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CATALYTIC INTERMOLECULAR HYDROGEN TRANSFER IN THE HYDROGENATION OF HETEROCYCLIC ALDEHYDES AND KETONES. A REVIEW

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Literature data and the investigation results of the present authors on the reduction of heterocyclic aldehydes and ketones using catalytic hydrogen transfer have been analyzed.

Catalytic hydrogen transfer holds a special position among the well known and commonly used methods for the catalytic hydrogenation of organic compounds in light of its several advantages relative to methods of homogeneous and heterogeneous hydrogenation using molecular hydrogen. Advantages of the method of transferring hydrogen from a donor to an acceptor for the reduction of various functional groups and multiple bonds include the simplicity of the apparatus required, avoidance of the use of a highly flammable gas, hydrogen, often under high pressure, mild conditions, high reduction selectivity, and ease of separating the products formed. The most important point is that this method permits us, in most cases, to increase the reduction selectivity of only one functional group in polyfunctional compounds by varying the combination of solvent, catalyst, and hydrogen donor. Furthermore, in several cases, reactions, which could not be carried out under the most vigorous conditions of catalytic hydrogenation with molecular hydrogen, may be achieved. Several reviews have appeared, in which the major types of catalysts and hydrogen donors used in heterogeneous and homogeneous reduction have been examined, temperature and solvent effects have been evaluated, and the major results on the reduction of unsaturated bonds and functional bonds have been summarized [1-4].

CATALYSTS

Group VIII metals as blacks or metal complexes or deposited on supports predominate as catalysts for the intermolecular hydrogen transfer to carbonyl compounds. The greatest number of studies have been devoted to triphenylphosphine complexes of ruthenium and rhodium (Table 1).

According to present concepts on the mechanism for intermolecular transfer in the presence of metal triphenylphosphine complexes, a hydrogen atom of the donor molecule is inserted into the coordination sphere of the metal complex and extrudes one of the ligands [1, 5]. Coordination of the acceptor molecule by the central metal ion is followed by hydrogen transfer to the acceptor, removal of the hydrogenated and dehydrogenated products, and regeneration of the original catalyst structure occur in a stepwise sequence.

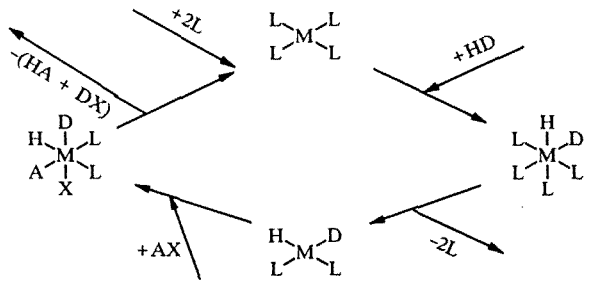

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TABLE 1. Catalysts Used in the Hydrogenation of Carbonyl Compounds by Hydrogen Transfer

Metal	Catalyst	Reference
Rh	$RhCl(PPh_3)_3$	[2, 3, 5—11, 13—15, 38, 39, 42, 59, 60, 62, 70, 75]
	$RhH(PPh_3)_4$	[3, 5, 10, 13, 16]
	$RhCl(CO)(PPh_3)_2$	[3, 5, 13, 38, 48]
	$RhH(CO)(PPh_3)_3$	[3, 16, 61]
	Rh-black	[3, 11, 17]
	Rh/C	[3, 11, 31]
Ru	$RuCl_2(PPh_3)_3$	[2, 3, 5—11, 13, 14, 16, 18—28, 37, 42, 48—50, 58, 60, 77]
	$RuH_2(PPh_3)_4$	[1, 3, 5, 10, 12, 13, 23, 25, 29]
	$RuHCl(PPh_3)_3$	[25, 29, 37, 48, 49]
	$RuCl_3$	[3, 12, 16, 28]
	Ru/C	[3, 11]
	Ru-black	[3, 11, 17]
Pd	$PdCl_2(PPh_3)_2$	[3, 5, 11, 13]
	Pd/C	[2, 3, 10, 11, 13, 54]
	Pd-black	[1—3, 10—12, 17, 23, 30, 31, 54]
Pt	$PtCl_2(PPh_3)_2$	[3, 5, 11, 13]
	$Pt(PPh_3)_4$	[5]
	Pt/C	[3, 11, 31]
	Pt-black	[3, 17]
Ir	$IrCl(CO)(PPh_3)_2$	[8, 16, 48, 63—67]
	Ir-black	[17]
Os	Os-black	[17]
Ni	$NiCl_2(PPh_3)_2$	[5, 13]
	Raney Ni	[2, 3, 24, 32, 33, 41]
Fe	$FeCl_2(PPh_3)_2$	[3, 5, 13]

TABLE 2. Hydrogen Donors Most Often Used in Catalytic Hydrogenation

Reduction reaction	Hydrogen donors
$R\text{-}CHO \longrightarrow R\text{-}CH_2\text{-}OH$	Cyclohexene [29], primary and secondary alcohols [13, 29, 61], 2-propanol [3, 8, 40, 44, 53, 55, 61], formic acid [25, 48]. HCOOH + trialkylamine [19, 29], formates [38, 50], dioxane [13, 29], tri-n-propylamine [13, 29], tetrahydrofuran [13, 29], tetrahydropyran [13], tetralin [13, 29]
$R\text{-}CHO \longrightarrow R\text{-}CH_3$	Cyclohexene [30], limonene [30], ammonium formate [54]
$R\text{-}CO\text{-}R^1 \longrightarrow R\text{-}CHOH\text{-}R^1$	Monoses [10], glucose [31], benzyl alcohol [9], glycols [23], 2,5-dihydrofuran [29], primary and secondary alcohols [6, 11, 13, 16, 18, 20, 26, 29, 35, 40, 61], 2-propanol [7, 8, 15, 17, 22, 32, 33, 40, 44, 53, 62], 2-pentanol [21], tetralin [13], tri-n-propylamine [13], HCOOH [25], HCOOH + Et_3N [51, 53], triethylammonium phosphite [24]
$R\text{-}CO\text{-}R \longrightarrow R\text{-}CH_2\text{-}R$	Cyclohexene [30], limonene [30], ammonium formate [54]

The above scheme shows that some positive charge on the metal atom (M), the presence of π-ligands (L) stabilizing the metal–hydrogen bond, and lability of the hydridic hydrogen in the donor molecule (HD) facilitate the intermolecular transfer of active hydrogen.

