfer catalysis conditions.

3. Semicatalytic, stereospecific cyclodehydration and/or reduction of α,β-unsaturated ketones by (η^5-cyclopentadienyl)vanadium tetracarbonyl under phase transfer conditions.

4. Unambiguous structural determination of the cyclic products from reaction of chalcone and (η^5-cyclopentadienyl)vanadium tetracarbonyl under phase transfer conditions with an implication to similar processes involving electron transfer mechanism.

5. Nickel cyanide and carbon monoxide catalyzed rearrangement of vinyl epoxides to α,β-unsaturated carbonyl compounds under biphasic conditions.

6. Phase transfer and nickel cyanide catalyzed carbonylation of vinyl epoxides to unsaturated δ-hydroxy acids.

7. Formation of a C-N bonds by the action of nitric oxide and palladium(0) or ruthenium catalysts on benzylic bromides under phase transfer conditions.

ATTACHED SPECTRA

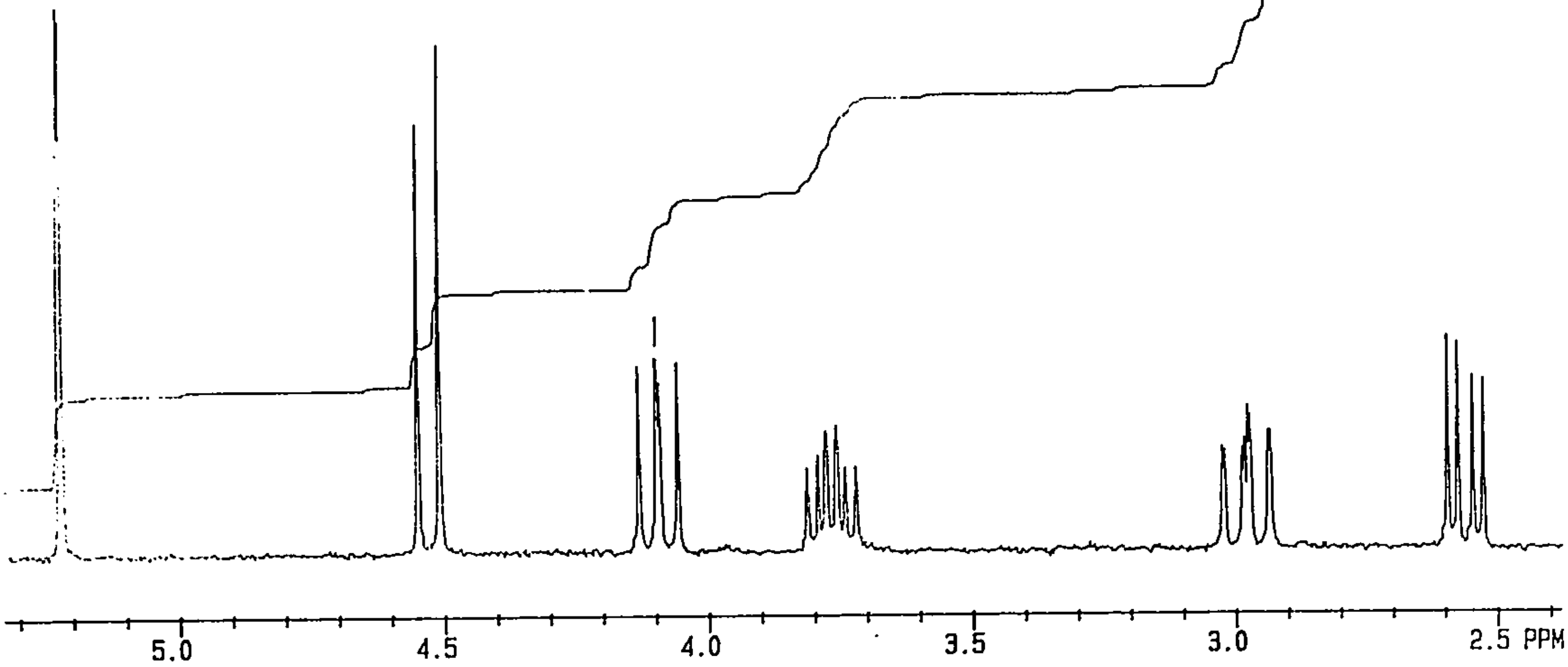
This section contains selected NMR spectra which were judged to be important pieces of evidence corroborating the structural assignments suggested in the result and discussion section.

