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Reducing Agent - Polymethylhydrosiloxane (PMHS)

Carbocation and Onium Ion Reagents

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ABOUT THE COVER

When our chemist - collector first saw this strange depiction of Lot fleeing Sodom, at an auction in Switzerland, it was attributed to a well known Flemist artist, David Teniers the Younger, a prolific painter of many peasant scenes, most of which our chemist finds boring. The painting seemed so strongly influenced by Rembrandt, that our chemist bought the painting, hoping to have found a work by one of that master's last students. Imagine our chemist's surprise - and, we suspect, slight chagrin - when cleaning showed the work to be stunningly beautiful, albeit fully signed by David Teniers.

The story of the destruction of Sodom emphasizes the value of the individual: if only there had been ten righteous in Sodom, the city would have been spared. Abraham understood what President Kennedy put so clearly: "One man can make the difference, and every man should try." Sodom is also a turning-point in the history of man. Until then, there had been no dialogue between God and man. With Abraham trying to save the righteous, man began to talk back to God with the fierce argument "Shall not the judge of all the earth rule justly?" We have not argued fiercely enough - though Teniers tried to do his part by hinting what he thought of the morality of his day, in painting the Cathedral of Notre Dame of Antwerp right in the center of Sodom.

To us it seems particularly fitting that this wild painting grace that issue of our ACTA which describes the strongest acids and the most powerful catalysts known to man. The wild beauty of the painting challenges our imagination as do the tremendous synthetic possibilities of the work of Professor Olah, and the sheer elegance and interest of Dr. Lipowitz's review.

COLLECTORS' ITEMS

Many of the early issues of the Aldrichimica Acta have become very rare.

Please do not throw your issues away. In time, we believe that complete sets will become valuable, and - if you do not want to keep them - there probably are chemists and biochemists near you who would be interested.

The Use of Polymethylhydrosiloxane (PMHS) as a Reducing Agent for Organic Compounds

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The scope of this review will be limited to a discussion of the use of polymethylhydrosiloxane (PMHS) as a reducing agent for organic compounds. It should be noted, however, that many other silyl hydrides have been utilized as reducing agents.

Polymethylhydrosiloxane (PMHS) is a convenient, readily handled and versatile reagent which can be used to reduce a variety of organic functional groups under mild, neutral conditions. Properties of PMHS are shown in Table I. In many cases, the use of a catalyst in conjunction with PMHS is required to effect reduction. Metals or metallic compounds are often used as catalysts. It is generally assumed that metal hydride intermediates are formed and function as the active reducing agents. In the case of organotin catalysts, which have been used most often, it is known that tin hydride intermediates are the active reducing agents.

Table I

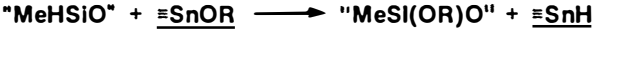
Typical PMHS Properties

Formula	$Me_3SiO(MeHSiO)_{\sim 35}SiMe_3$
H Equiv. Wt.	**65**
Density	**1.00**
Viscosity	**30 centistokes**
Appearance	**Water clear; odorless**
Flashpoint	**120°C**
Solubility	**Soluble in most organic solvents**[a]
Chemical Reactivity	**Stable and inert to air, moisture**[b]

a. Should not be used in halocarbon solvent because of the possibility of hydride-halide interchange on catalysis or with heating.

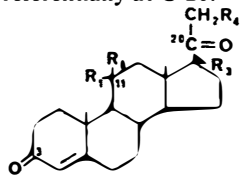
b. Becomes highly reactive in the presence of strong acids, strong bases and many metals and metallic compounds.

The major drawback to the widespread use of tin hydrides has been the difficulty in their preparation ($LiAlH_4$ reduction of tin chlorides or oxides) and storage. Storage is especially difficult for the reactive dihydrides, which are oxidatively and thermally unstable. However, tin hydrides can be readily prepared *in situ* simply by mixing PMHS and organotin alkoxides or stannoxanes.[1,2]



I. Reduction of Aldehydes and Ketones

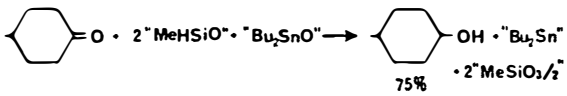
Aldehydes and ketones are readily reduced to carbinols by tin hydrides.[3] Some examples of marked selectivity have been found in tin hydride reductions of steroidal keto groups.[3a] For example, diphenyltindihydride preferentially reduces progesterone (1) at C-3 rather than C-20 in a ratio of 6.5 to 1, providing a facile route to the 3-hydroxy derivative. In contrast, sodium borohydride reduces preferentially at C-20.



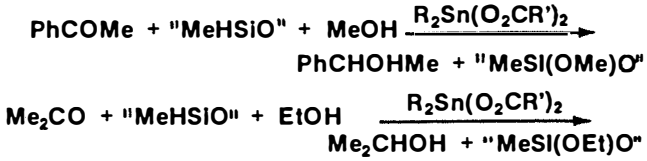
1. $R_1, R_2, R_3, R_4 = H$
2. $R_1 = H$; $R_2, R_3 = OH$; $R_4 = OAc$
3. $R_1, R_2 = O$; $R_3 = OH$; $R_4 = OAc$

Hydrocortisone (2) is reduced by diphenyltindihydride at C-20 in 63% yield and at both C-3 and C-20 in 14% yield. However, cortisone (3) is reduced at C-3 in 50% yield and at both C-3 and C-20 in 25% yield. The hindered 11-carbonyl in cortisone (3) could not be reduced even with excess diphenyltindihydride.

Grady and Kuivila[2] reported reduction of 4-methylcyclohexanone to 4-methylcyclohexanol by reaction with a tin hydride formed *in situ*.



However, two equivalents of PMHS and one equivalent of organotin oxide per mole of ketone are required. An advantage of the reaction is that no hydrolysis step is required, thus making it useful for moisture sensitive compounds. Nitzsche and Wick[4] had previously described reduction of ketones using one equivalent of PMHS and *catalytic* quantities of dialkyltindiacylates or other organometallics with alcohols as solvents. In this case, the solvent contributes a proton to the carbinol product and only one equivalent of PMHS is required. In the following examples, yields were excellent.



Similar results were obtained using a variety of organometallic catalysts, including Fe, Cu, Ni, Zn, Pb, Cd, and Hg acylates and Ti alkoxides. This suggests a multitude of potentially selective and specific reducing agents for a variety of functional groups.

We have found that PMHS and an organotin catalyst, bis-(dibutylacetoxytin)oxide (DBATO),[5] in an alcohol functions as a mild, convenient reagent for the specific reduction of aldehydes and ketones to carbinols in high yield.[7] Reductions are carried out in the presence of air and moisture (dry solvents are not necessary) and the reaction medium remains neutral during reduction and work-up.

$$R_1R_2CO + \text{"MeHSiO"} + ROH \xrightarrow{\text{DBATO}} R_1R_2CHOH + \text{"MeSi(OR)O"}$$

The rate of reduction is readily controlled by adjusting DBATO concentration or temperature. Table II lists reductions which have been carried out by this method at 80° in ethyl alcohol. Methyl vinyl ketone is primarily reduced at the carbonyl group to give methyl vinyl carbinol, with some reduction resulting from 1,4-addition of the tin hydride to give methyl ethyl ketone. Stereospecific reduction of 4-*tert.*-butylcyclohexanone takes place to give exclusively *trans*-4-*tert.*-butylcyclohexanol. Reduction of quinones occurs in high yield as shown by reduction of *p*-quinone to hydroquinone.

Table II

PMHS Reductions With 2 Mole % DBATO[a]

Substrate	Product	Yield
Ph_2CO	Ph_2CHOH	80[b]
PhCOMe	PhCHOHMe	81[b,d]
PhCHO	$PhCH_2OH$	100[c]
Me_2CO	Me_2CHOH	100[c]
CH_2=CHCOMe	CH_2=CHCHOHMe	65[c]
	EtCOMe	35[c]
4-*t*-butylcyclohexanone	*trans*-4-*t*-butylcyclohexanol	65[b] (100[c])
p-benzoquinone	hydroquinone	81[b]

a. At 80° in refluxing 95% ethanol.

b. Isolated yield.

c. GLC yield, using an internal standard.

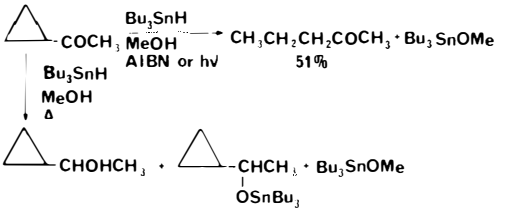
d. One hour reflux was required after PMHS addition.

Reduction appears to be specific for aldehydes, ketones and quinones at 80°, since representative esters (including lactones), amides, carboxylic acids, nitriles, alkyl halides and nitro compounds are not reduced.[7]

Aromatic aldehydes can be reduced to the carbinol using PMHS and DBATO catalyst. Reduction to the hydrocarbon occurs with PMHS and Pd on charcoal catalyst in an alcohol.[7]

$$PhCHO + 2\text{"MeHSiO"} + 2EtOH \xrightarrow[50^\circ]{Pd/C} PhCH_3 + 2\text{"MeSi(OEt)O"} + H_2O \qquad 84\%$$

Cyclopropyl methyl ketone can be reduced exclusively to propyl methyl ketone by tri-*n*-butyltin hydride in methanol with azobisisobutyronitrile (AIBN) or UV irradiation.[8] Without a radical initiator, thermal reduction of the carbonyl group takes place in a slower reaction.



Use of PMHS and a *catalytic* quantity of tributyltin oxide or alkoxide should be effective in this reaction since the tin hydride can be readily regenerated from PMHS and tributyltin methoxide.[1]

A recent report describes reduction of aldehydes and ketones to ethers in acidic alcoholic solution with triethylsilane.[9]

$$R_1R_2CO + Et_3SiH + R'OH \xrightarrow{H^+} R_1R_2CHOR' + Et_3SiOH \qquad >80\%$$

R' = Me, Et

Using sulfuric or trifluoroacetic acid, high yields (>80%) of ethyl and methyl ethers were obtained with ethanol or methanol. Higher alcohols gave lower yields. Reduction in water rather than alcohols gave almost quantitative yields of carbinol.

$$R_1R_2CO + Et_3SiH + H_2O \xrightarrow{H^+} R_1R_2CHOH + Et_3SiOH$$

The use of PMHS in these reductions has not been investigated.

Another recent report[10] describes the use of $(Ph_3P)_3RhCl$ to catalyze the rapid hydrosilylation of aldehydes and ketones under mild conditions.

$$R_1R_2CO + Et_3SiH \xrightarrow{(Ph_3P)_3RhCl} R_1R_2CHOSiEt_3$$

The alkoxysilane product can be readily hydrolyzed to give the carbinol.

$$R_1R_2CHOSiEt_3 \xrightarrow{H_2O} R_1R_2CHOH + Et_3SiOH$$

The utility of PMHS in these reactions has not been investigated.

II. Reduction of Halocarbons

Grady and Kuivila[2] reported *in situ* tin hydride reductions of a variety of halocarbons using PMHS and tributyltin oxide. In some cases, heat (100°) or UV irradiation was required to obtain high yields. Tin hydride

$$RX + \text{"MeHSiO"} + 1/2(Bu_3Sn)_2O \longrightarrow RH + Bu_3SnX + \text{"}MeSiO_{3/2}\text{"}$$

reduction of halocarbons is believed to proceed by the following radical chain mechanism.

Initiation (In• = initiator)

$$\underline{Sn}H + In\bullet \longrightarrow \underline{Sn}\bullet + InH \quad (1)$$

Propagation

$$\underline{Sn}\bullet + RX \longrightarrow \underline{Sn}X + R\bullet \quad (2)$$

$$R\bullet + \underline{Sn}H \longrightarrow RH + \underline{Sn}\bullet \quad (3)$$

In general, the rate of reduction seems to depend on the rate of abstraction of halogen from the alkyl halide (Equation 2).[3b] Thus the reaction rate follows the order:

$$RI > RBr > RCl > RF$$

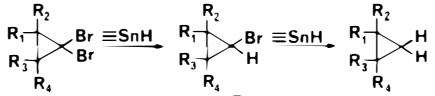
Iodides and bromides react rapidly and exothermally. Chlorides often require heating, a free radical initiator (preferably AIBN) or UV irradiation. Fluorides do not react.

The ease of reaction also depends on the stability of R•. Thus benzyl, allyl, and trichloromethyl halides, which give stable free radicals, are highly reactive. Radical rearrangements or fragmentation of radicals may occur. Tin hydride reactivities follow the order:

$$Ph_2SnH_2 > Ph_3SnH > n\text{-}Bu_2SnH_2 > n\text{-}Bu_3SnH$$

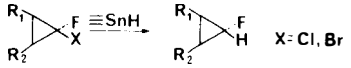
Stepwise reduction of polyhalides such as benzotrichloride has become a synthetically useful application of tin hydride reductions.

Using tin hydrides, *gem*-dibromocyclopropanes are reduced in high yield to the monobromides or to the hydrocarbon.

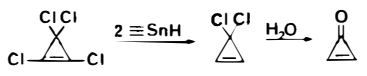


Bromo- and chloroalkanes, in general, can be reduced in high yield. Nitrile, ester and ketone functionalities do not interfere with reduction. Aromatic bromides, but not chlorides, are reduced in good yield. However, amino, keto, aldehyde and thiol functionalities interfere with reduction of aromatic bromides.

Reduction of *gem*-halofluorocyclopropanes with tributyltin hydride proceeds stereospecifically with exclusive reduction of halide.[11]



The first synthesis of cyclopropenone was carried out by reduction of tetrachlorocyclopropene with tributyltin hydride, followed by hydrolysis of the *gem*-dichloride.[12]



Alkyl and aryl bromides and reactive alkyl chlorides can be reduced by siloxanehydrides at 25° with a Pd on charcoal catalyst in a hydrocarbon or without solvent.[13]

$$PhBr \xrightarrow[Pd/C]{(Me_2SiH)_2O} PhH \quad 95\%$$

$$PhCH_2Br \xrightarrow[Pd/C]{(Me_2SiH)_2O} PhCH_3 \quad 95\%$$

$$PhCH_2Cl \xrightarrow[Pd/C]{(Me_2SiH)_2O} PhCH_3 \quad 95\%$$

Aliphatic bromides, but not chlorides, are reduced in high yield by triethylsilane and Pd/C.[13] The effectiveness of PMHS in these reductions has not been investigated, but should prove synthetically useful.

III. Aromatic Nitro Compounds

Nitzsche and Wick[4] reported the reduction of nitroaromatics to anilines using PMHS and various metal acylates or metal alkoxides as catalysts. Reductions using dibutyltin-dilaurate catalyst in refluxing ethylhexanol (b.p. 184°) were described in detail.

$$PhNO_2 \longrightarrow PhNH_2 \quad >95\%$$

$$m\text{-}C_6H_4(NO_2)_2 \longrightarrow m\text{-}C_6H_4(NH_2)_2 \quad >80\%$$

Reaction does not take place at 130°.[7]

Reduction of nitroaromatics can be carried out under milder conditions with PMHS and Pd/C catalyst in ethyl alcohol[7] or aqueous dioxane[13] at ambient temperature. Reduction of *m*-nitroacetophenone under these conditions was not successful.

$$PhNO_2 \xrightarrow[Pd/C\ EtOH]{PMHS} PhNH_2 \quad 89\%$$

$$PhNO_2 \xrightarrow[Pd/C\ aq.\ dioxane]{(Me_2SiH)_2O} PhNH_2 \quad 100\%$$

IV. Reduction of Olefins

Hydrogenation of α-and *cis*-olefins occurs readily at room temperature using PMHS and a Pd/C catalyst in ethanol[7] or in aqueous dioxane.[13]

$$\text{1-octene} \xrightarrow[EtOH]{} \text{n-octane} \quad 88\%$$

$$\text{cyclohexene} \xrightarrow[EtOH]{} \text{cyclohexane} \quad 100\%$$

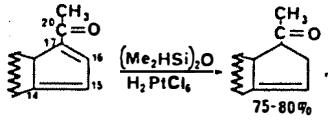
$$CH_2{=}CHCOCH_3 \xrightarrow[EtOH]{} C_2H_5COCH_3 \quad 100\%$$

$$\text{2-nonene} \xrightarrow[EtOH]{} \text{2-nonane} + \textit{trans}\text{-2-nonene} \quad 25\% \quad 75\%$$

(*trans/cis* = 3)

This reaction constitutes a safe, convenient reduction method. An inert atmosphere and bulky hydrogenation equipment are not required. Reduction follows the patterns observed for hydrogenations using gaseous hydrogen at one atmosphere and ambient temperature.[14]

A recent report[15] describes selective reduction of pregna-14,16-dien-20-ones to pregn-14-ene-20-ones in high yield by siloxanehydrides with a chloroplatinic acid catalyst.



V. Reduction of Phosphine Oxides and Phosphonic Esters

Reduction of a series of triarylphosphine oxides by PMHS has been reported.[16] Reductions were carried out by heating without a catalyst.

$$Ar_3PO \xrightarrow[\Delta]{PMHS} Ar_3P \quad >85\%$$

Reduction of a phosphonic acid ester has also been reported.[17]

$$C_4H_9PO(OEt)_2 \xrightarrow[\Delta]{PMHS} C_4H_9PH_2 \quad 90\%$$

VI. Miscellaneous Reductions

The feasibility of carrying out reductions using *in situ* preparation of tin hydrides from PMHS and readily available organotin oxides or alkoxides has been realized only for reduction of alkyl halides,[2] aldehydes and ketones[2,4,7] and nitroaromatics.[4] However, many other unique reductions of organic compounds by tin hydrides are known.[3]

Hayashi *et al.*[1] found that PMHS is a highly reactive silyl hydride for the preparation of tin hydrides. The reactivity order is:

$$\text{"MeHSiO"} > (Ph_2SiH)_2O > Ph_3SiH > Bu_3SiH$$

The following order of relative reactivities for readily available organotin compounds was found:

$$Bu_2Sn(OEt)_2 \sim Bu_3SnOEt > (Bu_3Sn)_2O \gg Bu_2SnO > (Ph_3Sn)_2O$$

A brief summary of additional types of organic reductions using tin hydrides will be given. The following reactions have not been reported to proceed with tin hydrides produced *in situ*, although many should be amenable to this technique.

A. Reduction of Acyl Halides

Reaction of acyl chlorides and bromides with tin hydrides, which proceeds by a radical mechanism, can follow two reaction paths.[18]

1. Aldehyde Formation

$$RCOCl \xrightarrow{\equiv SnH} RCHO$$

2. Reductive Acylation

$$2RCOCl \xrightarrow{2\equiv SnH} RCOOCH_2R$$

Aldehyde formation (path 1) is favored by bulky R groups; by carrying out reaction in dilute solution; and by use of acyl bromides. Reductive acylation (path 2) is favored by small R groups; reaction in concentrated solution (preferably solventless); and by use of acyl chlorides. The following examples illustrate the pronounced effect of variation in concentration and in halide used.

$$C_2H_5COCl \xrightarrow[25°]{Bu_3SnH} C_2H_5COOCH_2C_2H_5$$

no solvent 87%

$$C_2H_5COCl \xrightarrow[25°]{Bu_3SnH} C_2H_5CHO \quad 90\%$$

0.63M in methyl acetate

$$C_2H_5COBr \xrightarrow[25°]{Bu_3SnH} C_2H_5CHO + C_2H_5COOCH_2C_2H_5$$

no solvent 79% 21%

Good yields (> 80%) can often be obtained in either type of reaction by proper choice of experimental conditions.[18,19]

Reductive acylation to give mixed esters proceeds in high yield on addition of an aldehyde or ketone.[20] Yields are quantitative for reaction of acyl chlorides with aromatic ketones.

$$RCOCl + ArCOR' \xrightarrow{\equiv SnH} RCOOCHR'Ar \quad 100\%$$

R = Me, Et, Ph
R' = Me, Et, *i*-Pr

Acyl chlorides can be reduced to aldehydes under mild conditions using organosilicon hydrides and a Pd/C catalyst.[21]

$$RCOCl + \equiv SiH \xrightarrow{Pd/C} RCHO + \equiv SiCl$$

Unbranched acyl chlorides and aroyl chlorides give aldehyde yields of 40-70%. Good yields were obtained from acyl bromides with α-branching, but not from branched acyl chlorides. Utility of PMHS in this reaction has not been demonstrated.

Reductive acylations with acyl fluorides and trialkylsilanes which proceed thermally have been reported.[22]

$$2RCOF + 2R'_3SiH \xrightarrow{\Delta} RCOOCH_2R + 2R'_3SiF$$

B. Reductive Cleavage of Benzoate Esters

Benzoate esters are reduced by tin hydrides using radical initiators or UV irradiation.[23]

$$PhCOOR \xrightarrow{\equiv SnH} PhCOOSn\equiv + RH$$

Yields increase as the stability of R• increases. Thus, yields of greater than 70% are obtained for R = *tert.*-Bu, $PhCH_2$, Ph CH, Ph_3C, cinnamyl.

C. Reduction of Isocyanates

Isocyanates undergo *polar* addition of tin hydrides to the C=N double bond.[24] Addition may occur in either direction.

$$PhN{=}C{=}O + \equiv SnH \longrightarrow PhN(Sn\equiv)\text{-}CHO$$

$$n\text{-}C_6H_{13}N{=}C{=}O + \equiv SnH \longrightarrow n\text{-}C_6H_{13}NHC(=O)Sn\equiv$$

On hydrolysis, both types of reaction products give the formamide.

$$\left.\begin{array}{l} RN(Sn\equiv)\text{-}CHO \\ RNHC(=O)Sn\equiv \end{array}\right\} \xrightarrow{H_2O} RNHCHO$$

D. Hydrogenation of α,β-Unsaturated Esters, Ketones and Nitriles

α,β-Unsaturated esters, ketones and nitriles undergo hydrogenation at the C=C double bond using tin hydrides in methanol, preferably with UV irradiation.[25,26]

$$\underset{R_2}{\overset{R_1}{\diagdown}}C{=}CHZ + R_3SnH + MeOH \xrightarrow{h\nu \text{ or } \Delta} \underset{R_2}{\overset{R_1}{\diagdown}}CHCH_2Z + R_3SnOMe$$

Z = CN, COOR, COR — 45-90%

α,β-Acetylenic esters can be reduced to the *trans*-olefin or to the ethylene.[26] Only methyl esters have been reduced in good yield. It may be possible to carry out

$$MeO_2C\text{-}C{\equiv}C\text{-}CO_2Me \xrightarrow[MeOH]{Bu_3SnD} \underset{H}{\overset{MeO_2C}{\diagdown}}C{=}C\underset{CO_2Me}{\overset{D}{\diagdown}} \quad (72\%)$$

$$MeO_2C\text{-}C{\equiv}C\text{-}CO_2Me \xrightarrow[Bu_3SnD]{MeOD} MeO_2CCD_2CD_2CO_2Me + Bu_3SnOMe \quad (68\%)$$

these reactions using PMHS and a catalytic quantity of organotin oxide or alkoxide.

The C=C double bond of mesityl oxide can be quantitatively reduced.[27]

$$(CH_3)_2C{=}CHC(=O)CH_3 \xrightarrow{\equiv SnH} (CH_3)_2CHCH_2C(=O)CH_3 \quad (100\%)$$

E. Reduction of Isonitriles

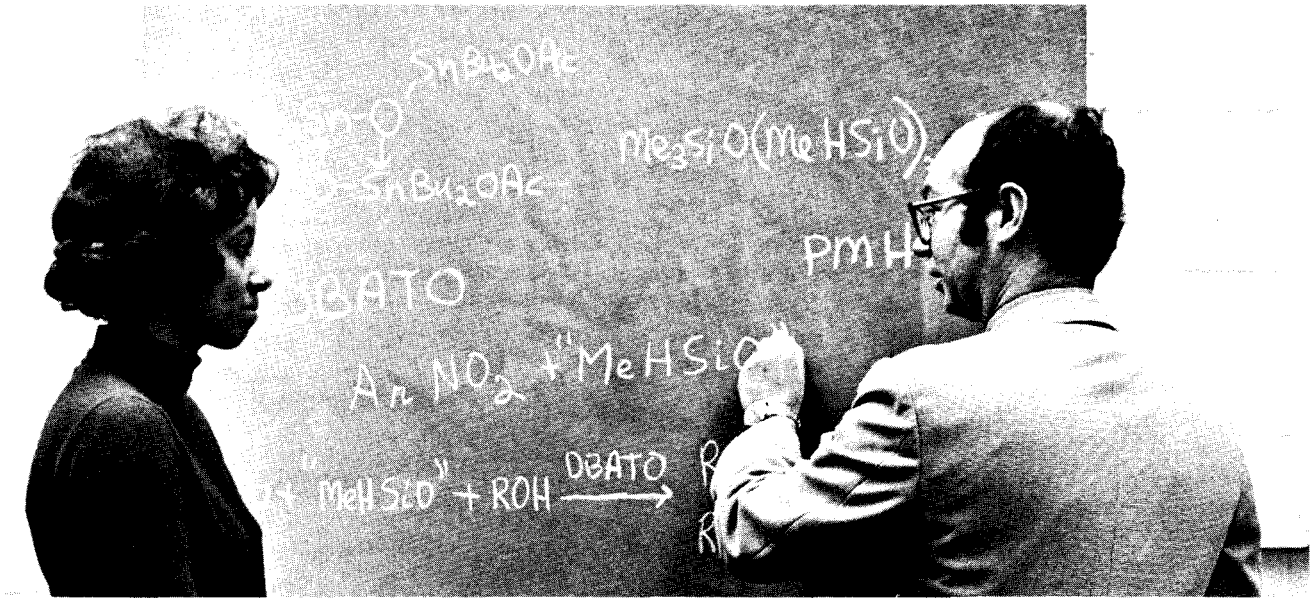
Isonitriles are reduced to the hydrocarbon with tin hydrides and a radical initiator.[28]

RNC + ≡SnH ⟶	RH + ≡SnCN
R = $PhCH_2$	97%
R = cyclohexyl	47%
R = *t*-butyl	45%

Nitriles do not react under these conditions.