Catalyst activity depends on the existence of free sites in the coordination sphere of the central metal ion or possibility that this ion will provide vacant sites upon loss of a ligand. Furthermore, the catalytic activity of complexes and

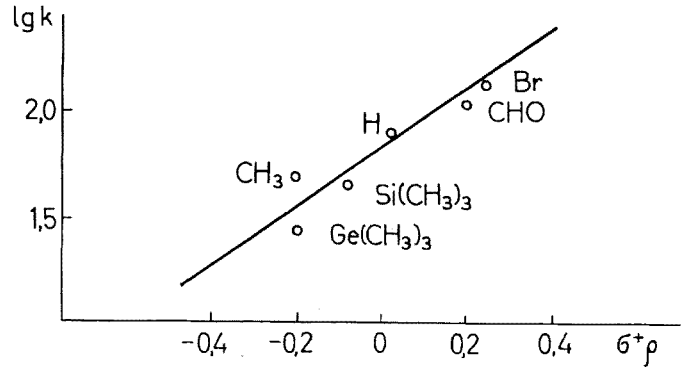


Fig. 1. Dependence of the hydrogenation rate constant on the Hammett substituent constant.

TABLE 3. Conversion of Dimethyl(2-furyl)germane in the Presence of Heterogeneous Catalysts

Catalyst	Hydrogen donor	Conversion, %	Selectivity for the formation of II
Raney Ni	2-Propanol	44	18
Pd/C	Cyclohexene	22	9,3
Raney Ni	H_2, P_{H_2} = 0,4 MPa	30	12

*Reaction conditions: T = 70°C for 3 h, the concentration of the substrate was $1 \cdot 10^{-3}$ mole/liter.

salts of transition metals is a consequence of identical energy levels of the substrate–metal, hydrogen donor–metal, and reduced substrate–metal bonds. A too strong bond of any of these pairs may account for lack of catalytic activity.

In examining the capacity of various homogeneous and heterogeneous catalysts in hydrogen transfer reactions, we cannot unequivocally determine which type of catalyst is most active relative to the carbonyl group. Thus, for example, heterogeneous Pd/C is inactive in the reduction of benzylacetophenone, while homogeneous catalysts, $RuCl_2(PPh_3)_3$ and $RhH_2(PPh_3)_3$ are active at 140°C [10, 23]. Homogeneous ruthenium and rhodium phosphine complexes are more active than the corresponding heterogeneous catalysts in the reduction of unsaturated cyclic ketones [11]. Processes involving catalysts have a number of advantages: relatively low reaction temperature, use of aqueous media, avoidance of the use of an inert gas, and use of cheap, available hydrogen donors. When heterogeneous catalysts are used, advantages include simple separation of the reaction products from the catalyst, which may be reused without marked alteration in activity.

HYDROGEN DONORS

Different hydrogen donors are employed depending on the type of reaction and catalyst used (Table 2). The hydrogen donor may be any organic compound having a sufficiently low oxidation potential, providing for the possibility of transferring a hydrogen atom under mild conditions.

Alcohols, which are converted to aldehydes or ketones as the result of the transfer of two hydrogen atoms, are the most active hydrogen donors. 2-Propanol is the best alcoholic donor due to the high lability of the α-hydrogen atom bound to carbon. Primary alcohols are less efficient as donors than secondary alcohols due to the lower inductive effect of the single alkyl group. Carbon–carbon multiple bonds in various unsaturated compounds and functional groups such as the carbonyl group are reduced using alcohols.

Methanol and ethanol have been used for the reduction of ketones to give alcohols in conjunction with various rhodium and ruthenium complexes [16]. Among the three mechanisms examined for the adsorption of methanol on the catalyst, preference is given for the formation of a carbonyl–hydride complex:

TABLE 4. Hydrogenation of Aldehydes in the Presence of $[RuCl_2(PPh_3)_3-HCOOH]$ $[RuCl_2(PPh_3)_3-HCOOH]$*

Starting compound	Conversion	Selectivity for alcohol formation, %
Benzaldehyde	0,77	89
Furtural	0,62	92
5-Methylfurtural	0,37	91
Furan-2,5-dicarbaldehyde	0,99	99
Thiophene-2-carbaldehyde	0,38	93
5-Trimethylsilyl-2-furfural	0,35	92
5-Trimethylgermyl-2-furfural	0,31	90
5-Bromo-2-furfural	0,99	100
Pyridine-3-carbaldehyde	0	0
Pyridine-4-carbaldehyde	0	0

*Reaction conditions: a) $6\cdot10^{-3}$ mole ketone and 4 ml $Et_3NH^+H_2PO_2^-\cdot1.5H_2O$ were stirred in a nitrogen atmosphere until a homogeneous solution was obtained. Then, $6\cdot10^{-5}$ mole $RuCl_2(PPh_3)_3$ was added. The reaction was carried out for 4 h at room temperature at room temperature. b) mixture of $2\cdot10^{-2}$ mmole $RuCl_2(PPh_3)_3$, 16 mmoles HCOOH, and 16 mmoles of the corresponding ketone was heated for 3 h at 120°C.

TABLE 5. Catalytic Liquid-Phase Reduction of 5-Methylfurfural*

Catalyst	Reducing agent (hydrogen pressure, MPa)	Solvent	Yield of 5-methylfuryl alcohol, %
$RuHCO(PPh_3)_3$	H_2 (0,3)	EtOH	0
$RuHCO(PPh_3)_3$	$NaBH4+H_2$ (0,3)	EtOH	0
$RuCl(PPh_3)_3$	H2 (0,3)	EtOH	0
$RuCl_2(PPh_3)_3$	H_2 (0,3)	2-PrOH	0
$RuCl_2(PPh_3)_3$	HCOOH	Toluene	95
Ni-Raneynickel	H_2 (0,3)	EtOH	25 (67)*[2]
$RhCl_3\cdot4H_2O$	$NaBH_4+H_2$ (0,3)	EtOH	86 (3)*[3]
10% Pd/C	H_2 (0,3)	EtOH	0
10% Pd/C	C_6H_{10}	THF	0,6 (0,6)*[3]

*Reaction conditions: $25\cdot10^{-3}$ mmole catalyst, $25\cdot10^{-3}$ mmole $NaBH_4$ or 0.5 mmole HCOOH, 0.25 mmole 5-methylfurfural, 2.5 ml solvent maintained at 50°C for 5 h.

*[2]Tetrahydrofurfuryl alcohol.

*[3]2-Methylfuran.