The following is a list of the parameters employed in recording 2D spectra:

	HETCOR	**COSY**	**Relay COSY**
SW	16501.7	1991.2	4000
AT	0.124	0.257	0.128
NP	4096	1024	1024
D1	1.000	1.000	1.000
PW	9.6	5.6	11.0
PW90		11.0	
NI	128	256	256
NT	128	16	32
TAU			30 msec

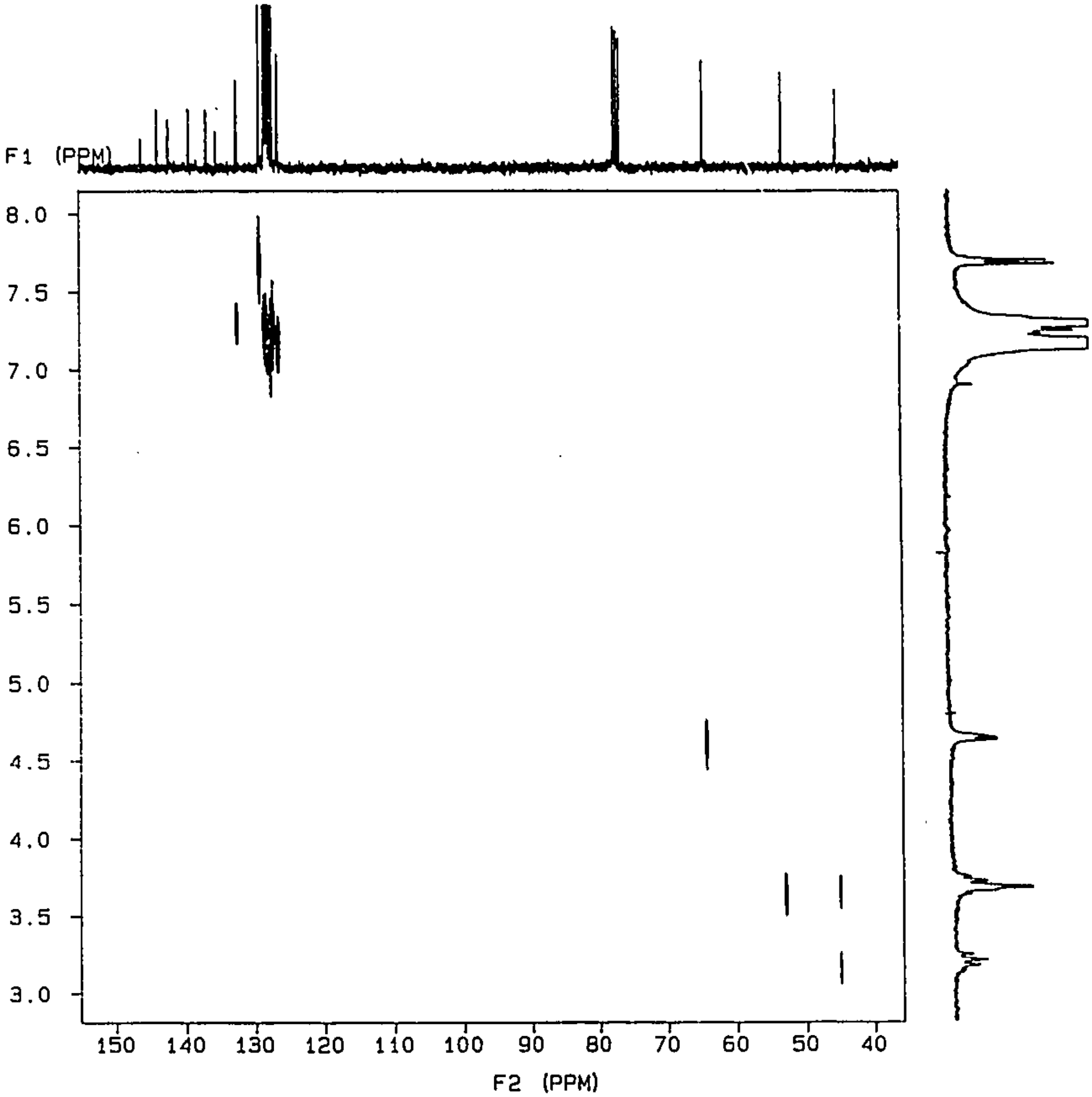
^{1}H NMR (300 MHz, $CDCl_3$, TMS) of compound **57** (R = Ph) - non aromatic region