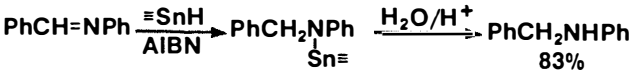
F. Reduction of Imines

Benzylideneaniline reacts with tributyltinhydride using a radical initiator (AIBN) to give a stannylamine, which

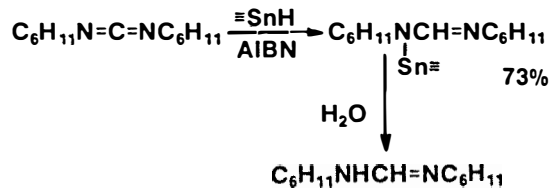


Sheryl A. Bowman and Jonathan Lipowtiz

can be hydrolyzed to an amine.[29]

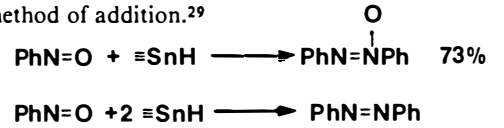


Dicyclohexylcarbodiimide gives a stannylamine, which yields an aminoimide on hydrolysis.



G. Reduction of Nitrosobenzene

Reduction of nitrosobenzene can give, upon hydrolysis, azoxybenzene, azobenzene or phenylhydroxylamine, depending on the ratio of nitrosobenzene to tin hydride and on the method of addition.[29]



If a dilute solution of nitrosobenzene is added to tin hydride, the hydroxylamine is obtained on hydrolysis.

VII. Preparation of Ziegler-Type Catalysts

A number of patents[30] have been issued describing the use of PMHS and related polymers as the reductive component in Ziegler-type catalysts, useful for polymerization of olefins.

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Carbocation and Onium Ion Reagents

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CARBOCATIONS

Carbocations[1], the positive ions of carbon compounds, are of substantial interest not only as intermediates in ionic reactions, but also as reagents in a multitude of synthetically important reactions. With the development of modern techniques including low nucleophilicity solvent systems, many of these carbocations can now be isolated as stable salts or prepared *in situ*, generally in superacidic solutions. Trivalent carbenium ion salts are very reactive species and their use as reagents in synthetic organic chemistry has become increasingly important.

Oxonium ions represent another important class of cationic reagents.[2] The preparation and study of numerous oxonium ion salts were pioneered by Meerwein.[2] While diarylhalonium ions have been known for years,[3 a,b] dialkylhalonium ions became known only recently[3c] but are rapidly gaining considerable interest.[3] In this review we will discuss primarily the formation and application of carbenium, oxonium and halonium ion reagents in organic synthesis. We shall also briefly discuss nitronium and nitrosonium salts. Space limitations will not allow the discussion of other classes of onium ions.

CARBOCATION REAGENTS

Alkylcarbenium Ions

Alkylcarbenium fluoroantimonates ($\overset{+}{R}\overset{-}{SbF_6}$) which were prepared and characterized in recent years[4], represent a new class of the most powerful cationic type alkylating agents.

The alkylcarbenium ion salts are generally prepared *in situ* from the corresponding alkyl fluoride and antimony pentafluoride at low temperature in sulfur dioxide or sulfuryl chloride fluoride (SO_2ClF) solution or from alcohols (olefins) in fluoroantimonic acid ($HF\text{-}SbF_5$) or Magic Acid® ($FSO_3H\text{:}SbF_5$) solution.

$$RF + SbF_5 \xrightarrow[-78^\circ]{SO_2 \text{ or } SO_2ClF} \overset{+}{R}\overset{-}{SbF_6} \quad R = CH_3,\ C_2H_5,\ C_3H_7,\ C_4H_9,$$

$$ROH \text{ or } RCH{=}CH_2 \xrightarrow[FSO_3H\text{-}SbF_5,\ SO_2,\ SO_2ClF]{HF\text{-}SbF_5} \overset{+}{R}\overset{-}{SbF_6}$$

Methyl and ethyl[4] fluoroantimonate, as the rapidly equilibrating alkyl fluoride:antimony pentafluoride complexes, are of particular importance because of their unusual alkylating power.[5] They can alkylate all n, π and σ - donor systems.

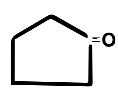
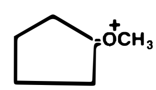
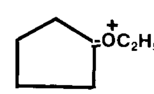
Methyl and ethyl fluoroantimonate in sulfur dioxide react with a variety of n-donor bases at low temperature (*ca.* -60°) to give the corresponding onium ions,[5,6] generally in almost quantitative yield.

$$RF + SbF_5 + (R')_nY\text{:} \xrightarrow{SO_2} (R')_n\overset{+}{Y}R\ \ \overset{-}{SbF_6}$$

R = methyl, ethyl:
Y = -O-, -S-, ⋛N:, -Cl:, -Br:, -I:
R = alkyl, aryl; n 1,2,3.

Some of the methylated and ethylated onium ions obtained are given in the following table:

Representative Methylated and Ethylated Onium Ions
Obtained with $CH_3F\text{-}SbF_5$ and $C_2H_5F\text{-}SbF_5$

Heteroorganic substrate	Methylated onium ion	Ethylated onium ion
$(CH_3)_2O$	$CH_3O(CH_3)_2^+$	$(CH_3)_2OC_2H_5^+$
$(C_2H_5)_2O$	$C_2H_5O(CH_3)(C_2H_5)^+$	$(C_2H_5)_2\overset{+}{O}C_2H_5$
CH_3OH	$CH_3O(CH_3)H^+$	$(C_2H_5)\overset{+}{O}(CH_3)H$
$(CH_3)_2C{=}O$	$(CH_3)_2C{=}OCH_3^+$	$(CH_3)_2C{=}OC_2H_5^+$
$(C_2H_5)_2C{=}O$	$(C_2H_5)_2C{=}OCH_3^+$	$(C_2H_5)_2C{=}OC_2H_5^+$
		
$(C_6H_5)_2C{=}O$	$(C_6H_5)_2C{=}OCH_3^+$	
$CH_3CH{=}O$	$CH_3CH{=}OCH_3^+$	$CH_3CH{=}OC_2H_5^+$
$C_6H_5CH{=}O$	$C_6H_5CH{=}OCH_3^+$	$C_6H_5CHC{=}\overset{+}{O}C_2H_5$
$HC(=O)\text{-}OH$	$HC(\text{O-}CH_3){=}OH^+$	$HC(\text{O-}CH_2CH_3){=}OH^+$
	$H_3C\text{-}O\text{-}\overset{+}{H}C{=}OH$	$H_3CCH_2\text{-}O\text{-}HC{=}OH^+$
$H_3C\text{-}C(=O)\text{-}OH$	$H_3C\text{-}C(\text{O-}CH_3){=}OH^+$	$H_3C\text{-}C(\text{O-}CH_2CH_3){=}OH^+$
$H_3C\text{-}N(=O)O$	$H_3C\text{-}\overset{+}{N}(=O)\text{-}OCH_3$	$H_3C\text{-}\overset{+}{N}(=O)\text{-}O\text{-}CH_2CH_3$
$H_3CCH_2CH_2\text{-}N(=O)\text{-}O$	$H_3CCH_2CH_2\text{-}\overset{+}{N}(=O)\text{-}OCH_3$	$H_3CCH_2CH_2\overset{+}{N}(=O)\text{-}OC_2H_5$
$C_6H_5\text{-}N(=O)\text{-}O$	$C_6H_5\text{-}\overset{+}{N}(=O)\text{-}OCH_3$	$C_6H_5\text{-}\overset{+}{N}(=O)\text{-}OCH_2CH_3$
$[(CH_3)_2CH]_2S$	$[(CH_3)_2CH]_2SCH_3^+$	$[(CH_3)_2CH]_2SCH_2CH_3^+$
$(C_2H_5)_2S$	$(C_2H_5)_2SCH_3^+$	$(CH_3CH_2)_3S^+$
tert-BuS-H	*tert*-BuSHCH$_3^+$	*tert*-BuSHC$_2$H$_5^+$
$(C_2H_5)_3N$	$(C_2H_5)_3NCH_3^+$	$(CH_3CH_2)_4N^+$

Although carbon monoxide is a relatively weak base, it reacts readily with alkyl fluoroantimonates under pressure to give the corresponding oxocarbenium ions in high yield.[3] Subsequent hydrolysis gives the corresponding carboxylic acids.

$$RF + SbF_5 + CO \rightarrow RCO^+SbF_6^- \xrightarrow{-H_2O} RCOOH_2^+SbF_6^-$$

$$R=CH_3,\ C_2H_5,\ i\text{-}C_3H_7 \qquad RCOOH \xleftarrow{-HSbF_6}$$

Methyl and ethyl fluoroantimonate also alkylate olefins. For example, the reaction of isobutylene, tri- and tetramethylethylene with CH_3F in SbF_5-SO_2 solution yields *tert.*-amyl and tetra- and pentamethylethyl cations, respectively. These ions are readily converted in usual reactions to a multitude of substituted products.

$$CH_3F\text{-}SbF_5 + H_2C{=}C(CH_3)_2 \xrightarrow{SO_2} CH_3\text{-}CH_2\text{-}\overset{+}{C}(CH_3)_2\ SbF_6^-$$

$$CH_3F\text{-}SbF_5 + CH_3HC{=}C(CH_3)_2 \xrightarrow{SO_2}$$

$$(CH_3)_2CH\text{-}\overset{+}{C}(CH_3)_2 \rightleftharpoons (CH_3)_2\overset{+}{C}\text{-}CH(CH_3)_2\ SbF_6^-$$

$$CH_3F\text{-}SbF_5 + (CH_3)_2C{=}C(CH_3)_2 \xrightarrow{SO_2}$$

$$(CH_3)_3C\text{-}\overset{+}{C}(CH_3)_2 \rightleftharpoons (CH_3)_2\overset{+}{C}\text{-}C(CH_3)_3\ SbF_6^-$$

Alkylation of aromatic hydrocarbons by alkyl fluoroantimonates even at -78° gives alkylated products in high yields (>80%).

$$ArH + R^+SbF_6^- \xrightarrow[-78^\circ]{SO_2ClF} ArHR^+SbF_6^- \xrightarrow[H_2O,\ 0^\circ]{NaHCO_3} ArR$$

$$R=CH_3,\ C_2H_5,\ C_3H_7,\ C_4H_9$$

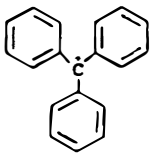
Alkyl fluoroantimonates are even capable of alkylating a wide variety of alkanes (σ-donors). These alkylation reactions involve electrophilic alkylcarbenium ion attack on both C-H and C-C bonds *via* two-electron, three-center bonded transition states.[1]

$$R^+SbF_6^- + R'_3C\text{-}H \rightarrow \left[R'_3C\cdots\overset{R}{H}\right]^+ \rightarrow R'_3CR + HSbF_6$$

$$R^+SbF_6^- + R'_3C\text{-}CR'_3 \rightarrow \left[R'_3C\cdots\overset{R}{CR'_3}\right]^+ \rightarrow R'_3CR + R'_3C^+SbF_6^-$$

Arylcarbenium Ions

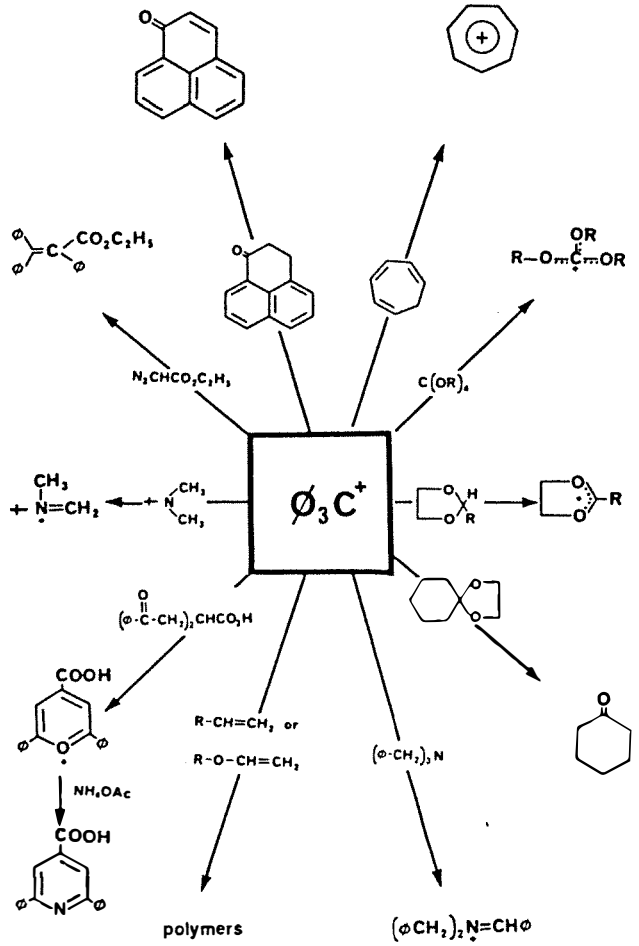
The first stable, long-lived carbenium ion observed is the triphenylcarbenium (trityl) ion.[7]



Many stable salts of triarylcarbenium ions are known.

The most frequently used trityl salt is the tetrafluoroborate. The perchlorate, although repeatedly mentioned in the literature, is less safe and could lead to an explosion. The hexachloroantimonate and the more soluble hexafluorophosphate salt are finding increasing use.

The triphenylcarbenium (trityl) ion is well documented as a hydrogen acceptor.[8] Dauben, *et al.*[9] used it to dehydrogenate cycloheptatriene to the tropylium ion. Tertiary methylamines are dehydrogenated to methyleneimmonium salts using trityl salts.[10] Acetals reduce the trityl cation by an intermolecular hydrogen process.[11] 1,3-Dioxolane and particularly the 2-methyl and 2-phenyl derivatives are converted by the trityl cation into dioxolenium salts.[11] Bartlett and McCollum[12] studied the hydrogen abstraction from alcohols by the trityl cation.



The trityl ion is reduced by formic acid to triphenylmethane. By using deuterated formic acid, a quantitative yield of $(C_6H_5)_3CD$ can be obtained.[13] Diethyl ether reduces the trityl cation, *via* intermolecular hydride abstraction, to give triphenylmethane, acetaldehyde, and ethyl halide.[14] Trityl salts were recently found by Barton[15] to be useful reagents for the deketalization of ketals, where the glycol function is smoothly oxidized to α-ketol. This reaction has special synthetic application in carbohydrate chemistry. In addition, trityl salts are useful in the synthesis of heterocycles, such as pyrilium salts,[16] and are efficient catalysts for the decomposition of diazo compounds.[17] A particularly useful application of trityl salts is as a cationic polymerization catalyst.[18]

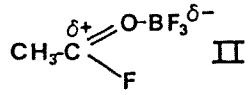
Phenylcarbenium ion salts other than the extremely stable trityl salts are also available and are finding applications.

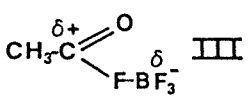
Volz[19] obtained tropylium ion from cycloheptatriene and diphenylcarbenium hexachloroantimonate, but the benzhydryl salt is rather unstable. Olah and Comisarow[20] recently described the phenyldichlorocarbenium ion $C_6H_5C^+Cl_2$ and the diphenylchlorocarbenium ion $(C_6H_5)_2C^+Cl$, both of which show remarkable stability as the isolated hexachloroantimonate salts.[21] These new stable carbenium ion salts offer numerous yet unexplored possibilities in synthetic chemistry, as well as in hydrogen abstraction and dehydrogenation reactions.

Acyl Cation Salts

In Friedel-Crafts acylation reactions, the acylating agent (acyl halide or anhydride) generally forms a highly polarized or ionic complex with the acidic catalyst. The nature of the acyl halide:Lewis acid complexes represented an intriguing problem until 1943. Seel[22] then provided the first conclusive evidence for the acetyl cation nature I of the isolated acetyl fluoride:boron trifluoride complex, in contrast to the two possible donor:acceptor forms II and III.

$$CH_3C\equiv O^+BF_4^- \longleftrightarrow CH_3C^+=O\ BF_4^- \quad \text{I}$$

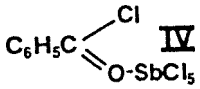

II


III

Olah and his coworkers[23] subsequently isolated a series of alkanoyl(cycloalkanoyl, aroyl) ions as the stable hexafluoro- or hexachloroantimonate and hexafluoroarsenate salts and the less stable tetrafluoroborate and hexafluorophosphate salts. Extensive spectroscopic studies (including ir, ^1H, ^{13}C and ^{19}F nmr spectroscopy) proved the structures, which were later substantiated by X-ray crystallography.[24]

Acyl chloride:antimony pentachloride complexes were isolated as early as 1901 by Rosenheim.[25] Meerwein[26] utilized these complexes in his studies of ether cleavages. Seel[27] first suggested, on the basis of conductivity data, the ionic structure for the acetyl chloride:antimony pentachloride complex, $CH_3CO^+SbCl_6^-$.

This structure was later verified by the spectroscopic studies of Olah.[23] In similar studies, the benzoyl chloride:antimony pentachloride complex was found to be the O-cooridinated, highly polarized donor:acceptor complex IV, which in solution also shows the presence of the ionic form V.


IV

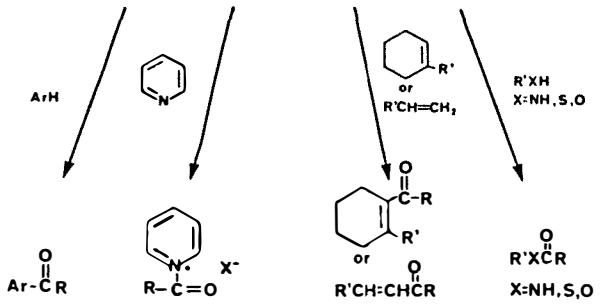
$C_6H_5CO^+SbF_6^-$ V

However, the crystalline form, according to the X-ray structural studies by Weiss,[28] is the donor:acceptor complex. In contrast, the benzoyl fluoride:antimony pentafluoride complex exists mainly as the ionic benzoyl cation $(C_6H_5CO^+SbF_6^-)$ in the crystalline form as well as in solution.

Regardless of the details of structure, the acyl chloride: antimony pentachloride complexes in various solvents such as nitromethane, nitrobenzene, sulfolane, etc. are remarkably active acylating agents. These complexes are capable of acylating aromatic and aliphatic hydrocarbons (arenes, alkenes, alkynes),[23, 29, 30] The complexes should find wide synthetic application.

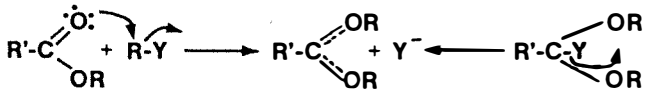
$$RCO^+SbX_6^-$$

$R = CH_3, C_2H_5, C_6H_5 \qquad X = F, Cl$

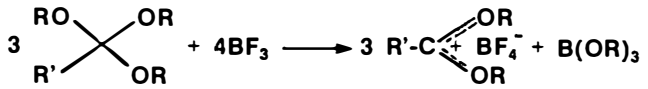


Dialkoxycarbenium Ions

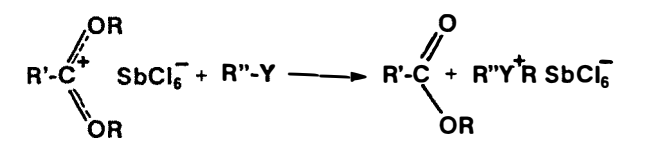
Dialkoxycarbenium ions were first prepared by Meerwein.[31] They can be prepared either by O-alkylation of esters or by cleaving orthocarboxylic acid esters.



The latter route is more convenient since orthocarboxylic esters are readily available.

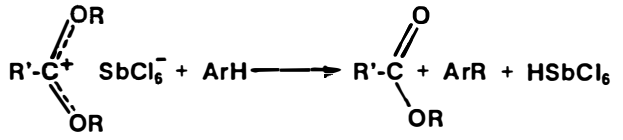


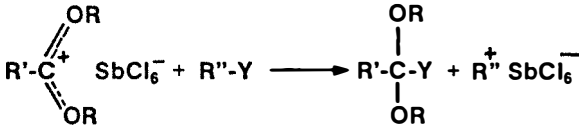
Acyclic dialkoxycarbenium salts are stronger alkylating agents than trialkyloxonium salts.[31, 32] This is shown by the fact that they can smoothly alkylate ethers to trialkyloxonium salts, while alkylation of carboxylic esters with trialkyloxonium salts is impossible.[32] Dialkoxycarbenium salts are capable of alkylating a variety of *n*-donor bases including some weakly nucleophilic carbonyl compounds such as acetophenone, benzaldehyde and esters.



Y = -C≡N:, >S=O, >C=O, >P:, -Ö-

The alkylation of aromatic hydrocarbons by dialkoxycarbenium salts has been reported.[33] In addition to alkylative reactivities, dialkoxycarbenium salts are capable of abstracting hydride or alkoxide ions.

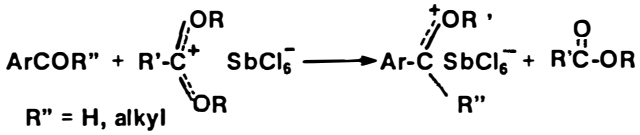




R" = Ar_3C; Y = H
R" = $(C_2H_5O)_3C$; Y= OC_2H_5

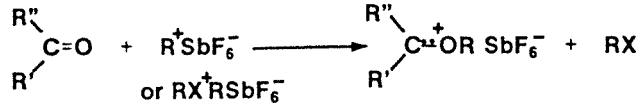
Alkoxy (aryloxy) carbenium Ions

Aryl aldehydes and aryl ketones can be alkylated by dialkoxycarbenium salts, but not by trialkyloxonium ions.[32]



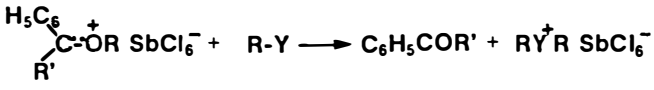
R" = H, alkyl

With stronger alkylating agents such as methyl or ethyl fluoroantimonate and dialkylhalonium salts, both aromatic and aliphatic ketones and aldehydes are alkylated to give alkoxycarbenium ions.[5]



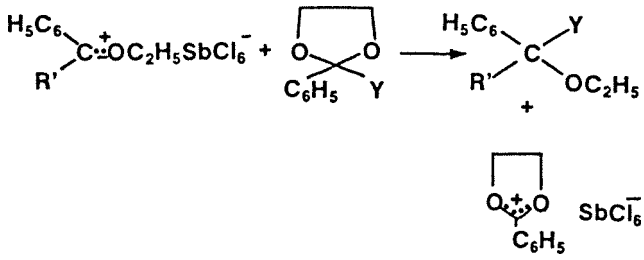
R', R" = H, alkyl, aryl
X = Cl, Br, I

Alkoxy (aryloxy) carbenium salts are capable of alkylating sulfoxides, ethers and amides to give the corresponding onium ion salts.[32]



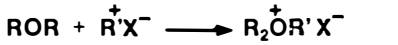
Y = >S:, -O:- ·$CONR_2$

Alkoxycarbenium salts are also used as anion acceptors.[32]



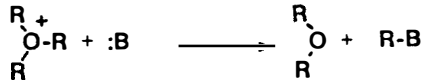
Trialkyloxonium Ion Salts

Meerwein[2,34,35] discovered trialkyloxonium ions and developed their synthetic preparations. They are generally prepared by alkylation of ethers by various alkylating agents including dialkoxycarbenium ions (generated from trialkyl orthoformates), epichlorohydrin, alkyl halides, etc.

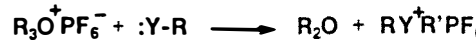


The original trialkyloxonium ion complexes prepared by Meerwein[2,34] were the tetrafluoroborate and hexachloroantimonate salts. The fluoroborate salts have limited stability and generally must be freshly prepared or stored under ether. The corresponding hexafluorophosphate salts[36] show improved solubility and stability which allows convenient storage (preferably in the cold) without the inconvenience of keeping them under ether (which in the case of the very volatile dimethyl ether is impractical). The alkylating action of trialkyloxonium salts has been known since their discovery by Meerwein in 1937. The general use of these powerful alkylating agents in organic synthesis has found increasing application.

Because of their ability to transfer alkyl groups readily, trialkyloxonium salts are strong alkylating agents and are of great preparative importance. Numerous inorganic and organic nucleophiles (:B) can generally be alkylated smoothly even at room temperature.