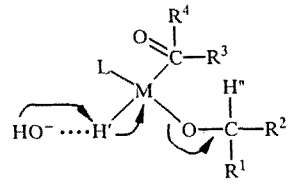
$$CH_3OH + M_n \longrightarrow M(H)_nCO_x$$

In addition to their relatively low donor capacity, a hindrance to the use of primary alcohols may lie in the circumstance that the aldehydes formed in the dehydrogenation of primary alcohols may poison the catalyst due to the formation of strong complexes [12, 37, 38]:

$$ML_n + RCHO \xrightarrow[-L]{} ML_{n-1}-\underset{\displaystyle R}{\overset{\displaystyle O}{\overset{\|}{C}}}-H \xrightarrow[-RH]{} ML_{n-1}-C\equiv O$$

As noted above, 2-propanol is the most efficient hydrogen donor. In addition to its compatibility with both homogeneous [5, 13, 39, 40] and heterogeneous catalysts [33, 41, 55-57], 2-propanol is inexpensive and may be separated from the reaction mixture rather simply similar to acetone, which is formed upon its dehydrogenation. A detailed study of the mechanism of the transfer of hydrogen from 2-propanol to ketones by the action of $RhCl(PPh_3)_3$ and $RuCl_2(PPh_3)_3$ was carried out by Freidlin et al. [7]. The mechanism of the catalytic action of the complex involves its dissociation with loss of

one ligand, oxidative addition of the alcohol, and cooperative addition of a ketone molecule with formation of an intermediate:



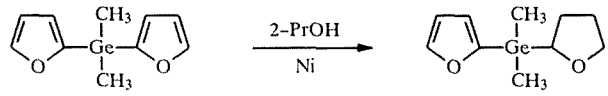
In this case, added KOH acts as a promotor. The attack of the OH^- nucleophile leads to loss of H′ as H^+ and enhancement of the electron density on the metal favorable for hydridic lability of H″. Special base activation is required for some homogeneous systems using the alcohol as a hydrogen donor [8, 21, 42].

The extent of reduction of aldehydes and ketones by 2-propanol is high in the presence of $RuH_2(PPh_3)_4$ at 140°C [13]. Ru, Os, and Ir blacks transfer hydrogen from 2-propanol to cyclohexanone derivatives [17]. In addition to the reduction of the carbonyl group in benzophenone, the consecutive hydrogenation of one of the benzene rings in diphenylmethane formed in the reaction occurs on Raney nickel in the presence of 2-propanol [33]. This result was attributed to the binding of diphenylmethane on the catalyst surface by means of the reaction of one of the phenyl rings with the residual aluminum ions, which are not hydrogenation sites. This provides for contact of the second ring with the hydrogenation sites. The explanation of the partial hydrogenation of diphenylmethane is not sufficiently convincing. According to the classical concepts concerning σ- and π-complex interaction [43], unsaturated compounds are preferentially bound on the surface ions of group VIII metals, which are hydrogenation sites. In this case, both rings in diphenylmethane are capable of being adsorbed on these sites. The hydrogenation of only one benzene ring occurs probably as a consequence of steric hindrance.

HYDROGENATION OF BISFURYLGERMANE

Information on the possibility of transferring hydrogen to heterocyclic compounds has appeared since the end of the 1980's and some of the methods proposed have already found preparative applications [27, 28, 34, 44, 45].

In previous work [34], we were the first to indicate the possibility of reducing the double bonds in dimethyldi-(2-furyl)germane (I) as the result of hydrogen transfer from 2-propanol as a donor. Raney nickel catalyzes the hydrogenation of one of the furan rings of germane I both under hydrogen transfer conditions and in an atmosphere of molecular hydrogen (Table 3).



I II

Furthermore, the hydrogenation of germane I gives rise to a series of hydrogenolysis products: dimethyl-(2-furyl)hydrogermane, dimethyl(2-tetrahydrofuryl)hydrogermane, and tetrahydrofuran.

Evaluation of the steric feasibility of the simultaneous reduction of both furan rings in dimethyldi(2-furyl)germane and a comparative quantum chemical study of the electronic structure of this germane and the reduction product, dimethyl-(2-tetrahydrofuryl)(2-furyl)germane(II), were carried out using the CNDO/2 program with parameters for a compound with group IV elements. The three-dimensional structure of the germane was represented as follows: the germanium atom is located at the center of a tetrahedron and the Ge–C bonds are directed toward its apices corresponding to sp^3 hybridization. The $Ge-CH_3$ bond length was taken to be 1.98 Å, while $Ge-C^{sp^2}{}_f$ and $Ge-C^{sp^3}{}_{THF}$ were optimized in our previous work [34]. If the furan ring is seen as a diolefin and we assume that the hydrogenation of five-membered cyclic hydrocarbons on Group VIII metals proceeds through a σ-adsorption complex, $C_{(4)}$ and $C_{(5)}$ of one of the furan rings are available for adsorption with subsequent hydrogenation. The subsequent hydrogenation of the second olefin bond in this ring proceeds with-

TABLE 6. Hydrogenation of Furan Ketones*

Ketone	Hydrogen donor	Alcohol yield, %
2-Fur—CO—CH_3	a) $Et_3NH^+H_2PO_2^-\cdot 1{,}5H_2O$	76
	b) HCOOH	10
CH_3—2,5-Fur—$COCH_3$	a) $Et_3NH^+H_2PO_2^-\cdot 1{,}5H_2O$	59
	b) HCOOH	5
2-Fur—CO—$CH(C_2H_5)_2$	a) $Et_3NH^+H_2PO_2^-\cdot 1{,}5H_2O$	67

*Reaction conditions: a) $6\cdot 10^{-3}$ mole ketone and 4 ml $Et_3NH^+H_2PO_2^-\cdot 1.5H_2O$ were stirred in a nitrogen atmosphere until a homogeneous solution was obtained. Then, $6\cdot 10^{-5}$ mole $RuCl_2(PPh_3)_3$ was added. The reaction was carried out for 4 h at room temperature at room temperature. b) A mixture of $2\cdot 10^{-2}$ mmole $RuCl_2(PPh_3)_3$, 16 mmoles HCOOH, and 16 mmoles of the corresponding ketone was heated for 3 h at 120°C.

out obvious difficulty. In this case, the simultaneous adsorption and hydrogenation of the corresponding bond in the second ring are possible only assuming an extraordinary correspondence of the pore shape and size and active site distribution on the catalyst surface to the three-dimensional structure of germane I, which is extremely unlikely. Thus, the hydrogenation of the second furan ring may be achieved only consecutively after hydrogenation of the first ring through desorption of the partially hydrogenated molecule, readsorption involving $C_{(4')}$ and $C_{(5')}$ with subsequent hydrogenation initially of $C_{(4')}=C_{(5')}$ and then of the residual $C_{(2')}=C_{(3')}$ bond of the second ring.

However, a quantum chemical calculation showed that after hydrogenation of the furan ring, the bond of this ring to Ge is markedly weakened, as indicated by the calculated equilibrium lengths (r_0) and two-centered components of the energy E for the bonds of germanium with the furan carbon atom (r_0 = 2.20 Å, $E_{Ge\text{-}C_f}$ = 0.906 a.u.) and tetrahydrofuran (r_0 = 2.25 Å, $E_{Ge-CTHF}$ = 0.826 au). These values were obtained by optimizing the corresponding bonds in germanes I and II. Two-centered energy components calculated in the framework of the CNDO/2 method are indices of the strength of the corresponding bonds.

Thus, it is natural to assume that the bond of germanium to the tetrahydrofuran ring under the reaction conditions is cleaved prior to realization of all the abovementioned consecutive steps required for hydrogenation of the second furan ring. Therefore, a partially hydrogenated form of germane I and its hydrogenolysis products are found in the products of the hydrogenation of germane I instead of the expected dimethylbis(2-tetrahydrofuryl)germane.

REDUCTION OF HETEROCYCLIC ALDEHYDES

The reduction of furfural as well as of aliphatic and aromatic aldehydes to the corresponding alcohols is carried out in the liquid phase in the presence of hydrated zirconium dioxide $Zr(OH)_4$ [44]. In the vapor phase, this catalyst is capable of reducing acids and ethers [57] in addition to aldehydes and ketones [53]. The steric structure of some ketones hinders their efficient reduction [44]. Primary, secondary, and tertiary alcohols were tested as hydrogen donors but only 2-propanol displayed suitable properties under the experimental conditions. The reaction rate data indicate first-order kinetics relative to the concentrations of the carbonyl substrates, 2-propanol, and the catalyst. The isotope effect determined indicates that the hydride transfer from adsorbed 2-propanol to the adsorbed carbonyl compound is the rate-limiting step.

A linear correlation between the Hammett $\sigma\rho^+$ constant and the reaction rate constant was obtained using the experimental data on the reduction of substituted benzaldehydes by 2-propanol in the presence of $Zr(OH)_4$ [35]. The value ρ = 1.35 confirms an electronic effect of the substituent on the reduction rate and indicates that the rate of attack of the 2-propanol hydrogen increases with increasing electron density deficit in the carbonyl group.

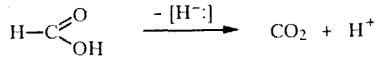
Analogous results were obtained in the reduction of furfural derivatives [28, 45] in the presence of $RuCl_2(PPh_3)_3$ with formic acid as the hydrogen donor (Table 4).

The introduction of various substituents at $C_{(5)}$ of the furan ring has a marked effect on the conversion. The rate of hydrogen transfer to aldehydes decreases in the following series: 5-bromofurfural > furan-2,5-dicarbaldehyde > furfural > 5-methylfurfural > 5-trimethylsilyl-2-furfural > 5-trimethylgermyl-2-furfural. An attempt was made to find a correlation of the reactivity of furan aldehydes with their structure using two independent Hammett equation parameters $\sigma\rho^+$ and ρ. Assuming no change in the hydrogen transfer mechanism, first-order kinetics, and constant reaction conditions, ρ describes only structural features of the reagent aldehydes.

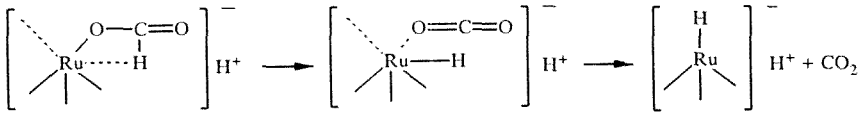
Figure 1 shows the linear correlation of the logarithm of the rate constant of the transfer of hydrogen to substituted furfurals on the Hammett substituent constant $\sigma\rho^+$. Using Hammett constants $\sigma\rho$ [46], we find $\rho = +5.9$ for substituents at $C_{(5)}$ in the furan ring. The correlation coefficient $r = 0.9531$ was determined by the method of least squares. The large positive value for ρ indicates a strong acceleration of the hydrogen transfer reaction upon the introduction of electron-withdrawing substituents Br and CHO into the furfural molecule, i.e., the rate increases with a shift in electron density from the reaction site. The presence of electron-donor substituents H, CH_3, $Si(CH_3)_3$, and $Ge(CH_3)_3$ leads to an increase in the electron density at the reaction site and thereby decreases the rate of reduction of furan aldehydes.

The selectivity for the formation of alcohols from benzaldehyde, furfural, and thiophene-2-carbaldehyde is virtually the same. The nature of the moiety attached to the carbonyl group lacks fundamental importance in the hydrogen transfer. Pyridinealdehydes do not react at all under analogous conditions due to inhibition as a consequence of deactivation of the catalyst by the substrate molecule, which forms a strong complex with the ruthenium complex. Similar inhibition was also reported by Khai and Arcelli [19].

Formic acid holds the greatest promise for use as a hydrogen donor in the hydrogen of the carbonyl group in the presence of the ruthenium complex catalyst among the group of donors such as formic acid, cyclohexene, indoline, and 2,5-dihydrofuran [28]. The ease of the removal of a hydride ion from formic acid is attributed not only to the effect of the free electron pair of the adjacent oxygen atom but also the significant stability of the carbon dioxide molecule formed:



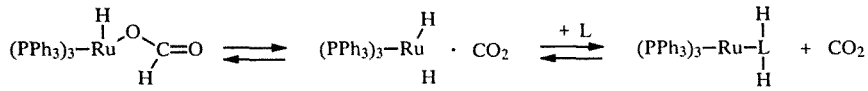
The decomposition of formic acid by the action of $Ru(PPh_3)_3Cl_2$ occurs through the formation of a formate complex with subsequent hydride transfer from the C−H bond as follows:



Thus, it is quite likely that the presence of electron-withdrawing substituents in furan aldehydes, which reduce the electron density in the aldehyde group, facilitate coordination of the substrate molecule with the ruthenium complex enriched with a hydride ion. Electron-donor groups, whose introduction causes a decrease in the rate of aldehyde reduction, have the opposite effect.

Table 5 gives a comparison of the efficiency of the reduction of 5-methylfurfural by various reducing agents. Metal complex catalysts are inactive relative to hydrogenation under the experimental conditions in a hydrogen atmosphere. The conversion of 5-methylfurfural in the presence of Raney nickel and $RhCl_3 \cdot 4H_2O$ is rather high. On the other hand, the use of formic acid permits us to carry out the hydrogenation on a metal complex catalyst with a 95% yield of 5-methylfurfuryl alcohol.

An increase in the aldehyde reduction rate (see Table 4) is observed upon adding triethylamine to a mixture of formic acid and $Ru(PPh_3)_3Cl_2$. The selective conversion of aldehydes to the corresponding alcohols at room temperature requires only 30 min. This property of $(C_2H_5)_3N$ may be attributed to an increase in the rate of migration of the hydridic hydrogen of the formate group to the metal with formation of an unstable ruthenium hydride complex with carbon dioxide. This complex readily eliminates carbon dioxide to give a hydride complex upon the action of agents such as Et_3N, Ph_3P, CO, N_2, and H_2 [47]:



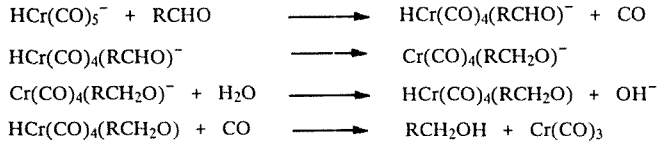
L = Ph_3P, N_2, H_2, CO

A study of various transition metal complexes in conjunction with formic acid showed that this reagent, similar to other donors, cannot be considered selective relative to some specific functional groups. We should note the efficient use of formic acid for the reduction of carbon–carbon multiple bonds [48, 49].

Joo' and Be'nyei [50] have described the catalytic decomposition of formic acid to give hydrogen and carbon dioxide in the presence of phosphine complexes of platinum, ruthenium, and iridium. The reduction of butyraldehyde to the corresponding alcohol is observed upon the introduction of this aldehyde into the indicated catalytic system.

The system containing triethylamine, formic acid, and $RuCl_2(PPh_3)_3$ rather selectively reduces aldehydes to the corresponding alcohols at room temperature. Steric factors, as indicated by Khai and Arcelli [19], play a significant role. The conversion in the reduction of mesitylaldehyde is only 27% after 30 min, while the corresponding yield of benzyl alcohol is 98%. The polarity of the substituents does not affect the rate of reduction and 4-methyl-2-bromo, 4-nitro-, and 2-methoxybenzaldehydes are reduced to alcohols with the same conversion.

Formate salts act analogously to formic acid. Unsaturated aldehydes may be reduced with high selectivity to unsaturated alcohols upon the transfer of hydrogen from $HCOOHa/H_2O$ in the presence of the Ru(II) complex under mild conditions (30-80°C) [50]. Aldehydes RCHO (R = 1-heptyl, p-toluyl, and p-anisyl) are converted to the corresponding alcohols using sodium formate in aqueous methanol in the presence of $Cr(CO)_6$ [80]. The reduction of aldehydes proceeds as follows:

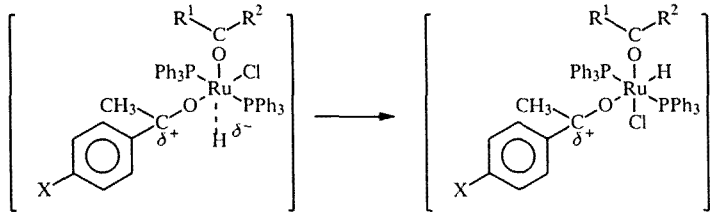


REDUCTION OF HETEROCYCLIC KETONES

2-Propanol is the most commonly used hydrogen donor for the reduction of ketones. The transfer of hydrogen from 2-propanol to the cyclohexanone carbonyl group is catalyzed by iridium [63-67], rhodium (62, 68-71], and ruthenium complexes [72, 74, 75, 80].

The use of immobilized complexes for the reduction of ketones holds promise. The reduction of cyclohexanone to cyclohexanol is carried out by the transfer of hydrogen from 2-propanol in an argon atmosphere in the presence of rhodium complexes $[RhCl(COD)]_2$, $RhCl(PPh_3)_3$, and $RhCl_3$ immobilized on silica gel modified by aminophoshine groups []75]. Cationic norbornadiene rhodium complexes immobilized on polystyrene [76] catalyze the transfer of hydrogen from 2-propanol to acetophenone. The nature of the ketone affects the hydrogen transfer rate, which decreases in the following series: cyclohexanone > acetophenone > cyclopentanone > 2-hexanone > cycloheptanone > cyclooctanone [21]. The yield of (+)-alcohol is 12% in the absence of asbestos and 19% (−)-alcohol in the presence of asbestos in the transfer of hydrogen from 2-propanol to acetophenone in the presence of a ruthenium complex with chiral ligands $[Ru(OAc)_2((+)\text{-diop})]_n$. Asbestos acts as a modifier of the asymmetric catalyst [79].

The activity of ruthenium phosphine complexes in the reduction of cyclohexanone by 2-propanol decreases in the series: $RuCl_2(PPh_3)_3$ > $RuCl_2(DPPTP)_3$ > $RuI_2(DPPTP)_3$ > $RuBr_2(DPPTP)_3$ > $RuH(CH_3CO_2)(PPh_3)_3$ [60]. An effect was found for the para substituents in 1-phenylethanol derivatives used as hydrogen donors. The negative value of ρ in the Hammett equation suggests an electron deficiency in the transition state and formation of a carbonium ion:



The transfer of hydrogen from 1-phenylethanol to aromatic ketones is a stepwise process and coordination of the donor in $RuCl_2(PPh_3)_3$ is preceded by prior orientation of the donor on it [20]. A kinetic isotope effect is found upon replacement of hydrogen in the hydroxyl group of the donor by deuterium, indicating that the α-hydrogen atom participates in the rate-limiting step.

The transfer of hydrogen from 2-propanol in the presence of $RuCl_2(PPh_3)_3$ and NaOH presupposes the consecutive formation of an anionic species, elimination of the β-hydrogen from the alkoxide ligand, leading to the formation of acetone and an anionic ruthenium hydride complex, rapid protonation of the anionic species, and then reduction of cyclohexanone by the dihydride derivative of the ruthenium compound [77].

Hydrogen transfer from methanol to 2-methyl-2-penten-4-one, which is an unsaturated ketone, is accomplished in the presence of a heterogeneous copper catalyst [78]. The use of such traditional heterogenous catalysts such as palladium, platinum, ruthenium, and nickel is impossible since carbon monoxide released upon the decomposition of methanol poisons such catalysts.

Carbonyl compounds are quantitatively reduced to the corresponding alcohols in the presence of formic acid and ruthenium complexes at 120°C over 3 h [25]. For example, the yield of α-propanol [I think this should be 2-propanol] upon the reduction of 2-propanone using $HCOOH-RuCl_2(PPh_3)_3$ is 94%. The selectivity for formation of the corresponding alcohols in the hydrogenation of 3-pentanone, cyclohexanone, and acetophenone is 86, 78, and 84%, respectively. Steric hindrance is quite important in the conversion of ketones. For example, the conversion in the hydrogenation of 3,3-dimethyl-2-propanone is 31%, while 3,3-dimethyl-3-pentanone is completely inactive. The catalytic activity under these conditions when using the following catalysts decreases in the series: $RuCl_2(PPh_3)_3$ > $RuHCl(PPh_3)_3$ > $RuHCl(CO)(PPh_3)_3$ > $RuH_2(PPh_3)_4$.

The corresponding alcohols are formed in good yield upon the reduction of aliphatic, alicyclic, and aromatic ketones (2-butanone, 2- and 3-pentanones, 3-methyl-2-butanone, acetophenone, benzophenone, and cyclohexanone) [51]. The addition of a tertiary amine to excess formic acid in the presence of $CpZrCl_2$ permits us to reduce even pinacolin, which has a bulky alkyl group, to pinacolyl alcohol in 68% yield at 150°C, while primary and secondary amines decrease the selectivity for alcohol formation, probably due to the facile formation of Schiff bases. Alcohols and the corresponding formates are formed under the same conditions in the hydrogenation of aldehydes (butanal, isobutanal, octanal, and benzaldehyde). A comparison of the catalytic activity of several complexes of group IVA metals was carried out: Cp_2ZrCl_2, Cp_2TiCl_2, $CpHfCl_2$, $CpZrCl_3$, $ZrCl_4$, Cp_2ZrHCl, and Cp_2ZrH. The greatest activity was found for Cp_2HfCl_2 and Cp_2ZrCl_2, while the least activity was found for $ZrCl_2$. Tertiary amines have greatest efficiency in this reaction.

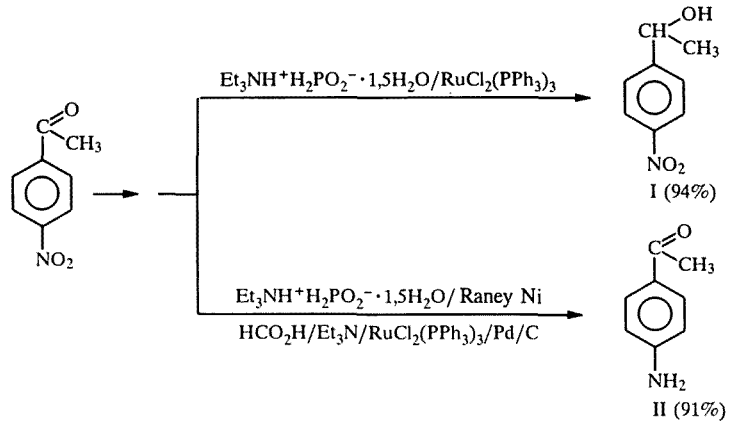
A method for enhancing the catalytic activity of systems, in which formic acid is the hydrogen source, is the replacement of this acid by formates or the addition of formic acid salts. Indeed, the use or ammonium formate as the hydrogen source leads to rapid reduction of aromatic aldehydes and ketones to the corresponding methyl derivatives [54].

The selective reduction of ketones is observed when the reaction is carried out in the presence of $Et_3NH^+ H_2PO_2^- \cdot H_2O$ and $RuCl_2(PPh_3)_3$ [24]. Such high selectivity relative to hydrogenation of the carbonyl group is not found for other catalysts such as Raney nickel. In this example, the nature of the transition metal plays the decisive role.

The extent of hydration of the agents ($Et_3NH^+H_2PO_2^- \cdot 1.5H_2O$ and $Et_3NH^+H_2PO_2^-$) affects the steric selectivity in the reduction. The thermodynamically less stable isomer is predominantly formed (cis/trans = 66/34) from 4-tert-butylcyclohexanone when the anhydrous reagent is used, in contrast to experiments, in which the hydrated reagent was employed to give cis/trans = 49/51.

The ease of hydrogen migration from the ruthenium complex to the ketone group of acetophenone and cyclohexanone derivatives depends on the nature of the substituent. Such behavior is not found in the reduction of aldehydes by the $HCOOH/Et_3N/RuCl_2(PPh_3)_3$ system [52]. The extent of reduction of ketones decreases in the following series: p-nitroaceto-

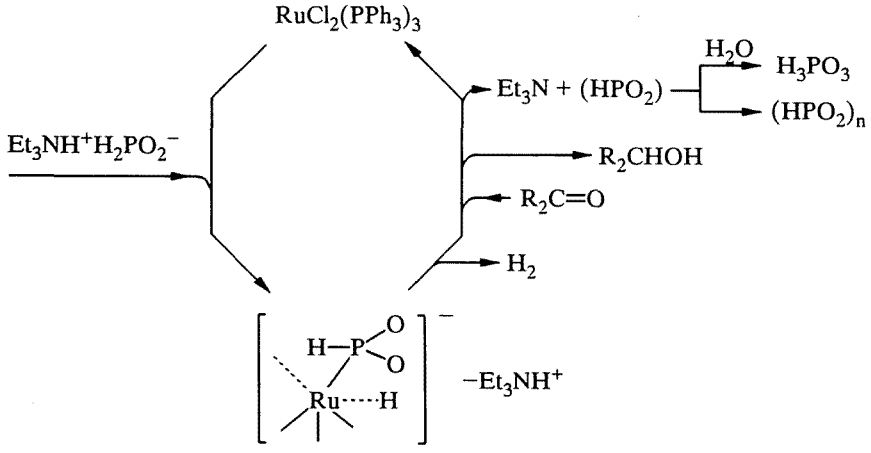
phenone > p-chloroacetophenone > acetophenone > p-methylacetophenone and cyclohexanone > 4-tert-butylcyclohexanone > 2-methylcyclohexanone.



The reduction of furan ketones and alcohols by hydrogen transfer has proven rather difficult in comparison with the reduction of other ketones, for which systems such as $HCOOH/RuCl_2(PPh_3)_3$ and $Et_3NH^+H_2PO_2^-\cdot 1.5H_2O/RuCl_2(PPh_3)_3$ are used [27]. Table 6 gives the results of the reduction of some furan ketones in the presence of $RuCl_2(PPh_3)_3$ by HCOOH or $Et_3NH^+H_2PO_2^-$ as the donor.

Catalytic hydrogen transfer from formic acid to the carbonyl group attached to a furan ring at 120°C for 3 h leads to formation of the corresponding alcohol in 5-10% yield. $Et_3NH^+H_2PO_2^-\cdot 1.5H_2O$ is the most efficient hydrogen donor relative to these ketones and the reaction requires 4 h at room temperature in this case. $RuCl_2(PPh_3)_3$ oxidizes H_3PO_2 to HPO_2 and is thereby partially converted into $RuHCl(PPh_3)_3$. In the presence of water, HPO_2 forms the polymer $(HPO_2)_n$, which is capable of adsorbing the catalyst, thereby reducing its activity. The presence of water molecules in the reaction medium leads to the formation of H_3PO_3. The catalyst activity is not altered in this case, which was observed in the reduction of furan ketones.

Scheme for ketone reduction



The intermolecular transfer of hydrogen to carbonyl group compounds examined above clearly illustrates the possibility of using this method in synthetic organic chemistry. Since ever more complex compounds are being studied, we may expect not only further development in our theoretical understanding of the reaction mechanism and the development of multifunctional substrates with catalysts and hydrogen donors, but also the broad introduction of this method into fine organic synthesis, especially in the synthesis of steroid derivatives and the preparation of determined enantiomers of optically active compounds.

REFERENCES

1. I. S. Kolomnikov, V. P. Kukolev, and M. E. Vol'pin, Usp. Khim., **53**, No. 5, 903 (1974).
2. G. Brieger and T. J. Nestrick, Chem. Rev., **74**, No. 5, 567 (1974).
3. R. A. W. Johnstone, A. H. Wilby, and J. D. Entwistle, Chem. Rev., **85**, 129 (1985).
4. Pillai S. Muthukumaru, J. Sci. Ind. Res., **47**, 460 (1988).
5. T. Nishiguchi, K. Tanaka, and K. Fukuzumi, J. Organometall., Chem., **193**, 37 (1980).
6. V. Z. Sharf, L. Kh. Freidlin, and V. N. Krutii, Izv. Akad. Nauk SSSR Ser. Khim., **10**, 2264 (1973).
7. V. Z. Sharf, L. Kh. Freidlin, and V. N. Krutii, Izv. Akad. Nauk SSSR Ser. Khim., **4**, 735 (1977).
8. A. Camus, G. Mestroni, and G. Zassinovich, J. Mol. Catal., **6**, 231 (1979).
9. Y. Sasson and J. Blum, Tetrahedron Lett., No. 24, 2167 (1971).
10. G. Descotes, J. P. Praly, and D. Sinou, J. Mol. Catal., **6**, 421 (1979).
11. J. Blum., J. Mol. Catal., **3**, 33 (1977).
12. T. Tatsumi, K. Kizawa, and H. Tominaga, Chem. Lett., No. 2, 191 (1977).
13. H. Imai, T. Nishiguchi, and K. Fukuzumi, J. Org. Chem., **41**, No. 4, 665 (1976).
14. Y. Blum, Y. Sasson, and S. Iflah, Tetrahedron Lett., No. 11, 1015 (1972).
15. Y. C. Orr, M. Mersereanu, and A. Sanford, J. Chem. Soc. Chem. Commun., No. 1, 162 (1970).
16. T. A. Smith and P. M. Maitlis, J. Organometall. Chem., **289**, 385 (1985).
17. H. B. Henbest and Z. Zurgiyah, J. Chem. Soc. Perkin Trans. I, No. 5, 604 (1974).
18. Y. Sasson, P. Albin, and J. Blum, Tetrahedron Lett., No. 10, 833 (1974).
19. B. T. Khai and A. Arcelli, Tetrahedron Lett., **26**, No. 28, 3365 (1985).
20. Y. Sasson and J. Blum., J. Org. Chem., **40**, No. 13, 1887 (1975).
21. V. Z. Sharf, L. Kh. Freidlin, V. N. Krutii, and T. V. Lysyak, Izv. Akad. Nauk SSSR Ser. Khim., No. 10, 2195 (1972).
22. A. Camus, G. Mestroni, and G. Zassinovich, J. Organometall. Chem., **184**, C10 (1980).
23. G. Descotes and I. Sabadie, J. Mol. Catal., **5**, 415 (1979).
24. B. T. Khai and A. Arcelli, J. Org. Chem., **54**, 949 (1989).
25. Y. Watanabe, T. Ohta, and Y. Tsuji, Bull. Chem. Soc. Japan, **55**, 2441 (1982).
26. G. Speir and L. Marko, J. Organometall. Chem., **210**, 253 (1981).
27. Zh. G. Yuskovets and M. V. Shimanskaya, "Use of metal complex catalysis in organic synthesis," Abstracts of the First All-Union Conference, Ufa (1989), p. 49.
28. Zh. G. Yuskovets and M. V. Shimanskaya, Khim. Geterotsikl. Soedin., No. 6, 745 (1990).
29. H. Imai, T. Nishiguchi, and K. Fukuzumi, Chem. Lett., No. 8, 807 (1975).
30. G. Brieger and T.-H. Fu, J. Chem. Soc. Chem. Commun., No. 19, 757 (1976).
31. G. Wit, J. J. Vlieger, A. C. K. Dalen, A. P. G. Kiebom, and H. Bekkum, Tetrahedron Lett., No. 15, 1327 (1978).
32. G. P. Boldrini, D. Savoia, E. Tagliavini, G. Trombini, and A. Umani-Ronchi, J. Org. Chem., **50**, 3082 (1985).
33. M. J. Andrews and C. N. Pillai, Indian J. Chem., **16**, No. 5, 465 (1978).
34. É. Lukevits, L. M. Ignatovich, Zh. G. Yuskovets, L. O. Golender, and M. V. Shimanskaya, Zh. Obshch. Khim., **57**, No. 6, 1294 (1987).
35. G. Tragale, M. Gargano, and M. Rossi, J. Mol. Catal., **58**, No. 5, 69 (1979).
36. A. Benyei and F. Joo, J. Mol. Catal., **58**, No. 2, 151 (1990).
37. Y. Sasson and G. L. Rempel, Tetrahedron Lett., No. 36, 3221 (1974).
38. I. S. Kolomnikov, I. L. Nakhshunova, F. Prukhnik, N. A. Belikova, and M. E. Vol'pin, Izv. Akad. Nauk SSSR Ser. Khim., **5**, 1180 (1972).
39. H.-A. Bruner, J. Unsin, R. Hemmer, and M. Reichhardt, J. Organometall. Chem., **369**, No. 36, 335 (1989).
40. K. Konishi, K. Makita, T. Aida, and S. Inoue, J. Chem. Soc. Chem. Commun., No. 10, 643 (1988).
41. S. Srivastava, J. Minore, C. K. Cheung, and W. J. Noble, J. Org. Chem., **50**, No. 3, 394 (1985).
42. V. Z. Sharf, L. Kh. Freidlin, B. M. Savchenko, and V. N. Krutii, Izv. Akad. Nauk SSSR Ser. Khim., **8**, 1894 (1976).
43. A. A. Balandin and A. M. Rubinshtein (eds.), Stereochemistry and Mechanisms of Organic Reactions [in Russian], Mir, Moscow (1968).

44. M. Shibagaki, K. Takanashi, and H. Matsuhita, Bull. Chem. Soc. Jpn., **61**, 3283 (1988).
45. Zh. Yuskovets and M. Shimanska, Fifth International Symposium on Furan Chemistry: Abstracts of Papers, Riga (1988), p. 107.
46. A. N. Egorochkin and G. A. Razuvaev, Usp. Khim., **61**, No. 9, 1480 (1987).
47. S. Komiya and A. Yamamoto, J. Organometall. Chem., **46**, 58 (1972).
48. I. S. Kolomnikov, V. P. Kukolev, V. O. Chernyshev, and M. E. Vol'pin, Izv. Akad. Nauk SSSR Ser. Khim., **3**, 693 (1972)
49. I. S. Kolomnikov, Yu. D. Koreshkov, V. P. Kukolev, V. A. Mosin, and M. E. Vol'pin, Izv. Akad. Nauk SSSR Ser. Khim., **1**, 175 (1973).
50. F. Joo and A. Be'nyei [Benyei], J. Organometall. Chem., **363**, C19 (1989).
51. N. Tatsuya, A. Joichi, J. Yasutaka, and O. Masayo, Technol. Reports Kansai Univ., **29**, 69 (1987); Ref. Zh. Khim., 19B4091 (1987).
52. B. T. Khai and A. Arcelli, J. Organometall. Chem., **309**, C63 (1986).
53. M. Shibagaki, K. Takahashi, H. Kuno, H. Kawakami, and H. Matsuhita, Chem. Lett., No. 10, 1633 (1988).
54. S. Ram and L. D. Spicer, Tetrahedron Lett., **29**, No. 31, 3741 (1988).
55. M. Shibagaki, H. Kuno, K. Takahashi, and H. Matsuhita, Bull. Soc. Chem. Jpn., **61**, 4153 (1988).
56. E. L. Amin, G. M. Anantharamaiah, G. P. Royer, and G. E. Means, J. Org. Chem., **44**, 3442 (1979).
57. K. Takanashi, M. Shibagaki, H. Kuno, and H. Matsuhita, Chem. Lett., No. 7, 1141 (1989).
58. Y. Sasson and J. Blum, J. Org. Chem., **40**, 1887 (1975).
59. V. Z. Sharf, L. Kh. Freidlin, I. S. Shekoyan, and V. N. Krutii, Izv. Akad. Nauk SSSR Ser. Khim., **4**, 834 (1977).
60. J. Rajaram, S. Vancheesan, and J. C. Kuriacose, J. Mol. Catal., **16**, 349 (1982).
61. R. Grigg, T. R. B. Mitchell, and S. Sutthivaiyakit, Tetrahedron, **37**, 4313 (1981).
62. V. Z. Sharf, L. K. Freidlin, I. S. Shekoyan, and V. N. Krutii, Izv. Akad. Nauk SSSR Ser. Khim., **5**, 1064 (1978).
63. A. Camus, G. Mestroni, and G. Zassinovich, J. Mol. Catal., **6**, 231 (1979).
64. G. Mestroni, G. Zassinovich, and A. Camus, J. Organometall. Chem., **198**, 87 (1980).
65. G. Zassinovich, A. Camus, and G. Mestroni, J. Mol. Catal., **9**, 345 (1980).
66. R. Spogliarich, G. Mestroni, and M. Graziani, J. Mol. Catal., **22**, 309 (1984).
67. F. Vinzi, G. Zassinovich, and G. Mestroni, J. Mol. Catal., **18**, 359 (1983).
68. R. Spogliarich, G. Zassinovich, G. Mestroni, and M. Graziani, J. Organometall. Chem., **179**, C45 (1979).
69. R. Spogliarich, A. Tencich, J. Kasper, and M. Graziani, J. Organometall. Chem., **240**, 453 (1982).
70. V. N. Krutii, S. A. Shelmakova, A. S. Gurovets, T. V. Vasina, D. B. Furman, V. Z. Sharf, and A. L. Liberman, Izv. Akad. Nauk SSSR Ser. Khim., **5**, 1111 (1975).
71. R. Uson, L. A. Oro, R. Sariego, and Esteruelas, J. Organometall. Chem., **214**, 399 (1981).
72. L. A. Oro, M. P. Lamata, and M. Valderrama, Transition Met. Chem., **8**, 48 (1983).
73. G. Zassinovich and F. Grisoni, J. Organometall. Chem., **247**, C24 (1983).
74. M. Bianchi, J. Organometall. Chem., **198** (1973).
75. V. F. Dovganyuk, V. I. Isaeva, and V. Z. Sharf, Izv. Akad. Nauk SSSR Ser. Khim., **6**, 1223 (1988).
76. L. A. Oro and R Sariego, React. Kinet. Catal. Lett., **21**, 445 (1982).
77. R. L. Clowdhyry and J.-E. Béckvall, J. Chem. Soc. Chem. Commun., **27**, 1063 (1991).
78. L. Prat, M. Rossi, M. Gargano, and N. Ravasio, Gazz. Chim. Ital., **122**, 221 (1992).
79. R. Chauvin, J. Mol. Catal., **62**, 147 (1990).
80. D. E. Linn, R. B. King, and A. D. King, Jr., J. Mol. Catal., **80**, 165 (1993).