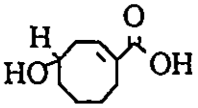
see page 66



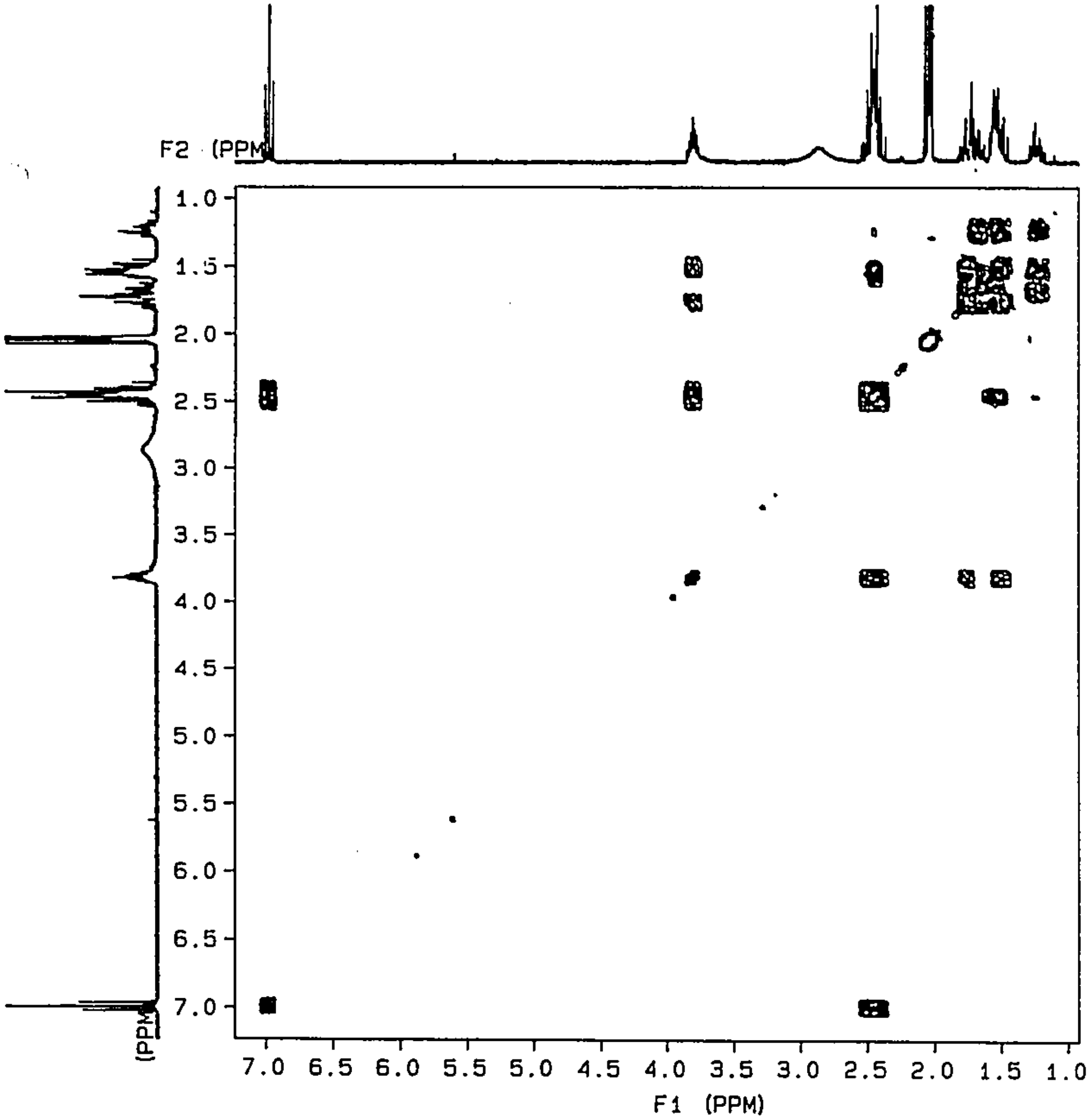
HETCOR (300 MHz, CDCl$_3$, TMS) of compound **61**

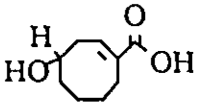
see page 69



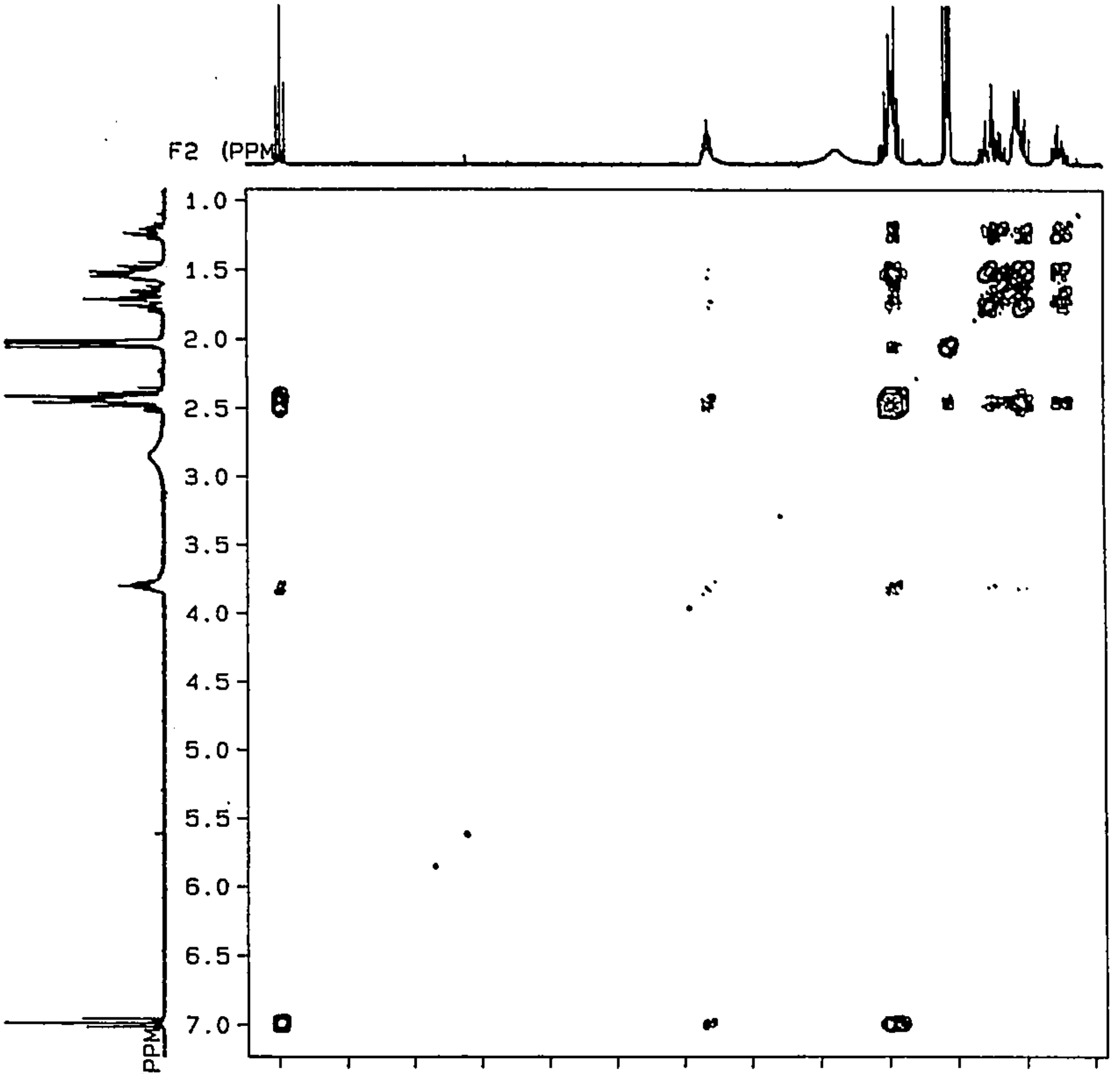
COSY (300 MHz, acetone-d_6, TMS) of compound 

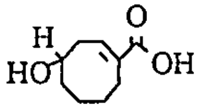
see Table 14 on page 86



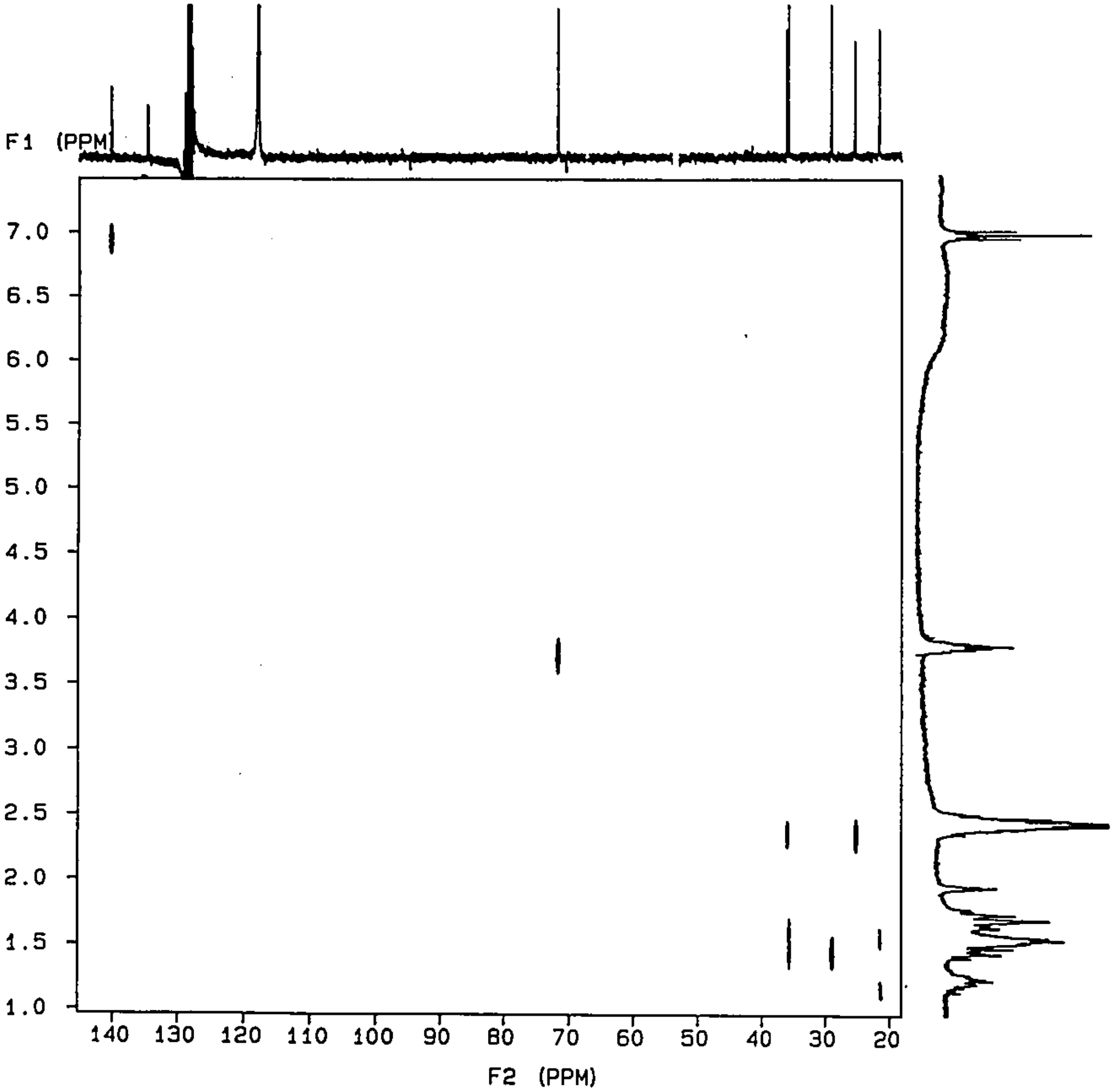
Single Relay COSY (300 MHz, acetone-d_6, TMS) of compound 

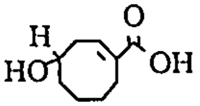
see Table 14 on page 86



HETCOR (300 MHz, CD_3CN, TMS) of compound 

see Table 14 on page 86



HETCOR (300 MHz, CD_3CN, TMS) of compound  (expanded spectrum)

see Table 14 on page 86