Trialkyloxonium salts are capable of alkylating a variety of heteroatom compounds. The nucleophile Y includes functional groups with O, S, N, and P.

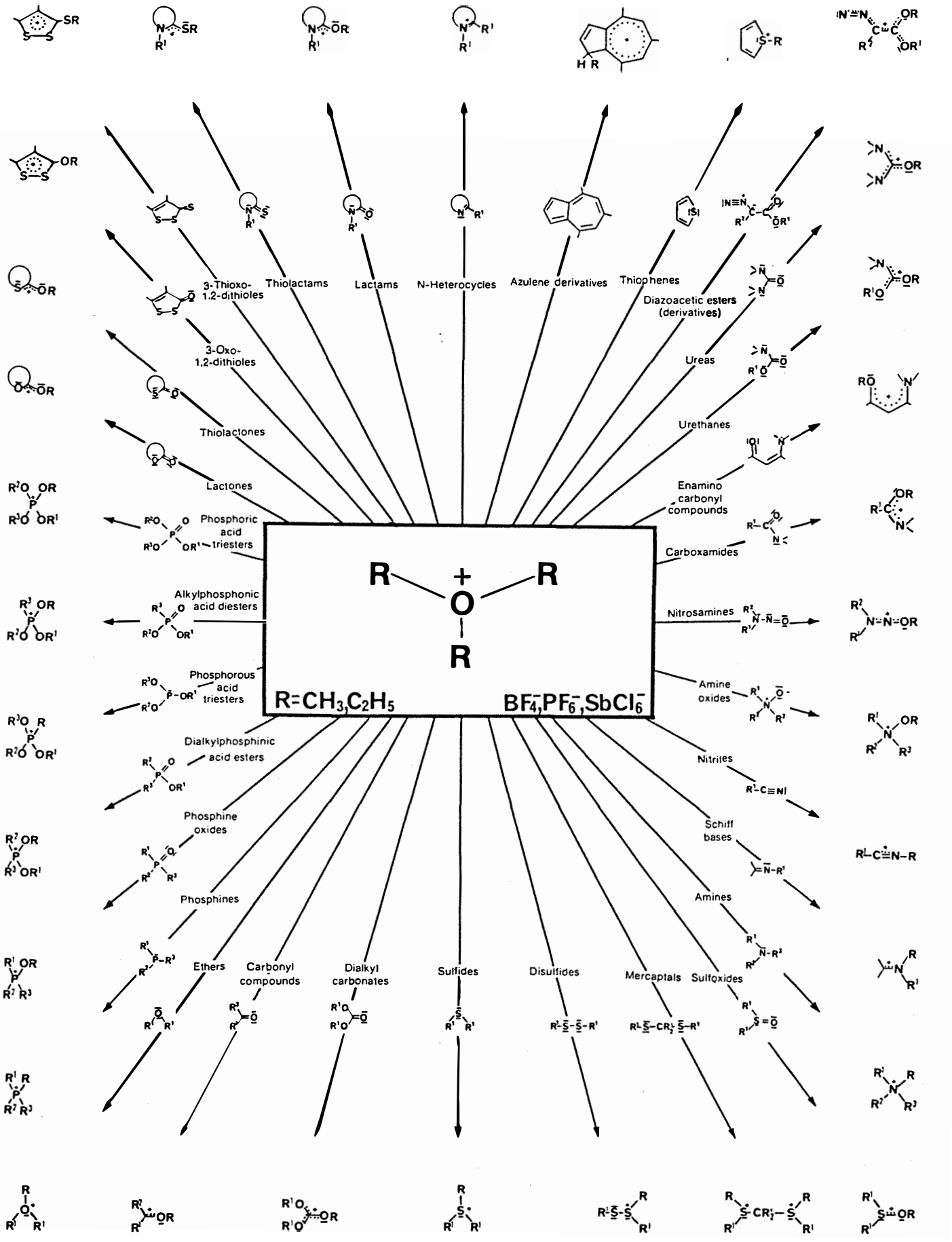


Y = -O:-, >C=O:, -S:-, -S(=O)-, >S=O:, >N:, >P:, -CN:, etc.

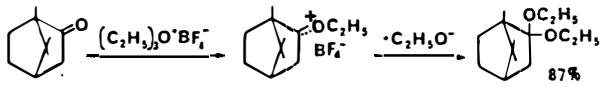
The resulting onium salts $RY^+R'\ PF_6^-$ are generally very reactive intermediates and can be used advantageously in synthesis. Many reported alkylations with trialkyloxonium salts can be seen in the following tabulation. (see p.11)

Hydroxy compounds, such as alcohols, phenols and carboxylic acids and/or their salts, react with trialkyloxonium salts to give O-alkyl derivatives. These alkylations are useful for hindered alcohols, such as pinacolyl alcohol[36] or when non-alkaline conditions are necessary, as in the case of chlorohydrins.[37] Ethers yield new trialkyloxonium salts. The product from epoxides depends on the initial structure. Thus, epichlorohydrin[38] gives a polymer whereas ethylene oxide affords dioxane.

Carbonyl compounds can be O-alkylated in the order:[39] lactams > amides > lactones > esters > ketones > alde-


3-Thioxo-1,2-dithioles
Thiolactams
Lactams
N-Heterocycles
Azulene derivatives
Thiophenes
Diazoacetic esters (derivatives)
3-Oxo-1,2-dithioles
Ureas
Thiolactones
Urethanes
Lactones
Enamino carbonyl compounds
Phosphoric acid triesters
Carboxamides
Alkylphosphonic acid diesters
Nitrosamines
Phosphorous acid triesters
Amine oxides
Dialkylphosphinic acid esters
Nitriles
Phosphine oxides
Schiff bases
Phosphines
Amines
Ethers
Carbonyl compounds
Dialkyl carbonates
Sulfides
Disulfides
Mercaptals
Sulfoxides
R=CH3,C2H5
BF4-,PF6-,SbCl6-

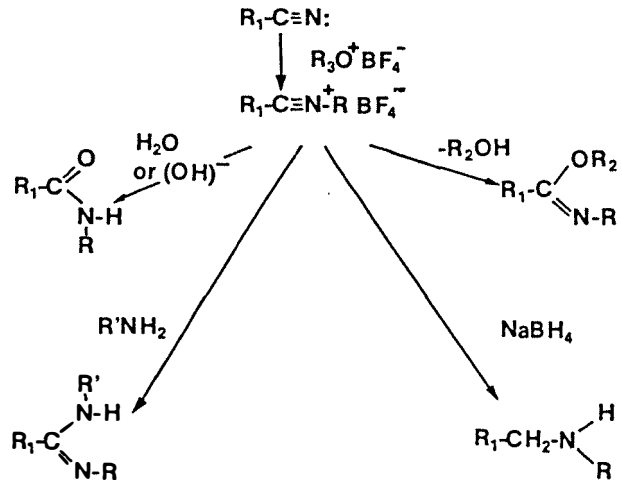
hydes. While most aldehydes and ketones yield only aldol condensation products, some ketones, such as camphor[37] can be O-alkylated, and subsequently reacted with ethoxide ion to give diethyl ketal in high yield.



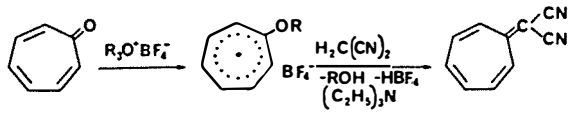
α,β-Unsaturated ketones, such as tropone,[40] are readily alkylated because of increased stabilization of the resulting cation. Esters are poorly alkylated but carbonates[41] can be alkylated because of additional stabilization of the products. The O-alkylation of amides results in imidate salts which react with amines to yield amidines.[42] Amine oxides, sulfoxides and phosphates[1] are readily O-alkylated.

The sodium salt of nitro compounds can be alkylated to give aci-nitronic esters[43, 44] which can rearrange to a mixture of oxime and oxime ether. Pyrazine and pyrimidine are alkylated to yield bis-quaternary salts.[45]

Meerwein and coworkers[46] obtained the first N-alkylnitrilium salts by alkylation of nitriles with trialkyloxonium salts. The carbon atom of the nitrile (C≡N) group is activated for nucleophilic attack. Thus, the action of water or hydroxyl ion on N-alkylnitrilium salts gives amides; alcohols give imidic esters; ammonia or primary amines yield amidines[46] while reduction with sodium borohydride in alcohol gives secondary amines[49].



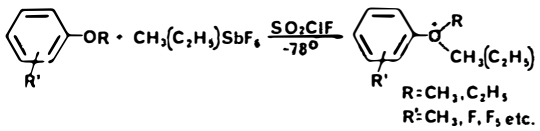
An interesting synthesis is the O-alkylation of tropone giving an alkoxytropylium salt, which when reacted with $H_2C(CN)_2$, yields heptafulvene.[48]



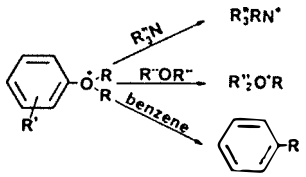
Phosphorus compounds such as triethyl phosphite are alkylated on the phosphorus atom. Sulfides readily yield sulfonium salts. Trialkyloxonium salts also can abstract hydrogen from acetals to give carbenium ions and are of great interest as cationic polymerization catalysts.[47]

Dialkylaryloxonium Ions

The preparation of dialkylaryloxonium ions has been achieved only recently.[50] Alkylation of a series of alkyl aryl ethers with methyl and ethyl fluoroantimonates in SO_2ClF at very low temperature yields the corresponding dialkylaryloxonium ions.



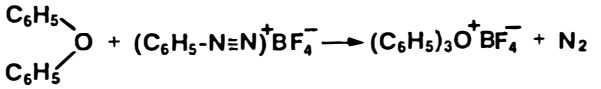
Dialkylaryloxonium ions show a similar chemical reactivity to trialkyloxonium ions. They react readily with amines, ethers and aromatic hydrocarbons at low temperature giving ammonium ions, trialkyloxonium ions and alkylarenes, respectively.



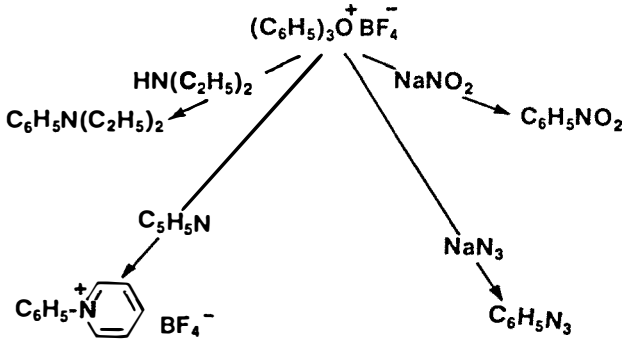
They show no intramolecular alkylating ability (O→C alkyl migration).

Triaryloxonium Salts

Nesmeyanov and Tolstaya[51] reported the preparation (in very low yields, <2%) of triaryloxonium ions by the action of benzenediazonium tetrafluoroborate on diphenyl ether.



The resulting triaryloxonium salts are extremely inert toward nucleophiles in comparison with trialkyloxonium salts. Long reaction time and severe conditions are needed for reaction with nucleophiles (amine, NO_2^- and N_3^-). The synthetic use of these salts as arylating agents is presently very limited.



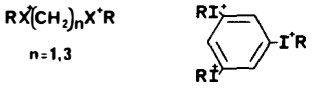
Halonium Ions

Halonium ions are important intermediates in electrophilic halogen additions and have been recognized more recently as a new class of alkylating agents. Alicyclic halonium

ions include (i) dialkylhalonium ions, RX^+R[55], (ii) alkylarylhalonium ions, ArX^+R,[56] and (iii) diarylhalonium ions, ArX^+Ar.[57]

Cyclic halonium ions including 3-membered ring ethylenehalonium ions,[52] 5-membered ring tetramethylenehalonium ions,[53] and 6-membered ring pentamethylenehalonium ions have been prepared.[54]

Furthermore, some open-chain di- and trihalonium ions have been prepared recently.[58]



Dialkylhalonium fluoroantimonate salts were first prepared by Olah and DeMember.[55] The same dialkylhalonium ions

$$2RX + SbF_5\text{-}SO_2 \xrightarrow{-60^\circ} RX^+RSbF_5X^-$$

R=CH_3, C_2H_5, C_3H_7
X=Cl, Br, I

can also be prepared from excess alkyl halide with anhydrous silver hexafluoroantimonate or related complex fluoro silver salts. Alternatively, methyl and ethyl

$$2RX + AgSbF_6 \longrightarrow RX^+RSbF_6^- + AgX$$

fluoroantimonate (in sulfur dioxide) react with alkyl halides to give the corresponding halonium ions.

$$R'X + RSbF_6^- \longrightarrow R'X^+RSbF_6^-$$

R' = CH_3, C_2H_5, C_3H_7
R = CH_3, C_2H_5

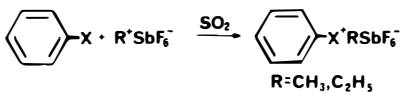
Cyclic three-, five-, and six-membered halonium ions were prepared from the corresponding alkylene dihalides in SbF_5-SO_2 solution at -78°.[52-54]

$$X(CRR')_nX + SbF_5\text{-}SO_2 \xrightarrow{-78^\circ} (CRR')_n^{X^+} \quad SbF_5X^-$$

X = Cl, Br, I
R, R' = H, alkyl
n = 2, 4, 5

Attempted preparation of 4-membered ring trimethylenehalonium ions resulted in ring contraction giving substituted three-membered ring halonium ions.[59]

Recently, Olah and Melby[56] reported the preparation of alkylarylhalonium ions from methyl and ethyl fluorantimonates with halobenzenes.



The preparation of diphenylhalonium ions ($C_6H_5X^+C_6H_5$) was reported by Nesmeyanov and coworkers.[57] The diphenylhalonium salts were obtained in low yield from the reaction of phenyldiazonium tetrafluoroborate with bromobenzene or chlorobenzene.

$$C_6H_5N_2^+BF_4^- + C_6H_5X \longrightarrow C_6H_5X^+C_6H_5 + BF_4^- + N_2$$

Diphenyliodonium ion was prepared in good yield from iodobenzenedichloride and phenyltintrichloride at room temperature.

$$C_6H_5ICl_2 + C_6H_5SnCl_3 \longrightarrow (C_6H_5)_2ICl + SnCl_4$$

Alkylation of a wide variety of hetero-organic compounds with dialkylhalonium ions gave the corresponding onium ion in quantitative yields.

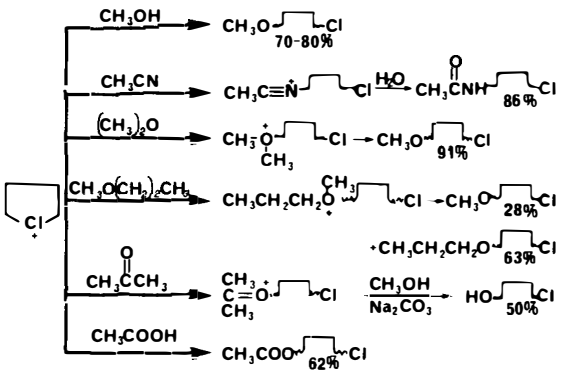
$$RX^+R + (R')_n\text{-}Y \longrightarrow (R')_nY^+\text{-}R + RX$$

SbF_6^- or $Sb_2F_{11}^-$	SbF_6^- or $Sb_2F_{11}^-$
X = I, Br, Cl	R' = CH_3, C_2H_5:
R = CH_3	Y = -O-, -S-, N:, -Cl:
R = C_2H_5	R = alkyl, aryl
	n = 1, 2, 3

The alkylation data show the general alkylating ability and synthetic utility of dialkylhalonium ions. The synthetic advantage of alkylation with dialkylhalonium ions over Meerwein's onium salts (see previous discussion) lies in their ease of preparation, the wide range of their alkylating ability and their selectivity, which can be varied by changing from iodonium to bromonium to chloronium ions. Furthermore, dialkylhalonium ions are effective C-alkylating agents for aromatic hydrocarbons.[60]

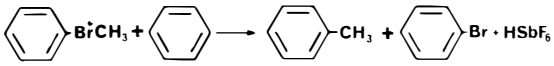
$$RX^+R\ SbF_6^- + ArH \longrightarrow ArR + RX + HSbF_6$$

Peterson and coworkers[61] reported the chemical reactivity of cyclic halonium ions, such as tetramethylenehalonium ions. For example, tetramethylenechloronium ion reacts with acetonitrile, giving the corresponding open chain -chloro nitrilium ion in high yield. On warming and treatment with water, the nitrilium ion is converted to the amide. Some other characteristic reactions of tetramethylenechloronium ion are diagramed below.

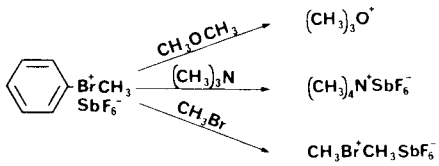


Alkylarylhalonium Ions

Alkylarylhalonium ions were shown to be good general alkylating agents for both π - and *n*-donor bases.[56] For example, methylphenyl bromonium ion reacts with benzene in sulfur dioxide at low temperature to give toluene.



Under similar condition, it reacts with dimethyl ether, trimethylamine and methyl bromide to give trimethyloxonium ion, tetramethylammonium ion and dimethylbromonium ion, respectively.



Phenylation with diphenylbromonium and diphenylchloronium salts was reported by Nesmeyanov and coworkers.[57] Thus, metallic mercury and thallium are phenylated.

$$(C_6H_5)_2BrI + Hg \xrightarrow{i\text{-}C_3H_7OH} C_6H_5HgI$$

$$[(C_6H_5)_2Br]^+BF_4^- + Tl \xrightarrow{\text{acetone}} (C_6H_5)_2TlF$$

Furthermore, diphenylhalonium salts phenylate inorganic compounds ($NaNO_2$, NaN_3 and KCN) and organic amines (diethylamine and pyridine) under varying conditions.

$$(C_6H_5)_2BrI + NaX \xrightarrow{H_2O} C_6H_5X + C_6H_5Br + NaI$$

$$X = NO_2, N_3, CN$$

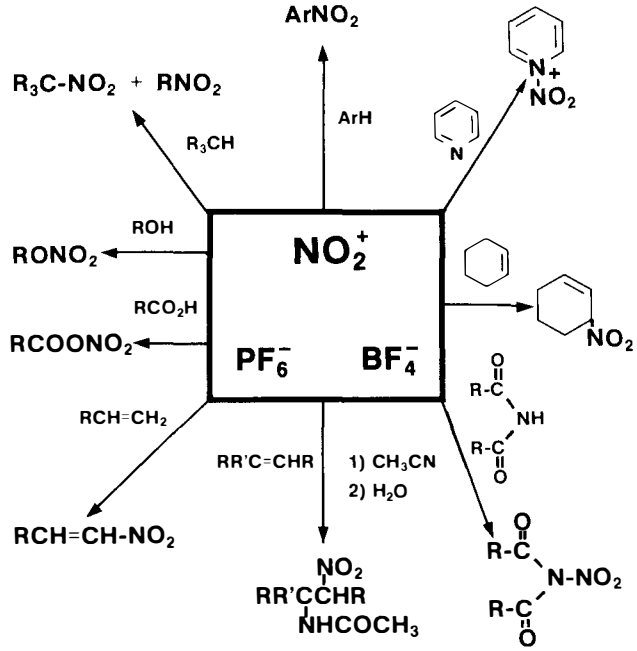
$$(C_6H_5)_2BrI + (C_2H_5)_2NH \xrightarrow{H_2O} C_6H_5N(C_2H_5)_2$$

$$(C_6H_5)_2\overset{+}{C}l\ BF_4^- + C_5H_5N \xrightarrow[200^\circ]{\text{Sealed tube}} (C_5H_5\overset{+}{N}C_6H_5)BF_4^-$$

George A. Olah

Nitronium and Nitrosonium Salts

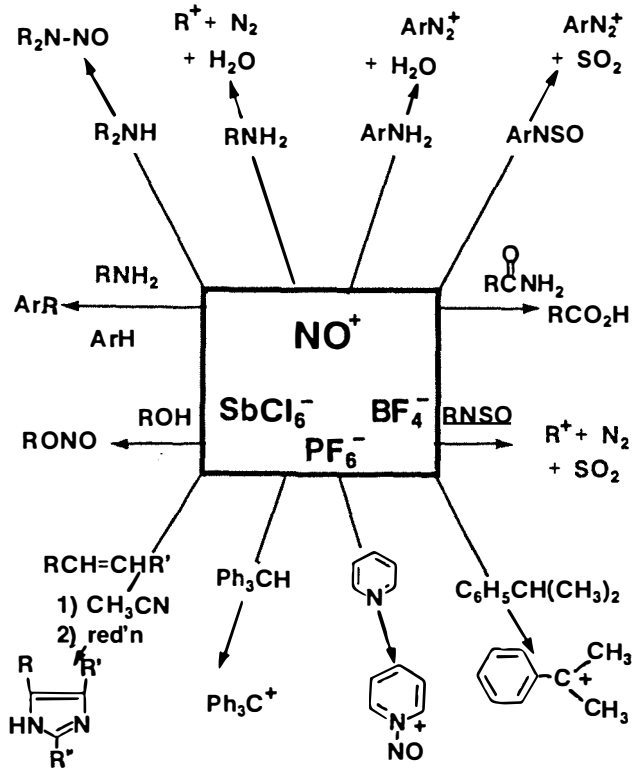
The fundamental studies of Ingold and Hughes[62] established that the reactive nitrating agent in electrophilic nitrations is the nitronium ion, NO_2^+. Olah and Kuhn[63] introduced stable nitronium salts as the most efficient nitrating reagents in aprotic, organic solvents. The most frequently used nitronium salts are the tetrafluoroborate, which is generally used as a 0.5 mole solution in sulfolane (tetramethylenesulfone), and the hexafluorophosphate which is quite soluble in nitromethane.



These nitronium salts nitrate and polynitrate all possible aromatics,[63, 64] alkenes[64] and even alkanes.[65] Alkenes react in acetonitrile with nitronium salts to give acetamido derivatives.[66] In a similar manner substituted aliphatic compounds such as alcohols produce alkyl nitrates,[67] carboxylic acids produce acyl nitrates,[63] and imines yield N-nitroimides.[63]

Although nitronium salts with low nucleophilic counterions such as PF_6^- and BF_4^- are stable, they are very hygroscopic due to their high reactivity with nucleophiles, and must be handled with careful exclusion of moisture.

Electrophilic nitrosation and diazotization may involve active reagents such as $H_2NO_2^+$ and NO^+.[62] Nitrous acid is rather unstable, and usually must be generated *in situ*. Alkyl nitrites and nitrosyl halides are, however, used for the same purpose in non-aqueous media. The nitrosonium salts (NO^+) are remarkably stable and considerably less hygroscopic than the related nitronium salts. They find applications in non-aqueous diazotizations,[68, 69] deaminations,[70, 71] and as hydrogen abstracting agents[70] in syntheses.[72] Suitable non-aqueous solvents for their reactions are nitromethane, acetonitrile, liquid sulfur dioxide, etc.



A brief review can give only a glimpse of the very broad field of carbocation and onium ion reagents, many of which could not be discussed. It can be expected that the field will continue its rapid growth and the synthetic chemist will find many new applications for these reactive reagents.

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ABOUT THE COVER

Our chemist-collector had often commented on his preference for paintings of people, especially biblical people, to paintings of landscapes or still life. So we were rather surprised that he had purchased the landscape (oil on canvas, 63 x 80 cm), depicted on our cover. However, when we saw the landscape, we understood: a truly great landscape - by Rembrandt, or Hercules Seghers, or Jacob Ruisdael, whose work this is - gives us a better understanding of the universe, just as a truly great portrait gives us a better understanding of man.

It seems appropriate that this painting appear on that issue of our Acta dealing with one of the most important developments in synthetic organic chemistry, hydroboration. There is great beauty in each, and both inspire the imagination.

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The Versatile Boranes

Clinton F. Lane
Aldrich-Boranes, Inc.

Diborane, sodium borohydride, and the organoboranes remained as little more than laboratory curiosities for many years after their discoveries. The full potential of this area of chemistry is becoming apparent through the investigations of Professor H.C. Brown of Purdue University. This review will now summarize the major contributions of Professor Brown and should indicate that the boranes are indeed the most versatile organometallics known.

USE OF BH_3·THF AS A REDUCING AGENT

Diborane, a potentially useful reducing agent, is a pyrophoric gas and therefore is seldom used in the laboratory. Aldrich-Boranes now produces borane in tetrahydrofuran, a powerful and convenient laboratory reducing agent. The borane tetrahydrofuran addition compound[1] in tetrahydrofuran is stabilized with sodium borohydride to minimize the loss of hydride due to cleavage of the solvent.[2]

Reductions by $NaBH_4$ and $LiAlH_4$ appear to involve a transfer of hydride ion from the anion to an electron-deficient center of the functional group.[3] Conversely, BH_3 is a strong Lewis acid and reduction by BH_3 appears to involve a preferred electrophilic attack on the center of highest electron density.[4] Consequently, a reagent with such different reducing characteristics would be expected to be exceedingly useful in selective reductions. An extensive study of the reducing properties of BH_3·THF was therefore carried out by Professor Brown and co-workers.[5,6]

Both aliphatic and aromatic aldehydes and ketones are rapidly reduced at room temperature. Lactones and epoxides are readily reduced, but the reactions are considerably slower than those of aldehydes and ketones. Esters are only slowly reduced and nitro compounds fail to react. Also, acid chlorides are unreactive with BH_3·THF. Presumably, this is due to the electron-withdrawing influence of the chlorine substituent.

Perhaps the most interesting observation is that both carboxylic acids and nitriles are rapidly reduced by BH_3 · THF. Indeed, carboxylic acids are reduced considerably faster than ketones. On the other hand the sodium salts of carboxylic acids do not react.

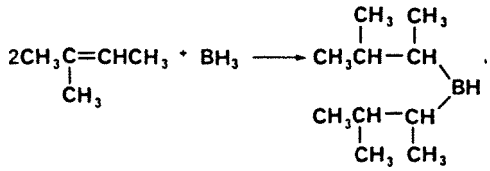
The results for the reaction of BH_3·THF with various representative substrates are summarized as follows:

Substrate	*Product*
aldehyde	alcohol
ketone	alcohol
acid chloride	no reaction
lactone	glycol
epoxide	alcohol
ester	alcohol (slow)
carboxylic acid	alcohol (fast)
carboxylic acid salt	no reaction
amide	amine
nitrile	amine
nitro	no reaction
olefin	organoboranes (fast)

A study of the relative reactivity of a number of representative groups toward BH_3·THF indicated the following order of reactivity[7]: carboxylic acids > olefins > ketones > nitriles > epoxides > esters > acid chlorides. On the other hand, the order of reaction with sodium borohydride is: acid chlorides > ketones > epoxides > esters > nitriles > carboxylic acids.

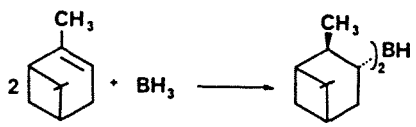
With such markedly different reactivities, it is apparent that the judicious use of either BH_3·THF or $NaBH_4$ permits the reduction of one group in the presence of a second, or *vice versa.*

The hydroboration[8] of trimethylethylene rapidly forms the dialkylborane, known as disiamylborane[9] (eq 2).



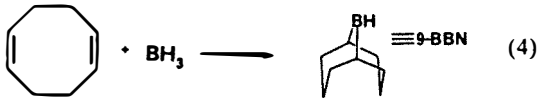
(2)

The addition of a third mole of olefin proceeds only relatively slowly. Similarly, α-pinene undergoes hydroboration to form diisopinocampheyl borane[10] (eq 3);



(3)

and 1,5-cyclooctadiene undergoes intramolecular hydroboration to give 9-borabicyclo[3.3.1]nonane (9-BBN)[11] (eq 4), which is now produced by Aldrich-Boranes, Inc.



(4)

These dialkylboranes might be expected to act as highly selective reducing agents. Consequently, a detailed study of the reducing capabilities of disiamylborane was carried out by Professor Brown and co-workers.[12] The results indicate the following characteristics:

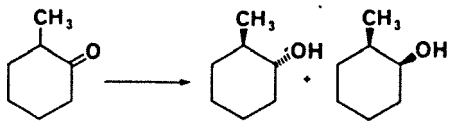
Substrate	*Product*
aldehyde	alcohol
ketone	alcohol
acid chloride	no reaction
lactone	hydroxyaldehyde
epoxide	very slow reaction
ester	very slow reaction
carboxylic acid	no reaction
carboxylic acid salt	no reaction
tert-amide	aldehyde
nitrile	very slow reaction
nitro	very slow reaction
olefin	organoborane

Similar results would be expected for other dialkylboranes.

Especially noteworthy is the partial reduction of lactones with disiamylborane to give, upon work-up, hydroxyaldehydes. The corresponding reduction with BH_3·THF or with $LiAlH_4$ goes rapidly past this stage to yield the diol.

Another highly selective use of dialkylboranes is for the reduction of tertiary amides which yield upon hydrolysis the corresponding aldehydes. Reduction of amides with BH_3·THF proceeds completely to the amine stage.

Finally, dialkylboranes (because of their increased steric size) are especially valuable as stereoselective reducing agents[13] (eq 5).*



$LiAlH_4$	75%	25%
BH_3	74%	26%
R_2BH	6%	94%

(5)

These new hydride reducing agents permit many selective reductions. Moreover, by an intelligent choice of reducing agent it is frequently possible to reduce one group in the presence of a second, or to carry out the reverse operation. The amount of data which has accumulated in this area is overwhelming. To simplify the task of becoming acquainted with the major possibilities, Table I summarizes the observed reactivities of the main functional groups toward these reagents. The symbol (+) indicates a rapid reaction at 0-25°C, the symbol (-) indicates slow or insignificant reaction at 0-25°C, and the symbol (±) indicates a variable rate depending upon structure.

Table I-Summary of the Behavior of Various Functional Groups Toward the Hydride Reducing Agents

	$NaBH_4$ in Diglyme	$NaBH_4$+ LiCl ($LiBH_4$) in Diglyme	BH_3 THF	R_2BH THF	$LiAlH_4$ THF
Aldehyde	+	+	+	+	+
Ketone	+	+	+	+	+
Acid Chloride	+	+	-	-	+
Lactone	-	+	+	+	+
Epoxide	-	+	+	±	+
Ester	-	+	±	-	+
Carboxylic Acid	-	-	+	-	+
" Acid Salt	-	-	-	-	+
tert-Amide	-	-	+	+	+
Nitrile	-	-	+	-	+
Nitro	-	-	-	-	+
Olefin	-	-	+	+	-

From this summary, it is evident that $NaBH_4$ will reduce an acid chloride group in the presence of an ester group, while BH_3·THF will reduce the ester in the presence of the acid chloride. Similarly, $LiBH_4$ will reduce the ester group in the presence of the nitrile group, while BH_3·THF will do the opposite. With BH_3·THF it is simple to reduce a carboxylic acid group, without attack on a nitro group. Numerous other selective reductions are possible as indicated by the summary. However, the reactivities of the various functional groups can be greatly altered by the structures containing them, so that these generalizations must be used with caution in predicting the behavior of greatly modified systems.

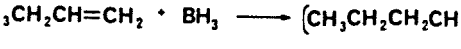
Use of BH_3·THF as a Hydroboration Agent

The hydroboration reaction involves the addition of the hydrogen-boron bond to the carbon-carbon double or triple bond, producing the corresponding organoborane (eq 6).

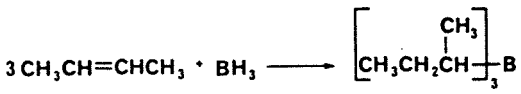

(6)

Systematic study of the hydroboration reaction by Prof. Brown and co-workers[8] has revealed that the reaction is essentially quantitative with remarkably wide applicability, involves a *cis* anti-Markovnikov addition from the less hindered side of the double bond, and can tolerate almost all functional groups.

The hydroboration of most alkenes proceeds directly to the fully alkylated borane, R_3B[8], *e.g.* eq 7 and 8.

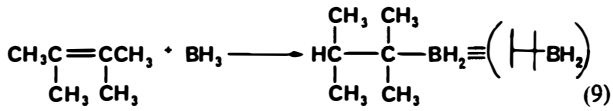

(7)

* An even more stereoselective reducing agent is now available in the form of $M(2\text{-butyl})_3BH$. See page 37 of this Acta for details on "Selectride".

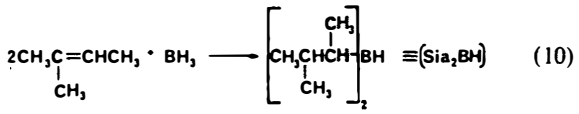


(8)

However, in some cases, the hydroboration can be readily controlled to yield partially alkylated boranes[14-20] (eq 9-13).



(9)



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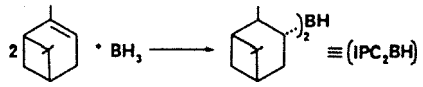
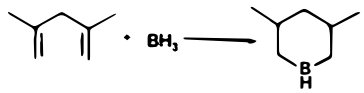


(11)

(12)



(13)

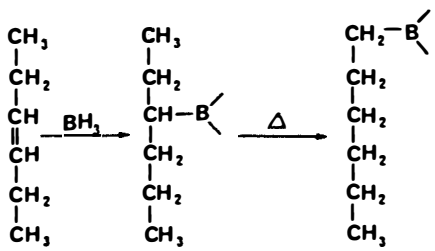
These partially alkylated boranes have become quite valuable for various synthetic applications to be discussed in this review.

Synthetic Uses of Organoboranes

The development of the hydroboration reaction has made the organoboranes readily available and has stimulated a detailed exploration of the chemistry of organoboranes by Prof. Brown and his students at Purdue University. In the initial stages of his investigation Prof. Brown has emphasized only the reactions of interest in organic synthesis. Progress in this area has been rapid and many new reactions of major significance to synthetic chemistry have been discovered. An attempt will now be made to summarize some of the more promising developments in this area.

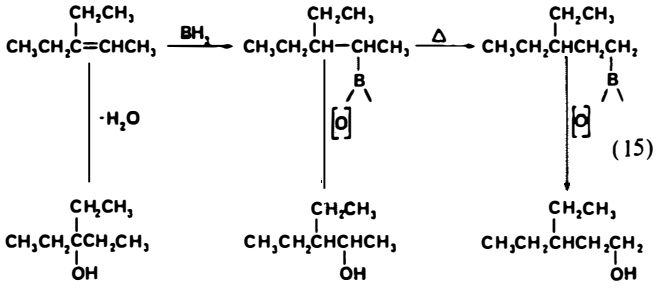
1. Isomerization

At 160°C organoboranes undergo a facile isomerization which proceeds to place the boron atom at the least hindered position of the alkyl groups[21,22] (eq 14).



(14)

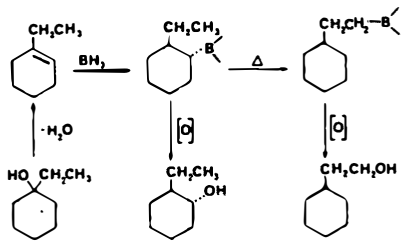
This makes possible a number of very valuable syntheses, not otherwise practical. For example, the following synthesis (eq 15)



(15)

may be readily achieved in essentially quantitative yield by utilizing hydroboration and isomerization.[22]

It is also possible to move the boron atom out of a ring and into a side chain[23] (eq 16).

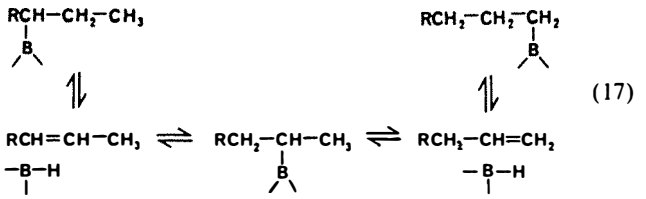


(16)

This ready isomerization of organoboranes under mild conditions makes possible a number of interesting syntheses of desired compounds from alternative, more readily available intermediates, such as the illustrated synthesis of 2-cyclohexylethanol from the readily available olefin, 1-ethylcyclohexene (eq 16).

2. Displacement

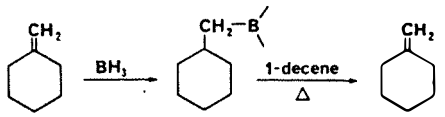
The mechanism proposed[21,24] for the isomerization reaction involves a series of eliminations and readditions, so thermodynamic equilibrium is readily established between all of the possible organoboranes (eq 17).



(17)

The predominant product is usually that derivative which places the boron atom at the least hindered position.

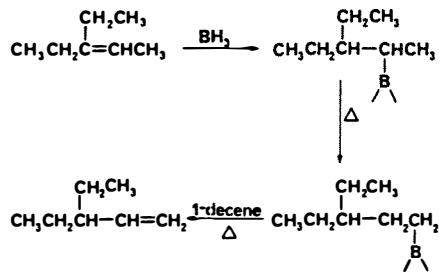
This mechanism indicates that the introduction of another alkene into the reaction mixture should result in capture of the boron hydride intermediate and incorporation of the new alkene into the organoborane product. By using a less volatile alkene, it is possible to distill out the original alkene (eq 18).



(18)

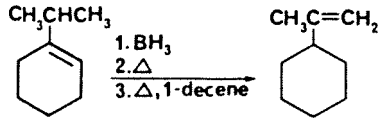
3. *Contrathermodynamic Isomerization*

By a combination of hydroboration, isomerization, and displacement, it is possible to carry out the contrathermodynamic isomerization of olefins[25, 26] (eq 19).



(19)

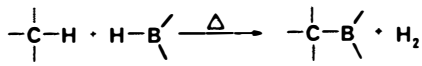
It is also possible to move in this manner a double bond from the endocyclic to the non-cyclic position[26] (eq 20).



(20)

4. *Cyclization*

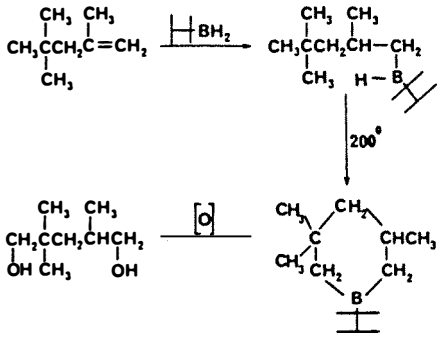
In addition to isomerization the organoboranes undergo other interesting reactions under the influence of heat.[27] Of these reactions the most promising is the ready reaction of a boron-hydrogen bond with a carbon-hydrogen bond to form hydrogen and a carbon-boron bond (eq 21).



(21)

Although this reaction is difficult when the two groupings are in separate molecules, it occurs readily within a single molecule, providing a ready entry into cyclic boron derivatives and to the corresponding compounds that can be prepared from boron intermediates.

The conversion of a terminal olefin into a 1,5-diol is representative of a synthesis which is possible *via* cyclization of a dialkylborane[28] (eq 22).



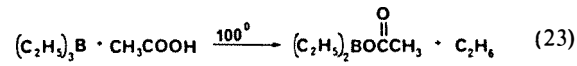
(22)

5. *Protonolysis*

Trialkylboranes are remarkably stable toward water, hydrogen sulfide, alcohols, and phenols. Temperatures > 200°C for extended lengths of time are necessary to achieve even partial hydrolysis of trialkylboranes using the above proton sources.[29] Interestingly, the addition of alkali to water even further stabilizes the trialkylborane toward hydrolysis.[30]

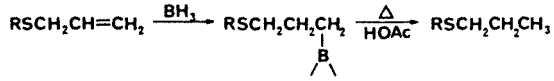
Treatment of trialkylboranes with concentrated mineral acids facilitates the hydrolysis. However, even heating under reflux with such acids brings about the protonolysis of only one of the three alkyl groups.[31]

Somewhat unexpectedly, organoboranes are more susceptible to attack by carboxylic acids than by mineral acids. Thus, it has been observed that under relatively mild conditions triethylborane can be converted into diethylboron acetate and ethane[32] (eq 23).

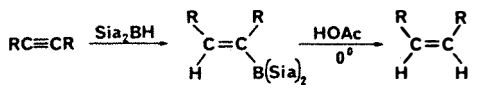


(23)

A detailed investigation of the action of carboxylic acids on organoboranes has revealed that two of the three groups can be removed by excess anhydrous acid at room temperature, and all three groups can generally be removed by refluxing the organoborane in diglyme solution with a moderate excess of propionic acid for 2 to 3 hr.[32] Consequently, this provides a convenient non-catalytic means of hydrogenating double and triple bonds in compounds where the usual catalytic hydrogenation is difficult[32,33] (eq 24, 25).

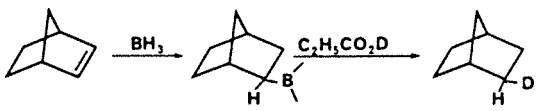


(24)



(25)

The protonolysis reaction appears to proceed with complete retention of configuration. Thus, tri-*exo*-norbornylborane undergoes deuterolysis to yield *exo*-deuteronorbornane[34] (eq 26).

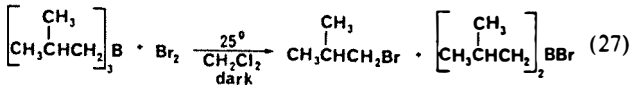


(26)

Also, complete protonolysis has been applied for the quantitative analysis of organoboranes.[35]

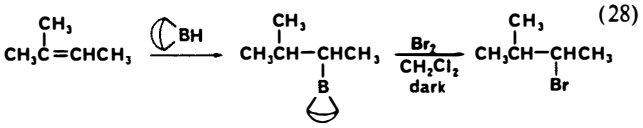
6. *Halogenolysis*

The rupture of the carbon- boron bond by direct reaction of bromine with neat trialkylboranes has proven to be surprisingly difficult.[31] However, the reaction is facilitated by the use of methylene chloride as a solvent and provides a convenient procedure for the anti-Markovnikov hydrobromination of olefins[36] (eq 27).



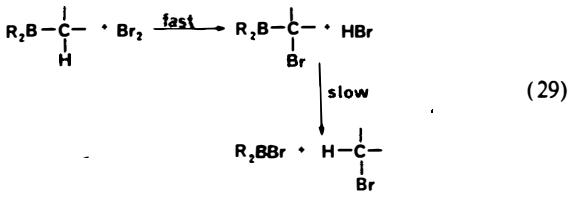
(27)

The use of B-alkyl-9-BBN derivatives provides a higher utilization of the alkyl group in many cases, and a good yield of the anti-Markovnikov bromide from the olefin[37] (eq 28).



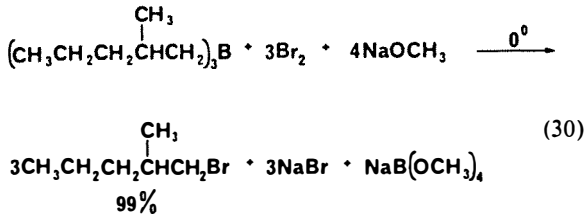
(28)

Investigation of this reaction (eq 27) revealed an unexpected feature - the reaction does *not* involve simple rupture of the carbon-boron bond by bromine. Instead, the reaction proceeds through a fast α -bromination of the organoborane followed by subsequent reaction of the intermediate with the HBr[36] (eq 29).



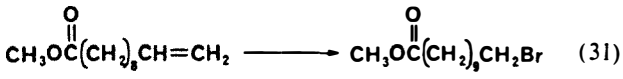
(29)

The difficulties in the brominolysis of organoboranes are largely overcome by treating the organoborane with bromine at 0°C in the presence of $NaOCH_3$ in CH_3OH[38] (eq 30).

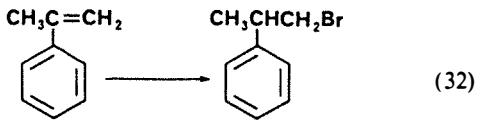


(30)

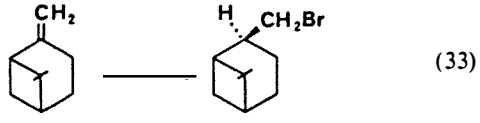
This reaction proved to be very general for the conversion of terminal olefins into primary bromides and a series of representative examples follow (eq 31-33).



(31)

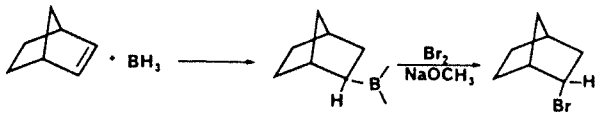


(32)



(33)

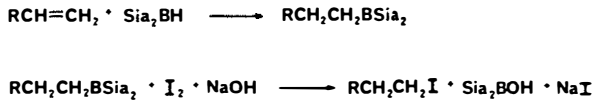
Hydroboration of norbornene gives the *exo* isomer predominantly (99.6%); but if tri-*exo*-norbornylborane is treated with bromine and sodium methoxide in methanol, *endo*-norbornyl bromide is formed preferentially[39] (eq 34).



(34)

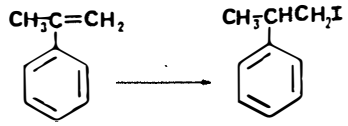
This now provides a convenient route to this and related bicyclic *endo* bromides, which are relatively inaccessible by other methods.

Similarly, the reaction of iodine with organoboranes is exceedingly sluggish.[40] However, the addition of sodium hydroxide in methanol to the organoborane and iodine brings about a rapid reaction; and by using disiamylborane, terminal olefins can be converted cleanly into primary iodides[41] (eq 35).

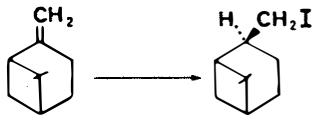


(35)

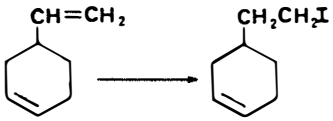
The reaction appears to be widely applicable, as shown by the following representative transformations (eq 36-38).



(36)



(37)



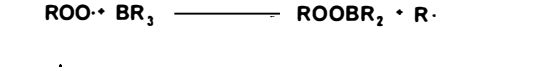
(38)

7. *Oxidation (O_2)*

Detailed study of the reaction of oxygen with organoboranes has revealed that the reaction proceeds through a free-radical chain, as illustrated in equations 39-42.[42 - 44]

(39)

(40)



(41)

(42)

By using the Brown□ apparatus,[45] Prof. Brown and co-workers have been able to control the oxidation and have developed convenient procedures for synthesizing alkylhydroperoxides or the corresponding alcohols. To obtain the hydroperoxide, the intermediate is oxidized at 0°C with H_2O_2 and the alkylhydroperoxide is separated from the alcohol by base extraction from the THF solution[46] (eq 43, 44).

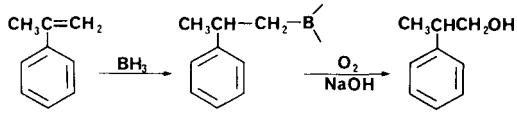
$$R_3B + 2O_2 \xrightarrow[-78^0 \rightarrow 0^0C]{THF} (RO_2)_2BR \qquad (43)$$

$$(RO_2)_2BR + H_2O_2 \xrightarrow[0^0C]{THF} 2ROOH + ROH \qquad (44)$$

By controlling the amount of O_2 introduced into the THF solution to the theoretical quantity followed by treatment with base, an essentially quantitative conversion to the corresponding alcohol is achieved[44] (eq 45).

$$R_3B + 1.5O_2 \xrightarrow[0^0C]{THF} (RO_2)_{1.5}BR_{1.5} \xrightarrow[H_2O]{NaOH} 3ROH \qquad (45)$$

Using this route many alkenes can be converted to their corresponding anti-Markovnikov alcohols (eq 46).



(46)

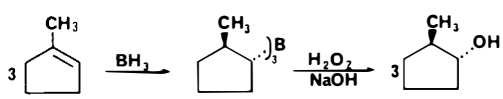
8. Oxidation (H_2O_2)

Oxidation of organoboranes with hydrogen peroxide in the presence of alkali is essentially quantitative and possesses remarkable specificity for the carbon-boron bond[47] (eq 47).

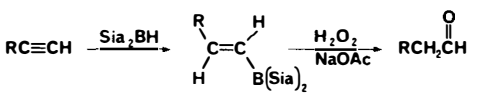
$$R_3B + 3H_2O_2 + NaOH \longrightarrow 3ROH + NaB(OH)_4 \qquad (47)$$

Hydroboration followed by *in situ* oxidation with alkaline hydrogen peroxide provides a remarkably simple and convenient procedure for the anti-Markovnikov hydration of double and triple bonds.[47] Also, the reaction proceeds with complete retention of configuration. Equations 48 - 50 illustrate typical examples.

$$3RCH{=}CH_2 \xrightarrow{BH_3} (RCH_2CH_2)_3B \xrightarrow[NaOH]{H_2O_2} 3RCH_2CH_2OH \qquad (48)$$



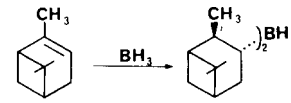
(49)

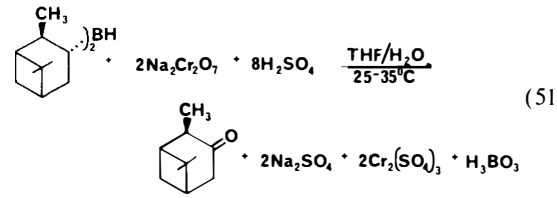


(50)

9. Oxidation (H_2CrO_4)

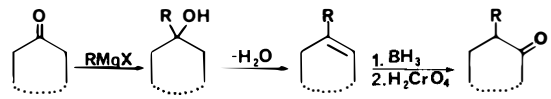
Using aqueous chromic acid, alicyclic organoboranes can be oxidized directly to ketones,[48] *e.g.* eq 51.





(51)

This oxidation reaction, when combined with other common synthetic reactions, provides the basis for a general synthesis of α-monoalkyl cyclic ketones (eq 52).

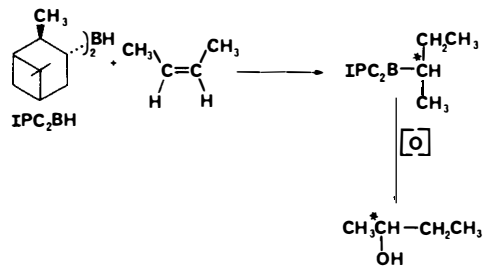


(52)

10. Asymmetric Synthesis

Optically active diisopinocampheylborane (IPC_2BH), which is readily synthesized by the hydroboration of optically active α-pinene (eq 11), reacts readily with *cis*-acyclic, cyclic and bicyclic olefins to yield diisopinocamphenyl-*sec*-alkylboranes. Oxidation with alkaline hydrogen peroxide then gives *sec*-alkanols with optical purities in the range of 65-91%.[49]

For example, *cis*-2-butene was converted into 2-butanol with an optical purity of 87%[49] (eq 53).



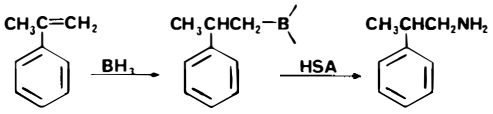
(53)

(+)-α-Pinene yields (-)-2-butanol ($[\alpha]_D$ -11.8°), and (-)-α-pinene yields (+)-2-butanol ($[\alpha]_D$ +11.7°).

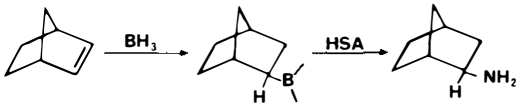
The reaction of IPC_2BH with *trans* and hindered olefins was found to be relatively much slower, proceeded with displacement of α-pinene from the reagent, and gave oxidized products of much lower optical purity.[50] Also, IPC_2BH can be used to convert 2-methyl-1-alkenes into optically active 2-methyl-1-alkanols.[51]

11. Amination

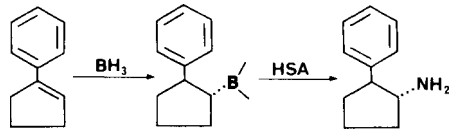
Organoboranes are converted by hydroxylamine-O-sulfonic acid (HSA) into primary amines.[52] Like alkaline hydrogen-peroxide oxidation, amination proceeds with complete retention of configuration.[53] Consequently, hydroboration followed by amination provides a highly satisfactory procedure for the simple synthesis of a wide variety of amines from the corresponding olefins. Typical examples are given in equations 54-57.



(54)



(55)

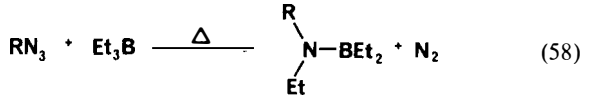


(56)

(57)

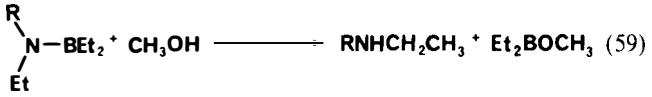
Dimethylchloramine provides a related route to the corresponding tertiary amines, $RN(CH_3)_2$.[54]

Recent developments by Brown and co-workers now provide a promising new route to the generally more difficultly synthesized secondary amines. A wide variety of organic azides were found to react readily with triethylborane in refluxing xylene[55] (eq 58).



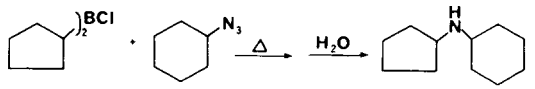
(58)

Hydrolysis of the intermediate with methanol then gave the corresponding secondary amine (eq 59).

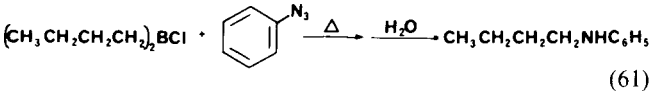


(59)

In contrast to this relatively sluggish reaction of organic azides with trialkylboranes,[55] organic azides were found to undergo a facile reaction with a wide variety of dialkylchloroboranes.[56] The dialkylchloroboranes are now readily available *via* hydroboration of olefins with chloroborane diethyl etherate.[57] Representative examples are shown in equations 60 and 61.



(60)



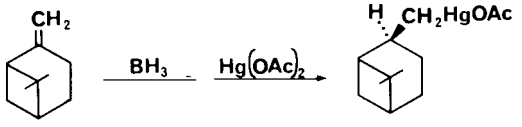
(61)

12. Metallation

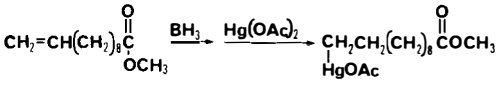
Organoboranes react with certain metallic oxides in aqueous suspensions to give the corresponding organometallics[58] (eq 62).

(62)

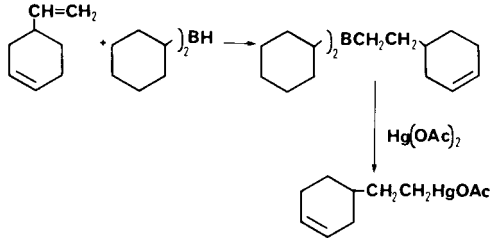
In tetrahydrofuran solution, organoboranes from terminal alkenes react with mercuric acetate with remarkable ease at 0°C to give primary alkylmercuriacetates.[59] The following transformations are representative (eq 63-65).



(63)



(64)

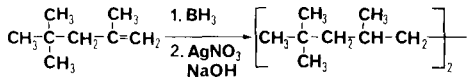


(65)

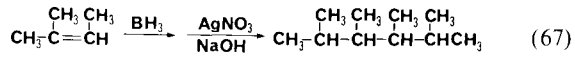
This hydroboration-mercuration reaction has also been used to prepare *sec*-alkylmercuriacetates,[60] alkenylmercuric salts,[61] and dialkylmercurials.[62]

13. Coupling

Treatment of organoboranes with alkali and silver nitrate at 0°C leads to coupling of the alkyl groups.[63-65] Presumably the reaction involves a metallation to give an alkyl silver compound which then undergoes the usual transformation into silver metal and the coupled product. Typical examples are shown in equations 66 and 67.



(66)

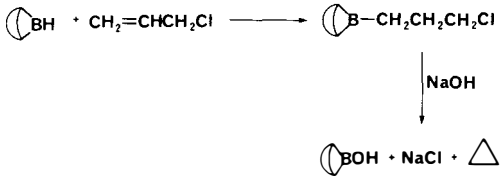


(67)

With two different alkyl groups, R and R', the coupling is essentially statistical,[65] with 25% R-R, 50% R-R', and 25% R'-R'.

14. Cyclopropane Synthesis

Hydroboration of allyl chlorides with 9-BBN[11] (eq 4) followed by treatment of the B-γ-chloroalkyl-9-BBN derivatives with NaOH provides a simple method for the synthesis of cyclopropanes.[66] Equations 68 - 70 indicate a few of the possibilities.

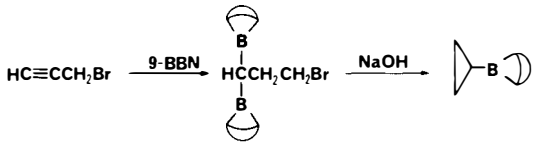


(68)

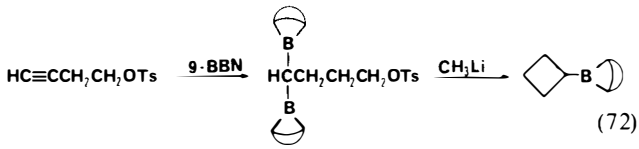
(69)

(70)

This approach can be extended to form derivatives of 9-BBN containing a cyclopropyl or cyclobutyl group attached to boron[67] (eq 71 and 72).



(71)

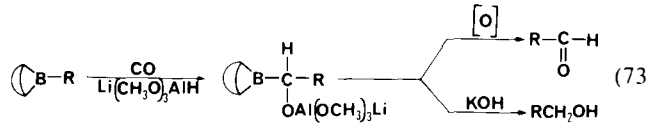


(72)

15. Carbonylation to Aldehydes

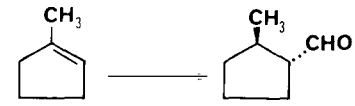
The reaction of organoboranes with carbon monoxide[68,69] has been developed by Prof. Brown and co-workers into a remarkably versatile approach to a wide variety of carbon structures.[70]

Treatment of an organoborane with CO in the presence of lithium trimethoxyaluminohydride provides an essentially quantitative yield of either the aldehyde or the methylol derivative.[71] Use of the B-alkyl-9-BBN derivative proved to be especially advantageous[72] (eq 73).

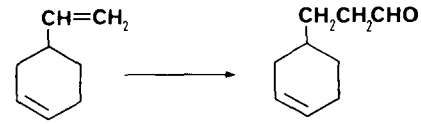


(73)

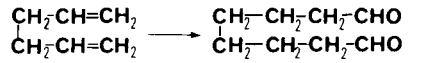
All the selectivity and stereospecificity of the hydroboration reaction can be utilized[72,73] (eq 74-76).



(74)

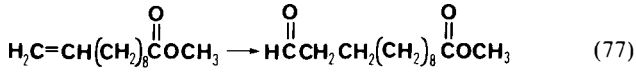


(75)

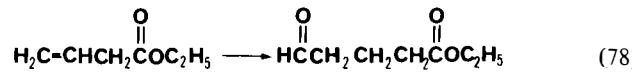


(76)

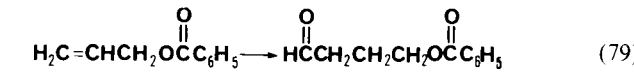
By using a less reactive reducing agent, lithium tri-*t*-butoxyaluminohydride, many functional groups can be accommodated.[74] Thus, the transformations shown in equations 77 - 80 have all been carried out successfully using hydroboration-carbonylation.



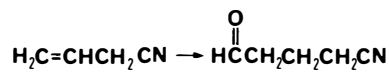
(77)



(78)



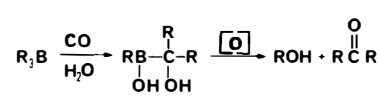
(79)



(80)

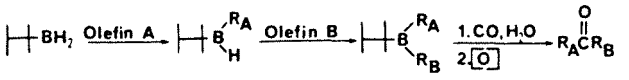
16. Carbonylation to Ketones

Carbonylation of organoboranes in the presence of water leads to an intermediate which can be readily oxidized to the corresponding ketones[75] (eq 81).



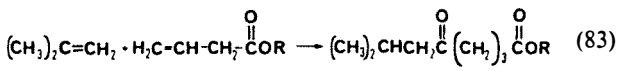
(81)

The use of thexylborane provides an elegant general route to ketones which avoids the loss of one of the three groups and allows the use of different alkyl groups[76] (eq 82).

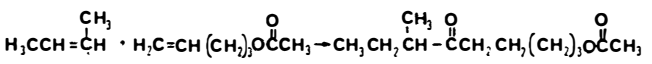


(82)

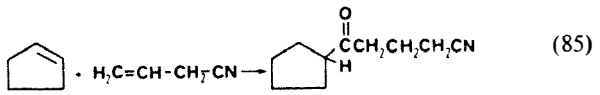
Using this procedure many types of functional groups and olefin structures can be accommodated[76,77] (eq 83 - 86).



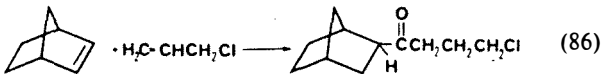
(83)



(84)

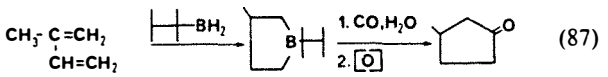


(85)

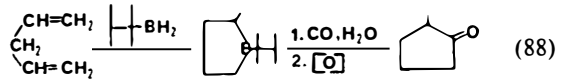


(86)

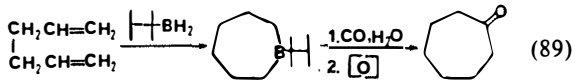
This method also provides a simple route to cyclic ketones,[78] as illustrated by equations 87 - 89.



(87)

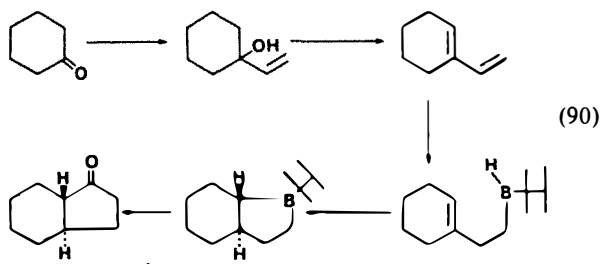


(88)



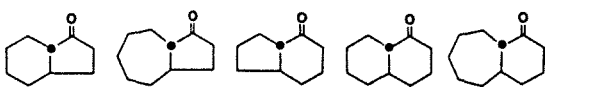
(89)

Finally, this hydroboration-carbonylation reaction provides the basis for a new annelation reaction of apparent wide applicability.[79] A specific example is illustrated in equation 90.

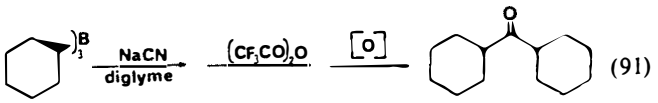


(90)

This annelation reaction has been successfully applied to the synthesis of the following ketones achieving an isomerically pure *trans*-fusion.



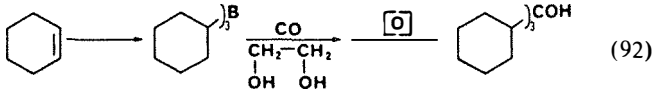
The conversion of organoboranes into ketones can also be accomplished with sodium cyanide and certain electrophilic reagents followed by oxidation.[80,81] Equation 91 illustrates the potential of this development.



(91)

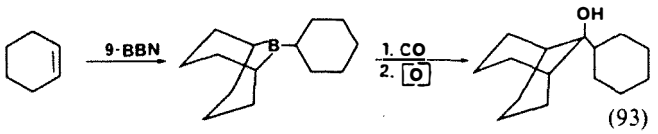
17. Carbonylation to Tertiary Alcohols

The carbonylation-oxidation of organoboranes provides a valuable new route to tertiary alcohols, which is capable of accommodating even highly bulky groups[82] (eq 92).

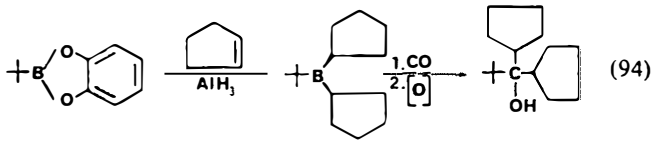


(92)

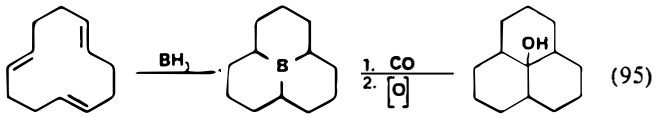
A few of the major possibilities of this new synthetic approach are indicated by the following syntheses[83-86] (eq 93-96).



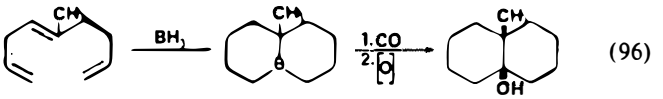
(93)



(94)

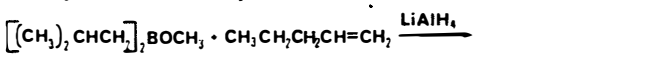


(95)

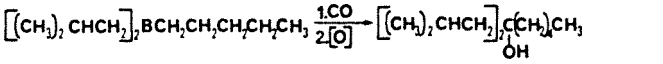


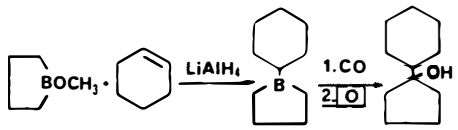
(96)

The full utilization of this new synthetic approach to tertiary alcohols requires the development of simple syntheses of mixed organoboranes, R R'R"B. Considerable progress has been made toward this objective by Prof. Brown and coworkers. Thus, the treatment of borinic acid esters with $LiAlH_4$ in the presence of the appropriate olefins yields the corresponding organoboranes readily convertible to the tertiary alcohols[87] (eq 97 and 98).



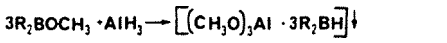
(97)



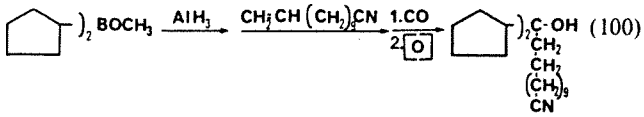


(98)

This procedure cannot be utilized for olefins containing groups reducible by $LiAlH_4$. Fortunately, this difficulty can be circumvented by using aluminum hydride. Relatively stable addition compounds of the dialkylboranes and aluminum methoxide are formed[88] (eq 99).

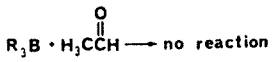

(99)

These addition compounds can be utilized to hydroborate olefins containing functional groups. The resulting trialkylboranes can then be converted into *tert*-alcohols[88] (eq 100).

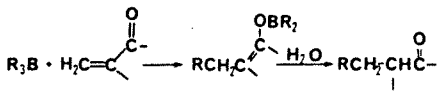

(100)

18. Conjugate Additions

Organoboranes do not add to the carbonyl group of simple aldehydes or ketones in the same way as Grignard reagents (eq 101).

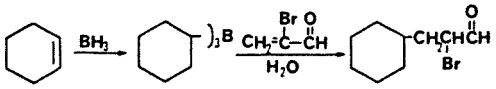

(101)

However, a rapid reaction occurs with acrolein,[89] methyl vinyl ketone,[90] and similar derivatives[91] (eq 102).


(102)

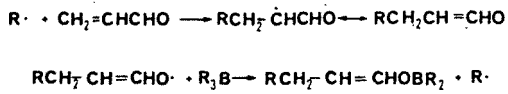
This reaction now provides a valuable means of lengthening a carbon chain by three carbon atoms.

Many α,β-unsaturated carbonyl derivatives were found to undergo this 1,4-addition reaction spontaneously, *i. e.*, without any added catalysts.[89-91] The following compounds undergo this reaction with a wide variety of trialkylboranes: acrolein, methyl vinyl ketone, 2-methylacrolein, 3-methyl-3-buten-2-one and 2-bromoacrolein. The reaction with 2-bromoacrolein is especially noteworthy and provides a simple, convenient route to α-bromoaldehydes[91] (eq 103).


(103)

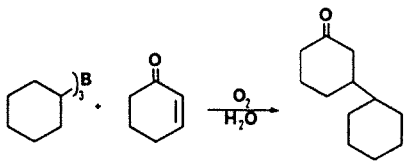
Other α,β-unsaturated carbonyl compounds such as crotonaldehyde, 3-penten-2-one, 1-acetyl-1-cyclohexene and 2-cyclohexen-1-one, failed to undergo this spontaneous reaction.

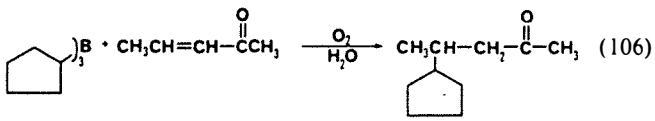
An investigation by Brown and co-workers revealed that the reaction involved a free-radical chain process[92] (eq 104).

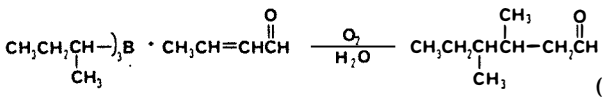

(104)

Consequently, even the facile reaction of acrolein with trialkylborane can be inhibited by a typical free-radical inhibitor, such as galvinoxyl.[92]

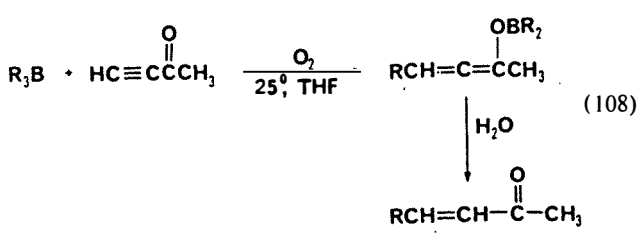
Once this free-radical reaction course was recognized, it became apparent that the 'inert' derivatives might involve reactions with shorter chain lengths. Indeed, in those cases irradiation of the reaction mixture with light, or the introduction of free-radical initiators, such as diacetyl peroxide, or merely the introduction of small quantities of oxygen, brought about satisfactory 1,4-additions[93] (eq 105-107).


(105)

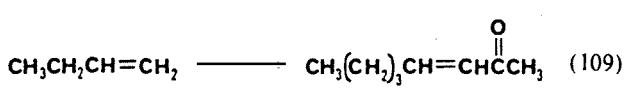

(106)

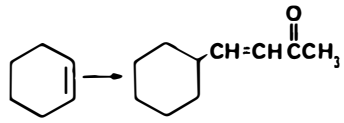

(107)

Acetylacetylene, which fails to undergo the 'spontaneous' reaction with trialkylboranes, readily undergoes addition in the presence of catalytic amounts of oxygen.[94] Hydrolysis of the allenic intermediate then produces the corresponding α,β-unsaturated methyl ketone (eq 108).

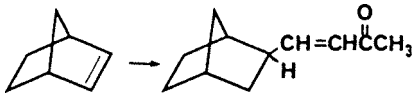

(108)

The reaction is one of wide generality, providing unsaturated methyl ketones from a wide variety of structural types of olefins[94] (eq 109-111).


(109)

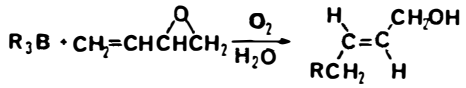


(110)



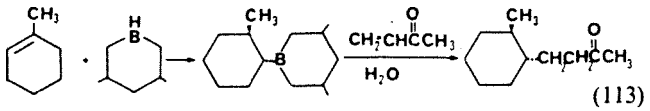
(111)

1,3-Butadiene monoxide also fails to react spontaneously with trialkylboranes. However, the reaction is readily induced by small amounts of oxygen or other free-radical initiators.[95] This provides a new four-carbon-atom homologation leading to the corresponding 4-alkyl-2-buten-1-ols in relatively high stereochemical purity (eq 112).

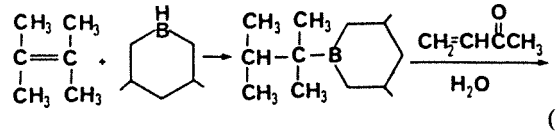


(112)

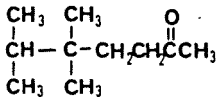
A serious limitation in applying these facile and highly general conjugate addition reactions of organoboranes lies in the requirement for the fully substituted organoborane, R_3B. It is difficult or impossible to obtain these derivatives when R is a bulky group. However, this limitation can now be circumvented by applying the B-alkyl-3,5-dimethylborinanes[96] (eq 113 and 114).



(113)



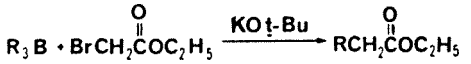
(114)



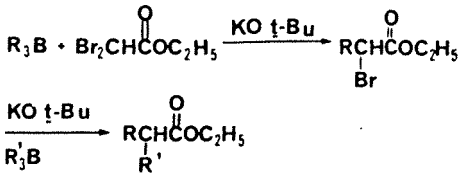
In addition to these free-radical conjugate additions, Prof. Brown and co-workers have investigated a number of other potentially useful synthetic reactions of trialkylboranes, which involve free-radical displacement reactions. These displacement reactions, including conjugate additions, have recently been reviewed.[97]

19. Alkylation and Arylation

α-Haloacetic acid esters can be readily alkylated by organoboranes under the influence of suitable bases[98-100] (eq 115 and 116).



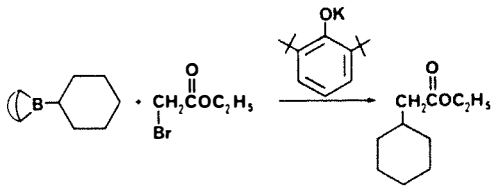
(115)



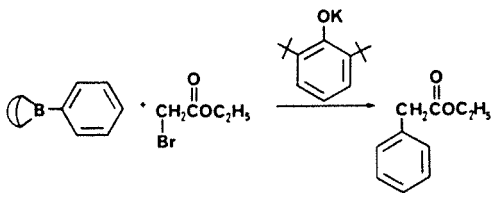
(116)

Since the products are usually unstable to the action of potassium *t*-butoxide, it is necessary to add this base last, carefully avoiding any excess. On the other hand, the products are usually stable to the potassium salt of 2,6-di-*t*-butylphenol. Consequently, this base can be used in excess and can be present initially in the reaction mixture.[101]

The use of B-alkyl-9-BBN or B-aryl-9-BBN provides for a more economical utilization of the organic group to be introduced[100,101] (eq 117 and 118).

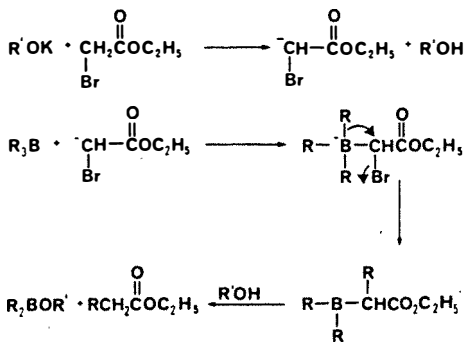


(117)



(118)

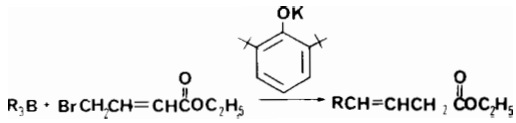
The reaction apparently involves the following mechanism[98] (eq 119).



(119)

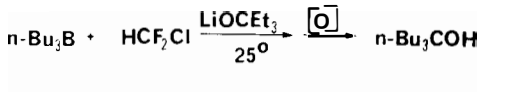
There is nothing about this mechanism which should restrict it to α-halo esters. Indeed, the following α-halogenated derivatives undergo this facile alkylation and arylation reaction:[98-105] ethyl bromoacetate, ethyl dibromoacetate, α-bromoacetone, α-bromoacetophenone, 2-bromocyclohexanone, chloroacetonitrile, dichloroacetonitrile, and ethyl 2-bromo-2-cyanoacetate.

Finally, it is also of interest that ethyl 4-bromocrotonate provides a new four-carbon-atom homologation[103] (eq 120).



$$R_3B + BrCH_2CH{=}CHCOC_2H_5 \xrightarrow{\text{OK}} RCH{=}CHCH_2COC_2H_5 \qquad (120)$$

In the above examples, the α-halocarbanion is formed by removing a proton from the activated α-position of an ester, ketone, or nitrile. It has recently been established that organoboranes can also react readily with chloroform, difluorochloromethane, and 1,1-dichlorodimethyl ether under the influence of a strong, highly hindered base, such as lithium triethylcarboxide[106] (eq 121).



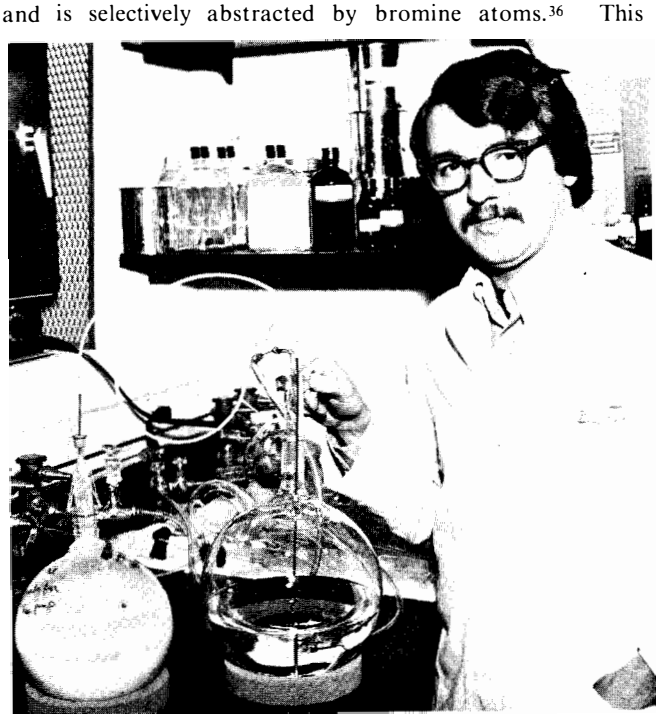
$$n\text{-}Bu_3B + HCF_2Cl \xrightarrow[25^\circ]{LiOCEt_3} [O] \rightarrow n\text{-}Bu_3COH \qquad (121)$$

Apparently a base of this kind can initiate the reaction by attacking the relatively inert hydrogen of the haloform without simultaneously combining with the organoborane present. The intermediate produced reacts with the organoborane to give an α-halo derivative which results in rapid migration of the alkyl groups from boron to carbon.

These alkylation and arylation reactions *via* reaction of organoboranes with α-halocarbanions have recently been reviewed.[107]

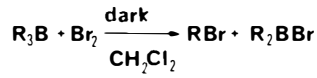
20. *Free Radical Bromination*

Still another route to such α-haloorganoboranes is the photochemical bromination of organoboranes. Apparently the hydrogen alpha to the boron atom is highly activated and is selectively abstracted by bromine atoms.[36] This



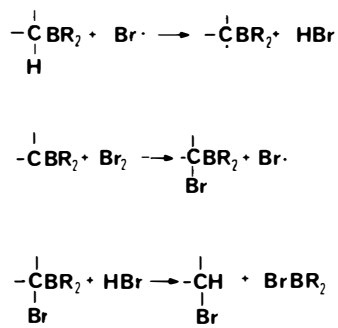
Dr. C.F. Lane

α-bromination reaction was discovered in the course of a study of the dark reaction of bromine with organoboranes.[36] The dark reaction is relatively sluggish and leads to the formation of dialkylboron bromide and alkyl bromide (eq 122).



$$R_3B + Br_2 \xrightarrow[CH_2Cl_2]{dark} RBr + R_2BBr \qquad (122)$$

However, the dark reaction does not involve a direct attack of bromine on the carbon-boron bond. Instead, bromine disappears at a faster rate than alkyl bromide appears. It was proposed that a free radical bromination of the α-position of the organoborane takes place selectively, followed by reaction of the α-bromoorganoborane with the hydrogen bromide produced in the bromination stage (eq 123).

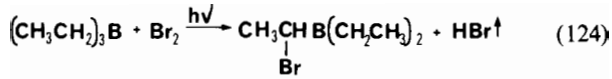


$$-\overset{|}{\underset{H}{C}}BR_2 + Br\cdot \rightarrow -\overset{|}{\underset{\cdot}{C}}BR_2 + HBr \qquad (123)$$

$$-\overset{|}{C}BR_2 + Br_2 \rightarrow -\overset{|}{\underset{Br}{C}}BR_2 + Br\cdot$$

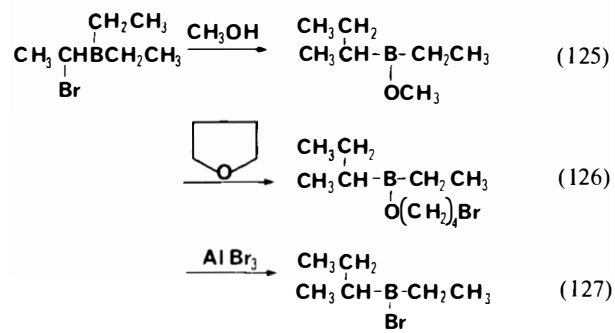
$$-\overset{|}{\underset{Br}{C}}BR_2 + HBr \rightarrow -\overset{|}{\underset{Br}{CH}} + BrBR_2$$

The α-bromination was found to be greatly accelerated under the influence of light.[108] Indeed, by carrying out the light-induced bromination in pentane under a slight vacuum to allow rapid removal of HBr, it is possible to synthesize α-bromoethyldiethylborane[109] (eq 124).



$$(CH_3CH_2)_3B + Br_2 \xrightarrow{h\nu} CH_3\underset{Br}{\overset{|}{C}}HB(CH_2CH_3)_2 + HBr\uparrow \qquad (124)$$

The α-bromoethyldiethylborane was found to be reasonably stable at room temperature in pentane and similar solvents, but rearranged with remarkable ease on the addition of nucleophilic reagents[109] or electrophilic reagents.[110] Typical examples are as follows (eq 125-127).



$$CH_3\underset{Br}{\overset{|}{C}}HB\overset{|}{C}H_2CH_3 \xrightarrow{CH_3OH} CH_3CH_2\text{-}\underset{OCH_3}{\overset{|}{B}}\text{-}CH_2CH_3 \qquad (125)$$

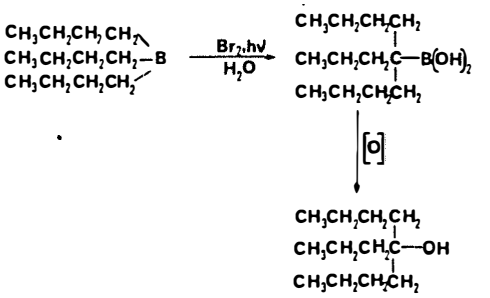
$$\xrightarrow{\text{O}} CH_3CH_2\text{-}\underset{O(CH_2)_4Br}{\overset{|}{B}}\text{-}CH_2CH_3 \qquad (126)$$

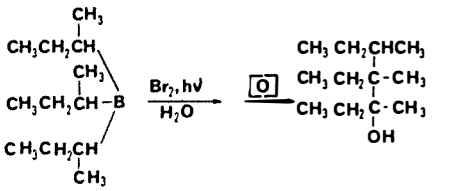
$$\xrightarrow{AlBr_3} CH_3CH_2\text{-}\underset{Br}{\overset{|}{B}}\text{-}CH_2CH_3 \qquad (127)$$

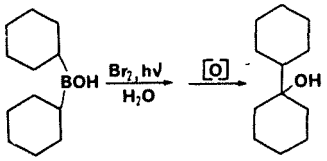
In addition to bromine, it was found that bromotrichloro-

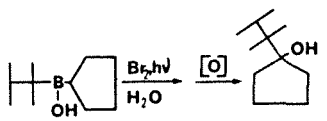
methane and N-bromosuccinimide could also be used for the α-bromination of organoboranes.[111]

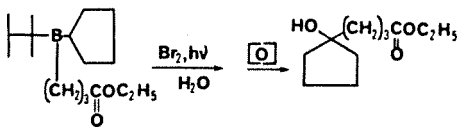
By performing the photobromination of the organoborane in the presence of a water phase to induce the rearrangement and absorb the HBr, one can achieve some remarkable syntheses[108, 112-114] (eq 128-132).


(128)


(129)


(130)


(131)


(132)

CONCLUSION

This review has only attempted to briefly summarize the major synthetic uses of organoboranes. For a more detailed discussion, the reader is directed to the recent books by Professor Brown.[8,115]

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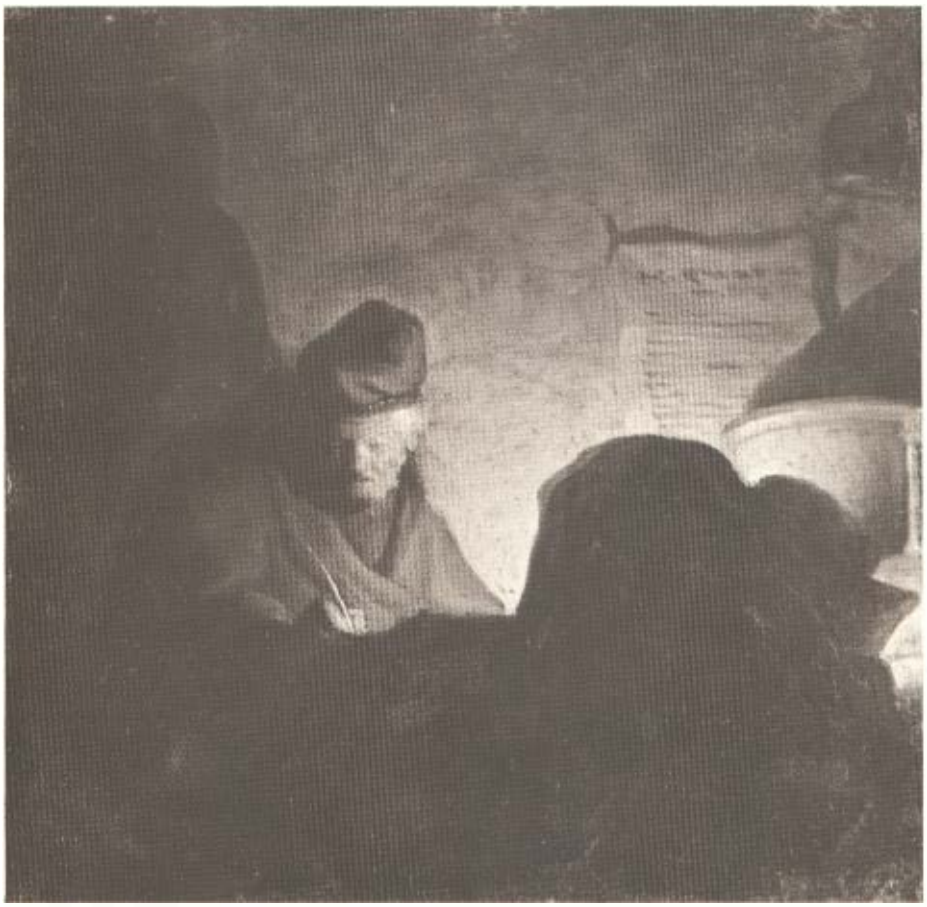

Wiswesser Line Notation

The Borane•amine Complexes

PUBLISHED BY THE ALDRICH CHEMICAL COMPANY, INC.

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ABOUT THE COVER

When we asked our chemist-collector to suggest one of his paintings which might relate both to the Wiswesser Line Notation and to Aldrich's work on hydroboration, we did not really expect an answer because these topics covered in this issue seem so unrelated. Thus, we were surprised when he quickly pointed to a small (oil on copper, 5 x 5 in.),early Rembrandt which he had purchased in Vienna years ago. What WLN and hydroboration have in common are their fundamental importance to chemists and the tremendous possibilities for development in each. In a similar manner, 'The Scholar by Candlelight', painted by Rembrandt in Leiden in his early twenties, clearly foreshadows some of his truly great works such as 'The Supper at Emmaus' in the Musée Jacquemart André in Paris, and 'The Flight to Egypt' (recently stolen from Tours), painted only a year or two later. Thus it is with WLN and hydroboration -- both are in their early stages of development, and both are bound to affect chemistry as fundamentally as Rembrandt affected art.

COLLECTORS' ITEMS

Many of the early issues of the Aldrichimica Acta have become very rare.

Please do not throw your issues away. In time, we believe that complete sets will become valuable, and - if you do not want to keep them - there probably are chemists and biochemists near you who would be interested.

CHEMICAL INFORMATION MANAGEMENT FOR THE 21ST CENTURY

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The 20th century is characterized by the profound change from flowery words and phrases to severely compressed identifications that more efficiently accomodate the information "explosion" of this era. Thus if people in ACS, EPA, FDA, ISI, NBS, NCI, NIH, NLM, and related organizations talked about ESR, GC, GLC, IR, LD50, MAC or TLV, NMR, and UV records, they would be dealing with the central problem in chemical information management--the "cosmic" addresses for the basic substances of these records. By the 21st century, such people also would have annually updated "chemical almanacs" about the size of the 1972 edition of *The Aldrich Handbook of Organic Chemicals* that would explain the meanings of these organizational and technical abbreviations, as well as very many other frequently used chemical terms such as "the Q1 equivalent" of antifreezes, "the Q2 concentration" of cocktails, "the QH content" of foods, "the QR coefficient" of germicides, and some 10,000 easily indexed structural identifications of the commonly met lab and shop environmental chemicals. Such "cosmic" identifications will be as commonplace to chemists as "Mr, Mrs, and Ms" now are to their secretaries. In the relentless competitions of "mass action" usage, these SHORTEST NECESSARY AND SUFFICIENT DESCRIPTIONS will survive like many work-horse Anglo-Saxon words have-- because they minimize the reading, writing and remembering effort for the users[1], and minimize the storage, retrieval and processing costs for the computers.

This seems an appropriate year to make these predictions, because our proposed solution to the chemical indexing problem was summarized in *C&EN* 20 years ago, and its key value for high-speed structure display was realized 10 years ago (demonstrated with a UNIVAC "dot-plot" program in February 1964). The first fundamental inspiration for our notation proposal was documented **thirty-five** years ago, in these 1938 notes on "Systematic Names," prepared for an invited discussion with Dr. A. M. Patterson at the National Meeting of the American Chemical Society at Baltimore in April 1939:

> "... The Geneva principle is to name the open-chain derivatives according to the **number of atoms** in the principal chain. It would seem desirable that closed-chain structures be named the same way--by the total number of atoms in the basic ring frame. Since the very same chain of atoms can, through ring closure, give rise to alicyclic and aromatic compounds, this geometrical connectedness can be profitably implied in the root name."

The tragic theme of history is that the young ignore its lessons and thereby are condemned to repeat its mistakes. After this encouraging 1939 meeting with Dr. Patterson, ten years passed before the revealing history on the origin and development of line-formula notations was gathered and reported at the 118th National Meeting of ACS at Chicago in 1950. This historic research was updated in 1961 for the hundredth anniversary of line-formula notations, and again in 1968 for a symposium on chemical notations[2]. Youthful ignorance of origins and developments in science and technology should not continue if humans are to enjoy the 21st century as a freedom-tolerating world community.

DEVELOPMENT OF LINE-FORMULA APPROACH

Computer identifications for chemicals in the 21st century will use the same short and simplified descriptions that the users will have learned in their first courses in general chemistry, because this directness and familiarity is overall "least effort." For example, the first chapters in their chemistries should explain how the science started in the 17th and 18th centuries through systematic examinations of naturally separated MINERALS (crystallized in deep layers from evaporated inland seas and lakes, or from colossal pools of lava) and METAL-BEARING ORES (studied with obvious enterprising motivations).

Mineral examples such as these--with short names that will survive for another century--were cited in Josiah P. Cooke's Harvard textbook of 1871, a full hundred years ago[3]; these selections indeed had name and synonym identifications in Martin Klaproth's "Chemischen Kenntniss der MINERALKORPER"[4] in 1807:

.AG	.AG3.SB	.BA..C-O3
.AU	.AG5.BI	.BA..S-O4
.BI	.AL2.O3	.CA..C-O3
.CU	.AS2.O3	.CA..S-O4
.FE	.AS4.S4	.CO..AS-S
.NI	.AS4.S6	.FE..AS-S
.PB	.AU2.BI	.FE..C-O3
.SN	.BI2.S3	..H3.B-O3
.TE	.CA..F2	.MG..C-O3
.AS4	.FE..S2	.MN..C-O3
.AG..G	.FE2.O3	.PB..C-O3
.AG2.S	.FE3.O4	.PB..S-O4
.CU..S	.MN..O2	.SB2.O.S2
.CU2.O	.MN3.O4	.SR..C-O3
.CU2.S	.SB2.O3	.SR..S-O4
.HG..S	.SB2.S3	.ZN..C-O3
.MN..S	.SI..O2	.AG..AS.S3
.NI..S	.SN..O2	.AG3.SB.S3
.PB..S	.TI..O2	.AG5.SB.S4
.ZN..S	.UR3.O8	.AL2.BE-O4

No chemist should need help in understanding these identifications, thanks mainly to the notational concerns of Jons Jacob Berzelius (1779-1848), "the organizer of chemistry." At a time when the tools of the chemist were the same primitive ones of the alchemist, he proved to be a master craftsman in chemistry: he analyzed over 2000 minerals and compounds, discovered more elements than any other individual (deter-

mining the atomic weights of 55 of them), made his own special glassware, introduced rubber tubing, the water bath, desiccator, wash bottle, filter paper, test tube, and separatory funnel. As a pioneering editor and abstractor, this "respected professor of chemistry of the Karolinska Medical Institute at Stockholm, Secretary of the Swedish Academy of Science, and uncrowned ruler of chemistry" insisted that "the chemical signs ought to be letters, for the greater facility of writing, and not to disfigure a printed book"[5]. He was indeed the "Rembrandt" of the chemical world, creating "a work of art--a thing of beauty that is a joy forever." Our chemical contribution is very modest by comparison. All we have done is standardize his symbol set and the "line-formula" citing method that first appeared in 1861 (13 years after his death), then combine these with a mathematically basic analysis of ring systems.

STANDARDIZATION OF ATOMIC SYMBOLS

The first and simplest step in this standardization is to implement his intent to distinguish at a glance the few commonplace NONMETALS from the many less frequently cited METALS. Cooke's Harvard text contained appended tables with **Ur** (like **Cr**) for uranium, **Va** (like **Ta**) for vanadium, and **Wo** (like **Mo**) for tungsten, 100 years ago. This grand oversight is matched by a much later one--in the 1921 M.I.T. Textbook by Norris[6] and in other Periodic Tables of the early 1920's) showing **Yt** (like **Yb**, both from the Swedish Ytterby sands) for yttrium. Since Berzelius started with **Po** and **So** for potassium and sodium, all that is needed to complete the standardization of two-letter symbols for ALL metals is to maintain the parallel with **Ka** for *kalium,* like **Na** for *natrium.*

CHLORINE NOTATION

Berzelius had proposed single-letter symbols for the commonly met but small number of NONMETALS--reserving the letters B, C, F, H, I, N, O, P and S (initially also *M* for the "muriatic" radical) for these most frequently cited elements. Now students occasionally slur the symbol of chlorine into a fusion that looks like G, and they might even misspell it as "GLORINE" with subconscious association of that 7th letter of the alphabet (which also appears in the word HALOGEN) for the element that "glorifies" the 7th Periodic Group. So the symbol **G** replaces the ambiguous symbol **Cl**.

BROMINE NOTATION

Bromine today is extracted in ton-a-day quantities from the sea, so when we suggested "extracting" from **Br** a letter in the alphabetically closed set covering E, F, G, H and I, a Syracuse University student many years ago very aptly showed how to extract the desired letter by proudly writing "SEA" on the blackboard and then rubbing out the two end letters! It also appears in the word haloGEn, right next to its companion letter **G**.

HYDROXYL NOTATION

Astronauts marvel at the beautiful blue color of our planet, caused by the bountiful abundance of that thermodynamically unusual vapor and liquid sea of AQUA. Surely the letter **Q** from this aqueous medium best describes its characteristic group--as an O-atom with a tiny H-tail.

AMINES AND THE IMINO NOTATION

Nitrogen parallels oxygen with a corresponding IMINO or IMIDE group, so this important NH-group is best denoted with the mid-letter M, pictured as a tilted N with a slender H-prop. When nitrogen appears as a doubly hydrogenated primary AMINO or AMINE (inorganic AMIDE or NH_2 anion) group, an end selection ends the inorganic A, B, C's of the symbolism with the letter Z--literally and figuratively an N on end (rotated 90°)!

COMPACT LISTING OF MINERALS

Now with a frequently useful Q for OH, M for NH, E for Br, G for Cl, and Z for NH_2, additional minerals identified by Klaproth in 1807 can be lucidly explained by the cation-anion formulations that first appeared with "ferrIC *vs* ferrOUS" types of names just about 100 years ago:

```
.AG..G              .CU2.C-03.Q2
.HG..G              .CU3.P-04.Q3
.NA..G              .PB2.C-03.G2
.Z&..G              .CA..S-04.QH2
.CU2.Q3             .CO..S-04.QH7
.MG..Q2             .CU..S-04.QH5
.MN..O.Q            .FE..S-04.QH7
.FE2.O.Q4           .MG..S-04.QH7
.FE4.03.Q6          .MG3.B7-013.G
.CU2.AS-04.Q        .PB5.P-04*3.G
```

In these examples of a computer-generated "compacted listing," Mitscherlich and Berzelius would have been delighted to see how the intercrystallizing or isomorphous (very closely related) minerals are automatically associated by simple alphabetization within each fixed-length set of records. Periods "fill" the separating blank spaces for simple cations and anions--with a reserved place for the first multiplier to guarantee simple scanning of the anionic descriptions. Compound anions are recognized at a glance by the bonding hyphen mark, and when necessary, these are multiplied with the Fortran mark and multiplier in a manner that does not mess up the sorting advantages. No artificial "connection-table" gyrations are needed to create these notations, because MINERALS AND INORGANIC SALTS are **aggregates of ions**; and here these descriptive units are cited one after another in an ordered manner, directly reporting the experimentally found compositions of these "aggregates."

CITING ORDER

Structural chemistry could not begin with this description of component parts like marbles in a bag, freely slipping and sliding around. Modern structural chemistry, as A. M. Butlerov first visualized in his 1861 paper on "The Chemical Structure of Compounds," is concerned with the connecting **arrangements of atoms** in molecules. For more than a century now chemists have speculated (sometimes wildly) on imaginary "stick-like" connections between atoms in molecules such as these:

```
NN    OCO    CNNC    NCSCN    NCOCCCN    OCCCCCO
OO    ONN    NCCN    OCCCO    NNNCCCN    SCCCCCO
OC    OSO    NCNC    SCCCO    OCNCCCN    SCCCCCS
ON    SCO    ONCN    SCCCS    SCNCCCN
SO    SCS    ONNO    SNSNS    SCNCCNC
```

These are linear chains of atoms connected to form molecules by a cementing cloud of electrons that has elongated spherical harmonic spatial patterns[7]. But why should the computer records be labored with these speculations? Moreover, the "chemical bondage" cannot explain why intermediate cases like OCCO, SCCO, SCCS or OCCCCO, SCCCCO, and SCCCCS do not exist! If the only experimentally confirmed details are the locations of the atomic groups (by beams scattering from those sharply defined centers), why force in more than we truly know? These end-to-end descriptions of unbranched molecules are the **simplest** necessary and sufficient descriptions, hence the preferred "cosmic" identifications and self-determined computer addresses. For the asymmetric cases, and for all "otherwise equal" citing alternatives in more complicated structures, a "highest first" resolving rule based on anciently familiar **alphabetic** order suffices. Indexing emphasis thus is automated as in arabic numeration, by first citing the highest-valued and most important mark on the left.

ALKYL CHAINS

Paraffin chains are so named because they have *par affinis*--least chemical affinity and therefore least indexing value; the FUNCTIONAL GROUPS attached to them determine the properties which determine the uses and values. So ALKYL CHAINS are denoted with ARABIC NUMERALS for the number of C-atoms in them, and the citing values ascend with 1,2,3,....A,B,C,... to X,Y,Z. The FUNCTION comes first, then the paraffinic or alkyl "tail."

UNSATURATION MARK

Unsaturations classically relate to dehydrogenations between **carbon** atoms, for E. Erlenmeyer was referring to **olefinic** double bonds and **acetylenic** bonds when he introduced the multiple bond marks in 1866. Thus when **carbon**-chain terminals are dehydrogenated, a single U-mark logically denotes the "single" unsaturation or dehydrogenation, and a UU-mark (logically and quantum-mechanically) denotes the "double" unsaturation or dehydrogenation (two **plus** the single bond line).

CARBONYL NOTATION

A **V**ery commonly met di**V**alent connecti**V**e that appears with the *paraffinis* groups (and causes frustrating nomenclatural gyrations in its great variety of combinations) is the ALDO- or KETO- or CARBONYL group. Within it is a classical C-to-O "unsaturation," so the etymologically related letter V (a Latin variant for "least effort" chiseling of U-marks in granitic monuments) is most appropriate for this -CO.- connective. When this V-mark is used (as VH) to signal ALDO- as well as KETO-groups (without H-mark), programmers should be cautioned that the aldo-V is two-connected like the keto-V only if the cited H is counted as a valid connection. When the H-details are ignored (traditionally giving "primary, secondary, ternary and quaternary" connecting differences among alkane carbons), the aldo-C is only 2-connected (to O and C) whereas the keto-C is 3-connected (to O, C and C).

DI-OXYGEN TERMINAL

DIOXO or DIOXYGEN branches with N- or S-atoms in nitro- and sulfonyl- and like groups classically have a **doubly unsaturated** hypothetical bonding pattern, so this logically and etymologically leads to a selection of the W-mark for **branched** dioxygen groups, because the medieval letter truly whispers this "double-U" meaning.

SIMPLE UNBRANCHED EXAMPLES

Now with single digits for the ever-present alkyl(ene) chains, single letters for five commonly met groups that first appeared as anions (E, G, M, Q, Z), and these last three (U, V, W) for unbranched aliphatic additions, chemists and computers have a powerfully efficient set of tools: **one** mark for each commonly met variable leads to an ultimate of simplicity and conciseness for thousands of linear combinations that show their connections with pictorial directness. Here is a "compacted listing" of items that were available 20 years ago.

WLN DESCRIPTIONS OF UNBRANCHED MOLECULES COMMERCIALLY AVAILABLE IN 1953

5H	G3	I8	Z3	2ØH	3V3	6M6	E1E	G1E	GV6
6H	G4	IG	Z4	28H	4M4	606	E2E	G1G	GV7
7H	G5	IH	Z5	2M2	402	6S6	E3E	G2E	GV8
8H	G6	Q1	26	202	404	6V1	E4E	G2G	I1Ø
E1	G7	Q2	Z7	2S1	4S1	7M7	E5E	G3E	I12
E2	G8	Q3	ZZ	2S2	4S2	7S7	EV1	G3G	I16
E3	I1	Q4	1ØH	2V1	4S4	7U1	EV2	G4G	I1I
E5	I2	Q5	12H	2V2	4U1	9V1	EV3	G5G	I3I
E6	I3	Q6	14H	32H	4V2	E1Ø	EV4	GV1	I5I
E7	I4	Q7	16H	3M3	4V4	E12	G1Ø	GV2	NC1
E8	I5	Q8	1M1	303	5M5	E14	G12	GV3	NC2
EH	I6	Z1	1S1	3S3	505	E16	G16	GV4	NC3
G2	I7	Z2	1V1	3V1	5V1	E18	G18	GV5	etc.

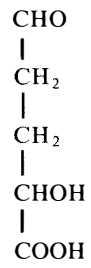
This "simplistic" listing, ordered by the lengths or "Hollerith numbers" of the records, automatically displays the simplest (2- and 3-mark) structure descriptions first, and provides easy visual scanning of both ends of the descriptions. No other kind of display can compress so much chemical information into such a small amount of line-printing space, so this method should enjoy a long-enduring profitable usage in the 21st century. Perhaps these simplest commercially available chemical descriptions are uninteresting, but for the same reason they should be very inexpensive: processed in huge quantities for the benefits of all chemists at **trifling** costs per entry!

BRANCHED CHAINS

Branching points are topologically unique features (nodes), so these deserve distinct single-letter marks for the most important or most frequently cited cases: Y-marks for the ternary or Y-branched CH-groups (with U if unsaturated), X-marks for the quaternary or X-branched C-atoms, and K-marks for the analogous quaternary N-atoms. These complete the eleven new aliphatic letters, with the five and three noted above.

Branched line-formula descriptions incorporate a subtle and tacitly understood **rightward**-unfolding polarization that has been followed ever since shrewd Josef Loschmidt published the first line-formula examples in his 1861 booklet on

Chemische Studien. Thus inorganic examples like FBFF and GPGG never are garbled into FFBF or GGGP citing sequences. This rightward polarization came naturally as a mechanical scanning of the earliest diagrams, in which the carbon skeleton extended vertically, like the human skeleton. Substituted groups were cited **after** the chain atom (like its associated H-atoms). The inset diagram (figure 1 in our 1952 *C&EN* report[8]) shows the "Origin of the Line-Formula delineation (*circa* 1861) as a television-like scanning of the vertical chain diagram, top to bottom and left to right, giving this delineation: CHO.CH_2.CH_2.CHOH.COOH (with a period marking the **end** of each scanned line)."

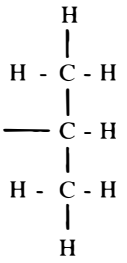


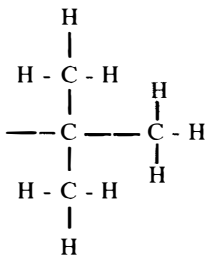
Selection of the letter Y for a Y-branched or 3-connected CH-group, as noted above, leads to YU or UY for the corresponding keto-like dehydrogenated acyclic C-branch, and to the letter X for the corresponding acyclic quaternary or 4-connected C-atom. Then all simple secondary alcohols are automatically indexed under the QY... marks, and simple tertiary alcohols under the QX...marks, with similar automated benefits for the corresponding halides and all other terminal functional groups. The letter X in turn suggests selection of its graphically related letter K for the corresponding quaternary N-atom.

METHYL CONTRACTION

Now Y, X and K are new and distinct branching symbols, so they can be defined as **methyl-branched unless otherwise specified**. This expressive conciseness for the ubiquitous "unit" alkyl group reflects the century-old custom of omitting the cluttering "unit" marks in chemical formulas: not H_2O_1 and $H_1N_1O_3$ and $H_1C_1N_1$ or the like, but simply H_2O and HNO_3 and HCN.

A terminating ...Y expresses the nine connections among the three C-atoms and seven H-atoms in the **isopropyl group** with maximum economy (see inset). The terminating ...X likewise is a "least effort" ultimate for the four C-atoms, nine H-atoms, and their twelve connections in the tertiary butyl group (2nd inset). This is the meaningful kind of symbol economy that is mandatory if the six million presently reported structures in the chemical world are to be widely available and **searchable** at low cost by the 21st century.





Contractions, like linguistic abbreviations, should not disturb the indexing first parts of any descriptions, so the corresponding methyl-branched groups are written as 1Y..., 1X..., and 1K... (for quaternary trimethylammonium) when they initiate a notation. No branch-ending punctuation is needed when these are the only branches in the description, and no additional explanations should be needed for the following simple isoalkyl and neoalkyl examples found in *The Aldrich Handbook of Organic Chemicals*:

```
2X  4Y  GX  QY   E1Y  NCX  Q2Y  SHY  Z3Y
2Y  5Y  GY  ZX   E2Y  NCY  Q3Y  VHY  ZVY
3X  6Y  IX  ZY   G2X  Q1X  QVX  WNY  (and others
3Y  EX  IY  2VY  GVX  Q1Y  QVY  Z1Y   among the
4X  EY  QX  3VX  GVY  Q2X  SHX  Z2Y   10,000 rarer
                                      chemicals)
```

These "curt, clear and complete" descriptions have enjoyed more stability during the past 20 years than the corresponding names, and the contrast in long-enduring usefulness seems likely to intensify much sooner than the 21st century!

BENZENE

BENZENE is a **R**esonating, **R**egular-hexagonal, a**R**omatic **R**ing, so the R-mark for this unit provides the greatest symbol economy of all, because in large collections this ring occurs **more frequently than all other rings combined**. It is subordinated to all other atomic group symbols because of this superprominence and its consequent negligible indexing value (nearly **two million** of the six million reported structures contain benzene rings without any other rings). A terminal ...R denotes the three double bonds, eleven single bonds, six C-atoms and five H-atoms in the **phenyl group** (often written with least effort as the Greek *phi* or ϕmark). Here are a few examples:

```
2R  8R  QR  1SR  2VR  5VR  G1R  Q1R  R1R  RVR  Z2R
3R  ER  RR  1VR  2XR  E1R  G2R  Q2R  R2R  SHR  Z3R
4R  FR  ZR  1XR  2YR  E2R  GVR  QVR  RMR  VHR  ZMR
5R  GR  1MR 1YR  3VR  E3R  NCR  QXR  ROR  WNR  ZVR
6R  IR  10R 2MR  4OR  EVR  ONR  QYR  RSR  Z1R  ZYR
```

REVIEW OF SYMBOLS

Chemists in the 21st century will be able to read these descriptions as easily as our children today read words like ace, ape, ark, art, asp, bad, bag, bar, bat, bay, bib, cab, car, cat, cog, cow, and so on. By that time the international professional competition will have convinced chemistry teachers and practicing chemists that they have an information-managing bargain with hundreds of such descriptions per printed page--at pennies per page (or less with reading equipment for microfilm cartridges or microfiche packets). Here is the learning requirement for the examples given thus far:

Letter:	E	G	K	M	Q	R
Meaning:	Br	Cl	$+N$	NH	OH	
Letter:	U	V	W	X	Y	Z
Meaning:	=		O_2			NH_2

ARABIC NUMERALS denote ALKYL CHAIN lengths (carbon count). K, X and Y are methyl-branched unless otherwise specified. ZERO is slashed as ϕ, leaving the far more frequently cited O unmarked.

BRANCHING TERMINATION

The **ampersand** here is the "**e**nd mark" for punctuating alkyl side groups and any others that do not end with the strictly terminal E, F, G, H, I, Q, W or Z groups. When some of these in turn--like iodine--are not terminal, they are set off

with **hyphens**, like all organometallic two-letter symbols. The ampersand is retained whenever a methyl-contracted Y, X or K group is **not** the last branch in the notation (or in a clearly "spaced" cyclic side group), simply to keep things clear when descriptions get complicated. The Aldrich *Handbook* again has many simple examples of notations with punctuated side groups, and others with the "understood" punctuation for E, F, G, H, I, Q, W and Z marks:

1Y&X	1N1&1	4N4&4	OSR&R	QY4&2
1Y&Y	1N1&R	4P4&4	Q1YGG	QY4&3
2Y&Y	1X&&X	8N8&8	QVYER	QY4&4
EYEE	1Y&1Y	EXEEE	QVYFF	QY4&R
EYER	1Y&2X	EYR&R	QVYGG	QY5&4
GPGR	1Y&2Y	FXFFR	QX&&Y	QY5&Y
GXGG	1Y&3Y	GPR&R	QX2&2	QY6&3
GYGE	1Y&MY	GX&&X	QX3&2	QY7&2
GYGG	1Y&SY	GXGGE	QX3&3	QYR&R
GYGR	1Y&UY	GXGGG	QX4&2	RNR&R
IYII	1Y&VY	GY&YG	QY&1Y	RPR&R
QBQR	2N2&1	GYG1G	QY&Y2	SPGGR
QY&X	2N2&2	GYGO1	QY&YQ	SUYGG
QY&Y	2N2&R	GYGVG	QY2&2	WS3&3
WSG1	2Y&1Y	GYGVR	QY2&R	WS4&4
WSGR	2Y&UY	GYR&R	QY2&X	WSR&R
WSQ1	2Y&Y2	OPGGR	QY2&Y	Z1YQR
WSQR	2Y2&2	OS1&1	QY3&2	ZMSWR
ZSWR	3N3&3	OS3&3	QY3&3	ZN1&1
ZY&X	3N3&R	OS4&4	QY3&R	etc.!

Of course there is no very simple way to describe very complicated structures, but there are far more 2- to 5-mark notations in the chemical world than equally short words in the English language. Yet while "apathy is our deadliest danger," chemists may have to wait until the 21st century before the **simplest** million reported chemical descriptions are widely and cheaply available for their "professional enhancement." There are over 1000 notations with **five or less** places in a file of 30,000 biologically screened compounds, so this same first fraction is more than a hundred thousand in the six million world total! Most of the high-volume, high interest, high-hazard chemicals are in this simplest fraction: must we wait another 25 years to structurally identify and reference the first few thousand in a $2 chemical almanac?

RING LOCANTS

LOwer **CA**se let**TE**rs were used to LOCATE ring positions in 1866 when Kekule[9] presented his historic discussion of benzene ring isomerism. These letters are more logical than numbers for such information, because positions are relative rather than absolute values, and in modern chemistry these citations frequently go past the single digit range, but seldom go past the alphabetic range. Lower-case meaning is indicated in computer applications without a penny of special hardware cost by prefixing such (upper case) letters with a blank **space**. This nonprinting signal serves as a shift key to denote lower-case meaning for the letter that follows; like the familiar space bar, this is the most frequently used keyboard signal. Spaces also serve handsomely to break up the units of information, just as words are clarified by putting spaces between them (a great discovery of the Middle Ages). Thus the notation logically shows a locant **between** the ring description and the substituent symbols, saying in effect, "and at this position there is a so-and-so group."

Phenylene (C_6H_4) segments of chains are distinguished by assuming the a-position for the first-cited substituent, thus giving ...R B... for *ortho-*, ...R C... for *meta-*, and ...R D... for the *para-* isomers. Kekule's student, William Körner, established these cleverly distinctive names just 99 years ago (1874), and the corresponding "computerized" O@-, M@- and P@- prefix marks deserve continuing usage with two-connected phenylene root names.

Locant marks, like atomic Y, X and K branches, can be defined as methyl-"filled" when not otherwise specified. Aldrich *Handbook* selections again show frequent usage of this contraction along with other locant-specifying short notations:

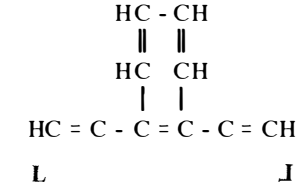
1R C	1OR B	FR DF	Q1R D	QR DG
1R D	1R CR	FR DR	QR B2	QR DI
2R B	1R DR	G1R B	QR B3	QR DQ
2R C	1VR C	G1R D	QR BE	QR DR
2R D	1VR D	GR BE	QR BF	QR DX
ER B	1XR D	GR BG	QR BQ	QVR B
ER D	1YR D	GR CE	QR BR	QVR C
FR B	2MR B	GR CG	QR BX	QVR D
FR D	2MR C	GR DE	QR BY	QYR D
GR B	2R B2	GR DF	QR C3	RR BR
GR C	2R C2	GR DG	QR CE	RR DR
GR D	2R D2	GR DR	QR CF	SHR B
IR B	E1R B	GVR B	QR CG	SHR C
IR C	E1R C	GVR C	QR CQ	SHR D
QR B	E1R D	GVR D	QR CX	VHR B
QR C	ER BE	IR DG	QR CY	VHR C
QR D	ER DE	NCR B	QR D2	VHR D
ZR C	FR BE	NCR C	QR D3	WNR B
ZR D	FR CF	NCR D	QR DE	WNR C
	FR DE	ONR B	QR DF	etc.

An important complementing pair of resolving rules should be emphasized here: **outside** the ring, the **highest** of otherwise equal marks are cited first (to put front emphasis on functions); **inside** the ring, the **lowest** sets of locants, etc., are chosen (to follow this well-justified tradition).

OTHER RINGS

The simplest features of aliphatic and benzenoid notations now have been illustrated with several hundred Aldrich *Handbook* selections, none of which required more than five typing columns. Distinctly longer notations will be needed to illustrate the simplest types of other cyclic compounds, because the rings themselves have many independent variables: carbocyclic or heterocyclic, aromatic or having a lone saturated C-atom, and saturated or having localized unsaturations. Each feature will be explained very briefly--with examples.

Beyond benzene, the **cyclic** part of a structure is traditionally and topologically the main feature and most useful indexing part, so the notations in this largest class all begin with a "ring-closing or ring-starting" mark, followed by the traditional ring number(s), heterogroup symbols, then the saturation character and finally the "ring-finishing" mark. The carbocyclic or "aLicyclic ring-closing L...J marks were inspired by Emil Erlenmeyer's historic (but contorted) 1866 diagram[10] for his postulated structure of naphthalene. In the inset diagram, his vertically extended ring has been swung up from his original lower position to more clearly display



his subtle "L- and J-shaped" angle-brackets that Erlenmeyer used to imply the ring closure. Beilstein's separation of a "he**T**erocyclic" kingdom justified the corresponding T...J marks, first used with the L...J in a 1951 demonstration deck of IBM cards. These punched-card substitutes for parentheses are still the users' choices, even though non-distinguishing parentheses (as in the 1954 manual) are more logical to set off this first part of the cyclic **connecting** specifications.

RING SATURATION

After the ring numbers and heterogroup symbols are cited, four distinct types of rings are denoted as combinations of two binary variables: minimum-maximum **hydrogenation**, and minimum-maximum notation marks. The minimum **marks** logically apply to the most frequently met extremes in hydrogenation: the aromatic, understood with no mark; and the fully saturated, distinguished with a "sa**T**uration" mark. In the 1954 manual, this mark was a "slash" or virgule ("capitalized letter symbols to denote atoms or atomic groups" and "punctuation marks to denote modes of connection or disconnection" or the like), but today it is a T-mark just before the ring-closing J-mark. This double usage of the T for a kind of "punctuation" was necessary with the primitive 1950 equipment, but the make-shift obviously would not be necessary today.

Aromatic monocyclic descriptions (with no lone saturated C-atoms) perhaps are most easily explained by citing many examples from the Aldrich *Handbook* (the parent ring is the catalog item in most cases, but some appear only as substituted derivatives).

```
L8J     T6NJ    T5NSJ    T5VMVJ    T5MNNNJ    T6MVMVMVJ
L7VJ    L4VVJ   T6MVJ    T5OVOJ    T6MVMVJ    T6MVMVVVJ
T5MJ    L6VVJ   T6NNJ    T5VOVJ    T6VMMVJ    L6VVVVVVJ
T5OJ    T5MNJ   T6OVJ    T5MVNJ    T5MMVMVJ   T6BHMBHMBHMJ
T5SJ    T5NOJ   T5NONJ   L6VVVVJ   T6NMVMVJ   T6BHOBHOBHOJ
```

Here adjacent heterogroups appear exactly as they would in an open-chain segment, but with the traditional "lowest first" choice inside the ring. If aromatic C-atoms separate the heterogroups, **spaced** letters locate them:

```
L6V DVJ    T6N CNJ     T5NN DSJ
T5M CNJ    T6N DNJ     T6NN DNJ
T5N CSJ    T6O DVJ     T6VM DNJ
T6M DVJ    T5MN DNJ    T6N CN ENJ
```

Connecting **positions** are considered before the symbols at those positions, so T6VM DNJ by this rule is correct and "lower on first counts" than T6MV ENJ.

"Extra hydrogen" citations (always with a locant, to avoid ambiguity with heterocyclic H-attachment) characterize those structures that are dehydrogenated to the aromatic limit and have just **one** remaining saturated C-atom:

```
L5 AHJ          T5NMV DHJ
L7 AHJ          T5NOV EHJ
L4V BHJ         T5MVMV EHJ
L6V BHJ         T5SVMV EHJ
T6M DHJ         T6MV DV CHJ
T3MM CHJ        T6MVMVV FHJ
T5OV CHJ        T6OV DV CHJ
T5OV EHJ        T6VMVMV FHJ
```

Fully saturated structures provide the greatest number of **mono**cyclic examples (parent ring systems) in the Aldrich *Handbook*. All end with ...TJ marks; all have **more than one** saturated C-atom, and none have any C-to-C unsaturations:

```
L3TJ    T5STJ    T9MVTJ    T6M CVTJ
L4TJ    T6MTJ    T5MVMTJ   T6M DMTJ
L5TJ    T6OTJ    T5MVOTJ   T6M DOTJ
L6TJ    T6STJ    T5OMVTJ   T6M DVTJ
L7TJ    T7MTJ    T5OSOTJ   T6O COTJ
L8TJ    T7OTJ    T5OSWTJ   T6O DOTJ
L4VTJ   T8MTJ    T5VMVTJ   T6O DSTJ
L5VTJ   T9MTJ    T5VOVTJ   T6S CSTJ
L6VTJ   L6VVTJ   T6MVMTJ   T6S DSTJ
L7VTJ   L7VVTJ   T6OSWTJ   T6S DVTJ
L8VTJ   T4OVTJ   T6VMVTJ   T7M DMTJ
L9VTJ   T5MVTJ   T6VOVTJ   T6M DSWTJ
T3MTJ   T5OVTJ   T5OPHOTJ  T6MV DOTJ
T3OTJ   T5SVTJ   T6OBHOTJ  T6MV DSTJ
T3STJ   T5SWTJ   L5V CVTJ   T6OV DOTJ
T4MTJ   T6MVTJ   L6V CVTJ   T6MV DMVTJ
T4OTJ   T6OVTJ   L6V DVTJ   T6VOV EOTJ
T5MTJ   T7MVTJ   T5M CSTJ   T6M CM EMTJ
T5OTJ   T8MVTJ   T5O COTJ   T6O CO EOTJ
                             T6S CS ESTJ
                             T8OSWO EOSWOTJ
```

The dioxygen symbol W, like H, is defined as a strictly terminal symbol and is cited **immediately after** the symbol of the atom to which it is attached, inside as well as outside the "ring-enclosing" marks.

UNSATURATED RINGS

Localized unsaturations characterize the fourth class of ring notations--those with maximum hydrogenation and maximum citing marks; the cited U-mark appears without a locant only in the special case of simple cycloalkenes, cycloalkynes, and their combinations that have no heterogroup:

```
L5UTJ      L7U CUTJ     T6O BUTJ
L6UTJ      L8U CUTJ     T7N AUTJ
L7UTJ      L8U EUTJ     T5SW CUTJ
L8UTJ      T5M BUTJ     T6NMV FUTJ
L5V BUTJ   T5M CUTJ     T5N CO AUTJ
L6U CUTJ   T5O BUTJ     T5N CS AUTJ
L6U DUTJ   T5O CUTJ     T6M CN BUTJ
L6V BUTJ   T6M CUTJ     T6O DO BUTJ
```

Benzyne is an exceptional structural type, justifying a **single** U **without** a T when this dehydrogenation is superimposed on an aromatic one: L6UJ. In all cases, localized unsaturations (like "extra" or indicated hydrogen) are cited as subordinated details that do not change the other "lowest locant," etc., measures within the ring-enclosing marks. This is equally true of any substituents; beyond the special case of benzene rings, **substituents** are cited in ascending order of locants, then "highest first" when locants are equal.

Thio- or imino- or methylene-type substituents on cyclic keto-groups provide a fifth type of ring, with a **cyclic** Y-mark here replacing the V-mark, and the necessary U-mark appearing outside the ring description:

```
L5YTJ AU1       L6V DYJ DUM       T6MVMVYVJ EUM
L5YTJ AUM       T5MYMTJ BUS       L6YYTJ AUM BUM
L6YTJ AU1       T5NMYSJ CUM       T5MYMV EHJ BUS
L6YTJ AUM       T5NYVOJ BU1       T5OYMV EHJ BUS
L7YTJ AUM       T5SYSTJ BUS       T5SYMV EHJ BUM
T6MYJ BUS       T6MYMVJ BUS       T5SYMV EHJ BUS
T6MYTJ BUM      T5MVMVYJ EUM      T5VOVY EHJ DU1
T6MYTJ BUS      T4VOY DHJ CU1     L6Y DYJ AU1 DU1
T7MYTJ BUS      T5MY DMTJ BUS     L6YVYTJ AUM CUM
```

Some of these are keto-like tautomers of enolic or mercapto-groups.

MACRO RINGS

Macro-rings stand out in this notation because two-digit ring sizes are set off with hyphens (avoiding ambiguity with sizes 33 and higher *vs* bicyclics). Again the Aldrich *Handbook* contains a good number of examples:

L-1Ø-TJ	L-13-VTJ
L-11-TJ	L-15-VTJ
L-12-TJ	T-13-MVTJ
L-1Ø-VTJ	L-11-UTJ
L-11-VTJ	L-12-UTJ
L-12-VTJ	L-12-U EUTJ
	L-12-U EU IUTJ

Substituents, as previously mentioned, are cited in ascending alphabetic order for all rings beyond the special case of benzene rings.

POLYCYCLIC RINGS

Chemical notation and nomenclature systems eventually "meet their Waterloo" in the polycyclic region, where seemingly endless complications keep compounding to a climax of frustrations. The strength of the WLN in this area was sensed in 1952:[8] "The most outstanding feature of this notation is that a single position-determining rule suffices for all kinds of polycyclic structures." This central advantage is based on a traditionally familiar aim--to seek a lowest possible set of ring measures, one that subordinates heterogroup variations. Each measure has a sharply defined priority, as stated by E. G. Smith in the official manual[11] of the Chemical Notation Association.

DETERMINING LOCANT PATH

The first requirement is that the locant path must be a continuous one through the largest possible number of ring positions (generally it is a peripheral loop or spiral through all of them). This aim maximizes the number of automatically defined connections--i to j to k...--and thus minimizes the necessary specifications of all other (nonconsecutive) links. For example, the elaborate tetracyclic steroid connecting pattern of 17 positions and 20 connections is compacted into a record of just four pairs of locants, each indicating a ring-closing link: (ei bj am aq). Chemists prefer to see the ring sizes directly, so this becomes (e5 b6 a6 a6) or simply (e5 b666) after omitting the understood **a**-locants.

The pathfinding rule was stated as follows in 1952: "All polycyclic ring positions are determined by starting the longest possible chain of ring positions at the point which gives the lowest sum for the **fusion** locants," "the name given here for the lowest position in each ring, relative to (this path)." In the above example, **e, b, a, a** are the fusion points, and their sum is 5 + 2 + 1 + 1 or 9.

All bicyclic fused and bridged ring paths thus start at one of the atoms common to both rings, for then the fusion locants are **a,a** (the same lowest position in each ring). In perifused systems where one "triple point" is common to three rings, this singular multicyclic junction or focal point is the starting point, and from here the locant chain proceeds through the shortest possible path to the furthermost ring. Some well-known examples that were included in the 1951 demonstration deck of IBM cards had these name identifications:

L57J	azulene	T56 BMJ D	skatole
L66J	naphthalene	T56 BMVVJ	isatin
T56 BMJ	indole	L B666J	phenanthrene
T66 BNJ	quinoline	L C666J	anthracene
T66 CNJ	isoquinoline	L B656 HVJ	fluorenone
T56 BNOJ	anthranil	L C666J BQ	anthranol
T66 BMVJ	carbostyril	L E6 B666J	chrysene
T66 BOVJ	coumarin		

Many additional examples are provided in "Educator" decks of IBM cards.

Free radicals are freely and easily described with the 1964 "dot-plot" extension of the carbyl C (for an unbranched C-atom); D for the diatomic, dehydrogenated, unbranched CH-group (pictured as a C-image and H-bar); L for the aLiphatic CH_2 Link; and T for the 3-connected or T-branched C-atom. With these the writer also urged the use of J for a Junction N-atom, the very frequently cited 3-connected nitrogen of tertiary amines, N-nitrosamines, and the like (rather than wasting this valuable atomic-symbol letter on a rarely cited "Jeneric haloJen"). But nine years have passed, and the other users still strangely oppose any change in "the sacred symbol set."

THE CHEMICAL NOTATION ASSOCIATION

The most bizarre aspect about this notation is that its designer no longer "owns and controls" it: that sensitive responsibility has been put in the hands of the Chemical Notation Association, an international association of more than 100 members. At the time of this writing, a "NATO/CNA Advanced Study Institute (ASI) on Computer Representation and Manipulation of Chemical Information" is planned to be held in Noordwijkerhout, near Amsterdam, from June 4 to 15, 1973, cosponsored by the North Atlantic Treaty Organization and the Chemical Notation Association.

Elbert G. Smith, more than any other individual, extended the spirit that this notation "was designed to be shared" with the chemical world. He started encoding the organic tables in the Hodgman and Lange Handbooks with the rudimentary instructions in the 1952 reports, helped edit the 1954 manual, wrote a faculty report demonstrating the notation's value in a table of phenylhydrazones (identification derivatives), built an experimental file of over 80,000 WLN descriptions--with other identification and reference data, wrote an attention-commanding report on substructure searching (with his set of 48 bit screens) when this file was 50,000-items strong, established the rule-controlling Chemical Notation Association, helped by his personal visits to establish the United Kingdom and Japanese chapters of CNA, and encoded the 15,000 *Ring Index* structures as part of his most time-consuming undertaking--to write a comprehensive WLN manual[11]. The royalties from this 6-year effort he turned over to the Chemical Notation Association. Smith's "Tutorial Lessons" provide 21 pages of the best kind of introduction to the WLN--learning by doing the stepwise decoding and encoding exercises[12].

Graham Palmer provided an excellent introduction to the WLN in 1970[13], which Usdin and Efron noted in 1972 with their own lucid summary[14]. Gibson and Granito also published a well-composed tutorial introduction to "Wiswesser chemical line-notation" in 1972[15]. Computer applications of

the WLN were summarized in 1969[16] and 1970[17], but so many advances have occurred since then that these reports now are regarded as obsolete.

UTILIZATION OF WLN BY ORGANIZATIONS

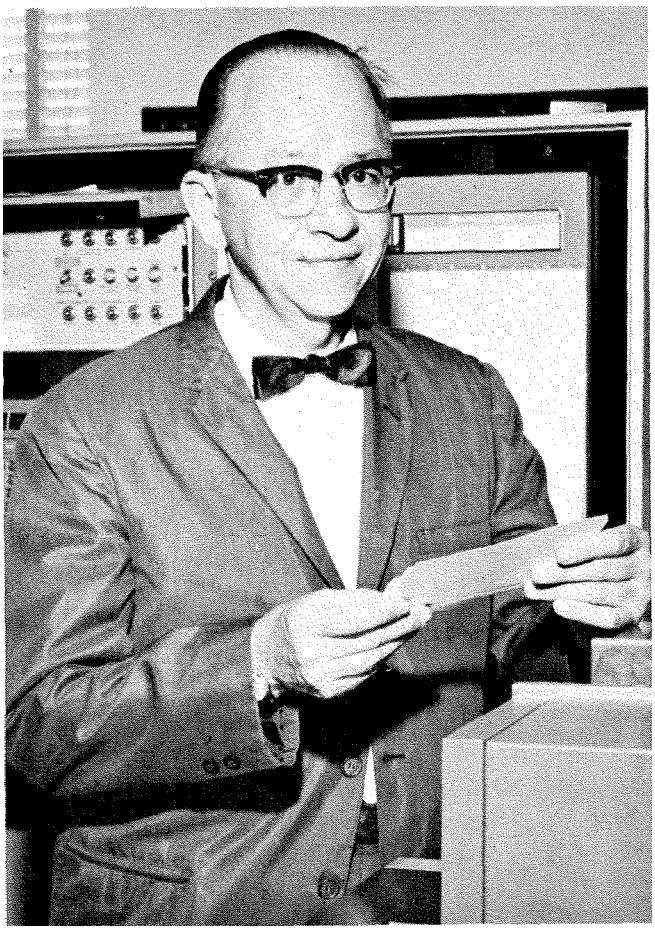
In the final analysis, the best "proof by test" of this information-managing tool is the extent to which others have published on their encouraging **uses** of it. The letter-symbol set was "finalized" at mid-century, in 1950. Only twelve reference citations on the notation appeared in the first ten years (1950-1959), then ten in the next five years (to 1964), followed by twelve in two years (1965-66), seven in 1967, and now there are some 150 citations from the organizations listed in Table I.

TABLE I.

ORGANIZATIONS THAT HAVE PUBLISHED OR PRESENTED PAPERS ON WLN

(An author index, keyed to these organizations and including the titles with journal or meeting citations, is given in a special report of the Committee on Chemical Information Management, Lehigh Valley Section of ACS.[18])

Aldrich Chemical Company
Althouse Chemical Division (C&K Corp.)
American Society for Testing & Materials
J. T. Baker Chemical Company
Biological Abstracts (BIOSIS)
Chemical Abstracts Service
Chemical Rubber Company
Ciba-Geigy Corporation
College of Charleston
Columbia University (Biological Sciences)
Diamond Shamrock Chemical Company
Dow Chemical Company
Drexel University
Excerpta Medica Foundation
Food and Drug Administration
GAF Corporation
Goodyear Tire & Rubber Company
Hebrew University (Israel)
Hoffmann-La Roche, Inc.
Horner Associates
Imperial Chemical Industries
Indian Institute of Science (India)
Institute for Scientific Information
Lehigh Valley Section of the ACS
Eli Lilly and Company
McCormick & Company, Inc.
Meta Information Applications, Inc.
Mills College (E.G. Smith)
Ministry of Defense of Israel
Monsanto Company
Moravian College (Bethlehem, Pa.)
National Bureau of Standards
National Cancer Institute
National Council of R & D (Israel)
National Institute of Mental Health
National Institute for Occupational Safety & Health
National Institutes of Health, DCRT
National Library of Medicine
Oesterr. Kunststoffinst. (Austria)
Ohio State University
Olin Corporation
Reading Chemists' Club (Reading, Pa.)
Remington-Rand Corporation (Norwalk, Ct.)
Sankyo Company (Tokyo, Japan)
G. D. Searle & Company, Inc.
Shippensburg (Pa.) State College
Simpson College (Indianola, Iowa)
Stanford Research Institute
State University of N. Y., Stony Brook
Tanabe Seiyaku Co. (Saitama, Japan)
Texas A&M University, TRC-API
United Kingdom Atomic Energy Authority
University of Sheffield (UK)
University of Pennsylvania
U.S. Army, CIDS Program (Edgewood Arsenal)
U.S. Army, Fort Detrick, VCD
U.S. Army, Industry Liaison Office (E.A.)
Wildlife Research Center, USDI (Denver)
Willson Products (Division of ESB Corp.)
Winthrop Laboratories (A. Addelston)



William J. Wiswesser

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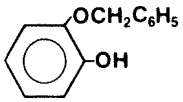
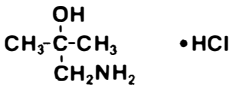
Medicinal Building Blocks

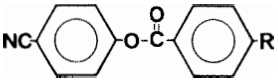


18,304-0 *o*-Benzyloxyphenol 10g $9.00 50g $28.00



This useful synthetic intermediate is derived from acetone cyanohydrin. We invite your inquiries for reduction products of other cyanohydrins.

Room Temperature Nematic Liquid Crystals



R=heptyl, butyl

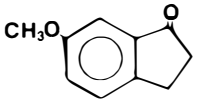
A 2:1 molar proportion of *p*-cyanophenyl *p*-heptylbenzoate and *p*-cyanophenyl *p*-butylbenzoate provides a room temperature nematic liquid crystal mixture exhibiting a low threshold voltage and strong positive dielectric anisotropy. These properties make these chemicals suitable for use in display cells in various electronic applications.

A. Boller *et al., Proc. IEEE,* **60**, 1002 (1972).

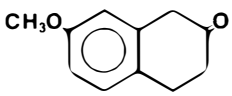
One of the Most Basic Dibasic Amines

K. Gerzon *et al., J. Med. Pharm. Chem.,* **1**, 223 (1959).

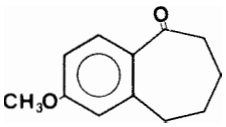
Methoxy-substituted Benzoalicyclic Ketones



17,525-0

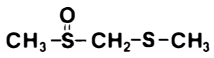


16,418-6



17,524-2

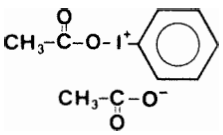
MMTS - A Versatile Reagent



Aldehydes[1] are obtained *via* the reaction of an alkyl halide with the carbanion obtained from MMTS and NaH, while the carbanion derived from MMTS and *n*-BuLi reacts with ketones to give α-hydroxyaldehyde dimethyl mercaptal *S*-oxide derivatives[2] which yield various types of α-hydroxyaldehydes. Phenylacetic acid esters[3] are obtained *via* the reaction of MMTS with aromatic aldehydes.

1) K. Ogura and G. Tsuchihashi,*Tetrahedron Lett.,* 3151(1971).
2) K. Ogura and G. Tsuchihashi, *ibid.,* 2681 (1972).
3) K. Ogura and G. Tsuchihashi, *ibid.,* 1383 (1972).

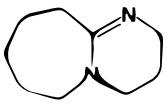
Versatile "New" Reagent



Iodobenzene diacetate is a reagent for the preparation of glycol diacetates from olefins,[1] azo compounds from aromatic amines,[2] *N*-arylacetamides,[3] phenyl ethers from phenols,[4] iodonium salts[5] and iodosobenzene.[6]

1) R. Criegee and H. Beucher, *Ann. Chem.,* **541**, 218 (1939).
2) K.H. Pausaker, *J. Chem. Soc.,* 1989 (1953).
3) G.B. Barlin and N.V. Riggs, *ibid.,* 3125 (1954).
4) K.H. Pausaker and A.R. Fox, *ibid.,* 295 (1957).
5) F.M. Beringer *et al., J. Amer. Chem. Soc.,* **81**, 342 (1959).
6) H. Saltzman and J.G. Sharefkin, *Org. Syn.,* **43**, 60 (1963).

Amidine For Organic Syntheses



A recent review[1] discusses the uses of DBU for the introduction of double bonds, and other reactions. More recently its utilization for the *O*-alkyl cleavage of hindered and simple methyl esters without the use of ionic nucleophilic reagents has been reported.[2]

1) Herman Oediger *et al., Synthesis,* 591 (1972).
2) E.J. Parish and D.H. Miles, *J. Org. Chem.,* **38**, 1223 (1973).

THE BORANE•AMINE COMPLEXES

Clinton F. Lane
Aldrich-Boranes, Inc.

Diborane (B_2H_6) is a very reactive gas which burns spontaneously in air and is rapidly hydrolyzed by water. Diborane is also a powerful reducing agent for both organic and inorganic substrates. The high reactivity of diborane is presumably due to its ready dissociation into borane (BH_3). The borane molecule is electronically unsaturated in that it has four orbitals available for bonding electrons but only three are occupied. Consequently, BH_3 behaves as a strong electron pair acceptor forming coordination complexes with suitable electron donor molecules. Of the various known complexes, the borane•amine complexes are particularly interesting because of their wide range of physical and chemical properties.

The first borane•amine complex was reported in 1937 and was prepared by the direct reaction of diborane with trimethylamine (eq. 1).[1]

$$2(CH_3)_3N + B_2H_6 \longrightarrow 2(CH_3)_3N \cdot BH_3 \qquad (1)$$

Since then almost all structural types of amines have been used to prepare borane•amines, and a wide variety of these complexes are now available from the Aldrich Chemical Company, Inc.

PHYSICAL PROPERTIES

An important feature of the borane•amines is their broad range of physical properties. Liquid, low-melting solid, and high-melting solid borane•amines are known. The borane•amines also have very low vapor pressures and can be purified by distillation and/or recrystallization. The physical constants of some of the typical borane•amines are summarized in Table I.

A very useful property of the borane•amines is their solubility in a wide variety of solvents as shown in Table II.

CHEMICAL PROPERTIES

All of the borane•amines produced by Aldrich-Boranes, Inc. are stable indefinitely at room temperature and are unaffected by dry air. The borane•amines prepared from primary and secondary amines are surprisingly resistant to loss of hydrogen (eq 2).

$$R_2NH \cdot BH_3 \longrightarrow R_2N\text{-}BH_2 + H_2 \qquad (2)$$

Borane•*tert*-butylamine does not lose hydrogen until heated to its melting point and borane•morpholine loses only 11.5% hydrogen after 20 hr at 69° in THF.[2] Borane•dimethylamine reportedly shows no evidence of thermal instability when heated to 110°.[3]

An attempted distillation of borane•pyridine at reduced pressure resulted in violent decomposition.[4] However, this complex has been stored for a year at room temperature without any detectable signs of deterioration.[5]

1. Hydrolysis

As shown in Table II, only the borane complexes with *N*-aryl amines (*N*-phenylmorpholine and *N,N*-diethylaniline) are hydrolyzed by water and alcohols. These two borane•amines react with atmospheric moisture. However, by careful and rapid handling, they may be transferred in air with only minimal loss of hydride activity. Naturally, an inert atmosphere and dry, aprotic solvents must be used for the bor-

Table I. Physical Constants for the Borane•amine Complexes

Borane•amine Complex	Mol. Wt.	mp, °C	bp, °C(mmHg)	Physical Appearance
Borane•*tert*-butylamine	86.97	96	decomp.	white, crystalline solid
Borane•*N,N*-diethylaniline	163.07	-30 to -27		clear, colorless liquid
Borane•dimethylamine	58.92	36	49(0.01)	white, crystalline solid
Borane•2,6-lutidine	120.99	110-112		white, crystalline solid
Borane•morpholine	100.96	93-95		white, crystalline solid
Borane•*N*-phenylmorpholine	177.06	97-99		off-white, crystalline solid
Borane•pyridine	92.94	10-11	decomp.	clear, light-yellow liquid
Borane•triethylamine	115.03	-4	97(12)	clear, colorless liquid
Borane•trimethylamine	72.95	94-94.5	172	white, crystalline solid

Table II. Solubility of Borane•amine Complexes at 25° [a,b]

Borane•amine Complex	H_2O	CH_3OH	Diethyl ether	THF	Di-glyme	Hexane	Cyclo-hexane	Benzene	Toluene	CH_2Cl_2
Borane•*tert*-butylamine	S	VS	S	VS	S	I	SS	S	S	S
Borane•*N,N*-diethylaniline	R	R	VS	VS	VS	VS	S	VS	VS	VS
Borane•dimethylamine	VS	VS	VS	VS	VS	I	I	VS	VS	VS
Borane•2,6-lutidine	SS	VS	S	VS	VS	I	SS	VS	VS	VS
Borane•morpholine	VS	VS	S	VS	VS	I	SS	S	S	VS
Borane•*N*-phenylmorpholine	R	R	VS	VS	VS	I	S	VS	S	VS
Borane•pyridine	SS	VS	VS	VS	VS	I	SS	VS	VS	VS
Borane•triethylamine	SS	VS	VS	VS	VS	VS	VS	VS	VS	VS
Borane•trimethylamine	SS	VS	VS	VS	VS	I	SS	VS	VS	VS

[a] R= Reacts, hydrogen evolved; I= Insoluble, <0.1 g / 100 ml solvent; SS= Slightly soluble, 0.1-1.0 g / 100 ml solvent; S= Soluble, 1.0-3.0 g / 100 ml solvent; VS= Very soluble, 3.0-25 g / 100 ml solvent.
[b] Reference 2 and unpublished results.

ane•*N*-arylamines. All of the other borane•amines are unaffected by hydrolytic solvents at neutral pH after a minimum of 12 hr at 25°.[2] Hydrolysis does occur in a 1 *M* hydrochloric acid medium in 50% water-50% ethylene glycol.[2] The hydrolysis times for the various borane•amines are listed in Table III.

2. Deuterium Exchange

The active hydrogens of borane•trimethylamine undergo a rapid exchange with deuterium when the borane•amine is stirred with acidic deuterium oxide (eq 3).[6]

$$(CH_3)_3N\cdot BH_3 \xrightarrow[DCl]{D_2O\ (excess)} (CH_3)_3N\cdot BD_3 \quad (3)$$

The exchange occurs much faster than hydrolysis, *e.g.*, after 6 hr, the deuterium content of the borane•amine is 98% while less than 6% has hydrolyzed.[6] Subsequently, this procedure was used to prepare large quantities of borane-d_3•trimethylamine which were used in the first convenient synthesis of sodium borodeuteride (eq 4).[7] Borane-d_3•trimethylamine can also be used to prepare B_2D_6 (eq 5).[8]

$$4(CH_3)_3N\cdot BD_3 + 3NaOCH_3 \xrightarrow[120\text{-}150^\circ]{diglyme} 3NaBD_4 + 4(CH_3)_3N + B(OCH_3)_3 \quad (4)$$

$$2(CH_3)_3N\cdot BD_3 + 2BF_3 \longrightarrow B_2D_6 + 2(CH_3)_3N\cdot BF_3 \quad (5)$$

3. Reaction with Thiols

A reaction that is related to hydrolysis is the conversion of borane•trimethylamine into trialkylthioborates (eq 6),[9] which can react with carboxylic acids in a new thioester synthesis (eq 7).[10]

$$(CH_3)_3N\cdot BH_3 + 3RSH \xrightarrow{100^\circ} (RS)_3B + 3H_2 + (CH_3)_3N \quad (6)$$

$$CH_3(CH_2)_4COOH + (C_2H_5S)_3B \xrightarrow[2\ hr]{C_6H_6} CH_3(CH_2)_4\overset{O}{\overset{\|}{C}}\text{-}SC_2H_5 \quad (7)$$

81% isolated

4. Reaction with Phosphines

When borane is used as the reference acid, the base strength of trimethylphosphine is greater than that of trimethylamine.[11] Since the reaction of a trialkylphosphine with a borane•amine is an equilibrium reaction, the amine must be continually removed to favor the borane•phosphine complex. Removal of a volatile amine by distillation then provides a convenient method for the essentially quantitative preparation of a variety of borane•phosphine complexes (eq 8,9).[4]

$$(C_2H_5)_3N\cdot BH_3 + (C_2H_5)_3P \longrightarrow (C_2H_5)_3P\cdot BH_3 + (C_2H_5)_3N\uparrow \quad (8)$$

$$(C_2H_5)_3N\cdot BH_3 + (C_6H_5)_3P \longrightarrow (C_6H_5)_3P\cdot BH_3 + (C_2H_5)_3N\uparrow \quad (9)$$

Table III. Hydrolysis of Borane•amines in 1 *M* Hydrochloric Acid in 50% Water-50% Ethylene Glycol at 25°C

Borane•amine Complex	Time (min) for total hydrolysis
Borane•*N*-phenylmorpholine	2 [b]
Borane•*N,N*-diethylaniline	3 [b]
Borane•*tert*-butylamine	4 [b]
Borane•pyridine	4 [c]
Borane•2,6-lutidine	6 [c]
Borane•dimethylamine	9 [b]
Borane•morpholine	120 [c]
Borane•triethylamine	390 [c]
Borane•trimethylamine	1000 [a,c]

[a] Extrapolated [b] Unpublished results [c] See reference 2.

5. Halogenation of Borane-amines

The preparation of partially halogenated borane•amines has been studied extensively. The reaction of borane•trimethylamine with hydrogen chloride[12,13] hydrogen bromide [13] or hydrogen fluoride[14] yields the corresponding monohaloborane•amine (eq 10-12). A dichloroborane•amine has also been prepared using mercuric chloride (eq 13).[12]

$$(CH_3)_3N\cdot BH_3 + HCl \xrightarrow[20\text{-}25^\circ]{C_6H_6} (CH_3)_3N\cdot BH_2Cl + H_2 \quad (10)$$

95%

$$(CH_3)_3N\cdot BH_3 + HBr \xrightarrow[35\text{-}40^\circ]{Et_2O} (CH_3)_3N\cdot BH_2Br + H_2 \quad (11)$$

75%

$$(CH_3)_3N\cdot BH_3 + HF \xrightarrow[0\text{-}5^\circ]{C_6H_6} (CH_3)_3N\cdot BH_2F + H_2 \quad (12)$$

$$(CH_3)_3N\cdot BH_3 + 2HgCl_2 \xrightarrow[35\text{-}40^\circ]{Et_2O} (CH_3)_3N\cdot BHCl_2 + 2Hg_2Cl_2 + 2HCl \quad (13)$$

6. Quantitative Analysis of Borane•amines

The most important chemical property of the borane•amines is their ability to act as excellent reducing agents. The rapid reduction of iodine to iodide has been developed into a practical method for the quantitative analysis of borane•amines.[15] A solution containing the borane•amine is buffered with sodium acetate and acetic acid. Analysis is then carried out by the addition of starch and titration with iodine solution. The end point of the titration is sharp, and the reaction proceeds rapidly and quantitatively (eq 14).[15]

$$R_3N\cdot BH_3 + 3I_2 + 3H_2O \longrightarrow R_3NH^+ + 6I^- + 5H^+ + B(OH)_3 \quad (14)$$

The uses of borane•amines in the hydroboration of olefins, reduction of organic functional groups, and reduction of metal salts are all discussed in detail in later sections of this review. Numerous important and interesting industrial applications are also included. As is apparent, the chemical properties of the borane•amines are quite diverse, and it has even been reported that borane•trimethylamine is an effective chemosterilant for houseflies.[16]

BORANE•AMINES AS STABILIZERS AND PURIFIERS

The excellent solubility and reducing properties of the borane•amines have resulted in numerous applications for the stabilization and purification of industrial materials.

Alcohols prepared by the hydrogenation of oxo process aldehydes are usually contaminated with carbonyl and/or unsaturated compounds. When these alcohols are used to prepare phthalic acid esters, the resulting plasticizers are usually colored. These undesirable contaminants and color-forming impurities are readily removed by treating the alcohols with borane•amines.[17,18]

Borane•amine complexes have been used extensively as stabilizing agents in polymer formulations. A copolymer of acrylonitrile and vinyl chloride was stabilized against heat and light degradation by the addition of borane•pyridine[19] or a borane•alkylamine complex.[20] Addition of a borane•pyridine–triphenylmethane violet dye reaction mixture stabilized a polyvinyl chloride resin and inhibited discoloration during both hot milling and subsequent oven aging.[21] Polyoxyalkylenes were also stabilized by the addition of a borane•amine.[22]

Borane•trialkylamines have been used to stabilize organic isocyanates against discoloration during storage[23] and to prepare thermally stable insulation material.[24] Borane•2,6-lutidine, when added to a bath containing an acid leuco vat dye, increased the stability of the acid leuco form.[25] