RECENT EXAMPLES OF SELECTIVITY IN CATALYSIS

by John H. MacMillan
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RECENT EXAMPLES OF SELECTIVITY IN CATALYSIS

by John H. MacMillan

Synthetic organic chemistry is in part a science of reactions of functional groups. Invariably the chemist will encounter synthesis where he wishes to react one functional group while keeping other active groups in the molecule intact. Chemists also desire "optical" selectivity, which is defined as preferential production of one enantiomer giving an optically active product. Stereoselective synthesis, i.e., preferential production of one structural isomer over another, and stereospecific synthesis, i.e., exclusive production of one isomer, are of obvious importance. In addition the selective incorporation of isotopes is important for mechanistic investigations. Transition metal catalysts have proven of enormous utility in these areas. This account will briefly summarize recent work, commenting on advantages over older procedures.

Recent work in asymmetric synthesis has involved the direct synthesis of optically active amines or alcohols. Corriu\(^2\) has shown \(\text{RhCl(Ph_3P)_3}\) to be a selective catalyst for hydrosilylation of carbonyl compounds.

\[
\begin{align*}
R_1R_2C=O + H_2SiR_3R_4 & \xrightarrow{\text{RhCl(Ph_3P)_3}} \text{R_1R_2C-HOSiHR_3R_4} \\
R_1R_2C^*HOH + HOSi^*HR_3R_4 & \xrightarrow{\text{H_2O}} \text{R_1R_2C^*HOH + HOSi^*HR_3R_4}
\end{align*}
\]

\(R = \text{alkyl or aryl}\)

Hydrosilylation is preferable to catalytic hydrogenation of the carbonyl group in cases where the product alcohol is a solid or is prone to hydrogenolysis. The liquid silated derivatives are analyzable by gas chromatography and are stable to further reduction. If \(R_1 + R_2\) and \(R_3 + R_4\), optical centers are produced on both carbon and silicon. Employing a Rh(I) catalyst and chiral ligand such as (+) or (−)DIOP (2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane)\(^3,4\) or \(^5\text{R-(+)}\text{PhCH_2PCH_2Ph}\) asymmetric syntheses have recently appeared which may be summarized as

Dr. John H. MacMillan was born in Massachusetts in 1944. He received his B.S. from Tufts University in 1966 and Ph.D. in organic chemistry from Northeastern University in 1970. He has done postdoctoral work at the University of Utah in low temperature diazirine chemistry and Temple University in organosilicon chemistry and lanthanide chemical shift reagents. Since July, 1973 he has acted as consultant to Sterling Chemicals, Inc. in organic and organometallic synthesis and homogeneous and heterogeneous catalysis.
follows,
\[ R_1R_2C = X + R_3R_4SiH_2 \xrightarrow{[\text{Rh(I)}]} [\text{Ligand}] \xrightarrow{\text{Chiral}} R_1R_2C^+HXSi^+HR_3R_4 \]

\[ R_1R_2C^+H^+ + HO Si^+HR_3R_4 \]

If \( X = \) oxygen, optically active silylated alcohol derivatives are produced which give optically active alcohols on hydrolysis\(^3,5\). Optical yields are quite variable, intimately depending on steric size of the \( R \) groups for both carbon and silicon, but yields of 30-50% are common. A good example\(^5\) is t-butylphenylketone which with \( \text{Rh(I)} \) and \( \text{RPhCH}_2\text{PCH}_3\text{Ph} \) gives the S-carbinol in 62% optical yield after hydrolysis. Induced asymmetry at silicon\(^3\) gives an optical yield of 31-55%. For \( X = N-R \) (imino groups) asymmetric hydroisilylation gives derivatives from which optically active amines are produced on hydrolysis in \( ca. 40-50\% \) optical yields.

\[
\begin{align*}
\text{Ph} & \quad \text{C} = \text{N-CH}_2\text{Ph} + \text{Ph}_2\text{SiH}_2 \\
\text{CH}_3 & \quad \xrightarrow{[\text{RhCl(C}_2\text{H}_4\text{)}_2]_2} \text{H}_2\text{O}
\end{align*}
\]

Good catalysts for the above reactions include \( \text{RhCl(Ph}_3\text{P})_3 \), \( [\text{RhCl}(\text{C}_8\text{H}_{14})_2]_2 \) or \( [\text{RhCl}(\text{C}_2\text{H}_4)_2]_2 \). Homogeneous Rh(I) catalyst systems such as \( \text{RhClO(Ph}_3\text{P})_3 \) with \( (-) \text{-DIOP} \) also effect asymmetric hydroformylation of olefins to aldehydes with \( ca. 20-30\% \) optical yields\(^6\). Kagan and coworkers\(^7\) have complexed a chiral phosphine on a polymer with \( [\text{RhCl}(\text{C}_2\text{H}_4)_2]_2 \), giving a heterogeneous type catalyst for asymmetric synthesis which may be filtered from the reaction and used again. This catalyst proved less efficient for hydrogenation of olefins to optically active alkanes than the non-bound catalyst, but of comparable efficiency for asymmetric hydrosilylation of carbonyl groups.

These new catalyst systems give enantiomerically enriched products directly in contrast to the classical procedures which involve complexation of the racemate with a chiral natural product, separation and chemical degradation of the resulting diastereomers.

Steroid chemists will find Nishimura's recent work\(^5\) of interest. Selective hydrogenation of steroid \( 1 \) with \( \text{RuCl}_2(\text{Ph}_3\text{P})_3 \) and base gives 2 with less than 4% fully saturated isomers 3 and 4.
Tris-(p-methoxyphenyl)phosphine or tri-(p-tolyl)phosphine in place of triphenylphosphine in the ruthenium catalyst produced catalysts which greatly accelerated the hydrogenation rate with little loss of selectivity. These new catalysts offer exciting possibilities for fast selective hydrogenations.

Fahey\textsuperscript{9} describes a selective hydrogenation of potential industrial application. 1,5,9-Cyclododecatriene (CDT) is selectively hydrogenated to cyclododecene (CDE) with Ru(CO)\textsubscript{2}(Ph\textsubscript{3}P)\textsubscript{2} or Ru(Et\textsubscript{2}S)\textsubscript{3}Cl\textsubscript{2}. Up to 98\% CDE is produced. CDE is a precursor for the polyamide monomers 1,12-dodecanedioic acid, 1,12-diaminododecane and 12-aminododecanoic acid lactam. CDE cannot be separated from cyclododecadiene or cyclododecene by distillation.

Two recent examples of deuterium incorporation with transition metal catalysts show greatly improved selectivity. Friedmann \textit{et al}\textsuperscript{10} report that Co\textsubscript{2}(CO)\textsubscript{9} selectively deuterates the 9, 10 position of anthracene giving tetradideuterated product. Also Regen\textsuperscript{11} describes RuCl\textsubscript{2}(Ph\textsubscript{3}P)\textsubscript{3} as a selective catalyst with D\textsubscript{2}O for deuterium incorporation at C\textsubscript{1} of primary alcohols. Alcohols deuterated at C\textsubscript{1} are valuable precursors to many materials such as 1-deuterated aldehydes, deuterated halides, organometallics or olefins. This method is one step under neutral conditions in contrast to older methods involving oxidation of alcohol to acid and reduction with LiAlD\textsubscript{4}.

Recent reports of stereoselective and stereospecific syntheses include the stereospecific epoxidation of geraniol (5) and related compounds with VO(AdAc)\textsubscript{2} or Mo(CO)\textsubscript{6} catalysts\textsuperscript{12}. Epoxidation occurred at the olefinic site closest to the hydroxyl group in con-
to the uncatalyzed process, where the more electron-rich 6,7-double bond was epoxidized.

\[
\text{VO(}\text{AcAc}_2\text{)} + \text{t-butOOH} \rightarrow \text{t-butOOH}
\]

Heck has pioneered in the development of Pd (II) catalysts for arylation of olefins with aryl iodies. Earlier work \(^1\) employing palladium acetate with a tertiary amine gave good yields only with aryl iodies and resulted in non-stereoselective mixtures of products. A recent paper \(^2\) describes the catalyst system Pd(II)\(\text{OAc}_2\)/Ph3P/Ph3N for stereoselective arylation of olefins with iodies or bromides.

\[
\begin{align*}
\text{Ph} & \quad \text{PhBr} \\
\text{Ph} & \quad \text{Ph} \quad \text{Pd(OAc)}_2 \quad \text{Ph} \quad \text{Ph} \quad \text{Ph} \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

Heterogeneous catalysts are less frequently employed for selective synthesis due to uncertainties regarding surface effects, pretreating, aging etc. However, significant work is continuing. Mitsui et al. \(^3\) report stereoselective hydrogenations of dialkylcyclohexanes to axial alcohols with Raney nickel or platinum black and to equatorial alcohols with PtO2. They also report 2,3 and 4-alkyl-substituted methylenecyclohexanes hydrogenate stereoselectively with Pt or Rh on C giving axial dimethylocyclohexanes \(^4\) (cis isomers from 2 and 4-substituted, trans from 3-substituted methylenecyclohexanes).

\[
\begin{align*}
\text{CH}_3 & \quad \text{Pt/C} \\
\text{H} & \quad \text{Pt/C} \\
\text{CH}_3 & \quad \text{Pt/C}
\end{align*}
\]

Palladium gives axial/equatorial ratios depending on catalyst concentration and reaction time while Raney nickel gives more axial than equatorial only on aged catalysts.

These stereoselective syntheses in substituted cyclohexanes are of interest not only for fundamental conformational studies but also
as model systems for selective syntheses from natural products such as menthol, steroids etc.

As a final example of selectivity we may note Corey's use of allyl ethers as protecting groups for alcohols.\(^1\)

\[
\begin{align*}
ROCH_2 - CH = CH_2 & \xrightarrow{\text{RhCl(Ph}_3\text{P)}_3} ROCH = CHCH_3 + pH_2 \\
R &= \text{alkyl or aryl} & ROH + CH_3CH_2CHO
\end{align*}
\]

Heating the allyl ether with RhCl(Ph\(_3\)P\(_3\)) results in quantitative double bond migration. Treatment at room temperature with mild acid cleaves the vinyl ether to alcohol in >90% yields. As examples the allyl ethers of 1-decanol and cholesterol form the alcohols in 96 and 90% yields. Previous methods of cleavage involved heating in strongly acidic or basic media. The present reaction conditions are so mild that alkyl and aryl ethers, esters and many common functional groups are unaffected. This technique may find application in natural product work, where often phenolic groups sensitive to oxidation must be protected.

In conclusion it is obvious that vigorous research activity in catalysis is continuing unabated. Perhaps the chemists' need for a specific catalyst for every desired reaction is no longer a dream and may approach reality within the next decade.

References


Continued on Page 8

**SELECTED HETEROGENEOUS CATALYSTS FROM STOCK**

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NEW LOW PRICES!

15-010 Bis(diphenylphosphino)acetylene

A new production technique developed by J. H. MacMillan, M. E. Strem, F. A. Fowler and G. Guy makes this commonly used ligand available at lower prices.

15-010 Bis(diphenylphosphino)acetylene

\[
\text{Ph}_2\text{P}=	ext{CPh}_2
\]

$2.00/g in 100 g lots \quad ($200.00)

$3.00/g in 25 g lots \quad ($75.00)

$4.00/g in 5 g lots \quad ($20.00)

Color and form: white solid
m.p. (min.): 80°
Stability: air stable

FOREIGN SALES REPRESENTATIVES

Italy
Fine Chemicals Dept.
PRODOTTI GIANNI S.R.L.
20138 Milano
Via Mecenate, N.30/14
Tel.: 50.97 (10 lines)

West Germany
M. BRAUNAGEL
7500 Karlsruhe 1
Postfach 1704
Salierstrasse 5
Tel.: (0721) - 811370

United Kingdom and Ireland
DIGBY CHEMICAL SERVICE
103 Ebury Street
London, SW1W 9QU
Tel.: 01-730-1400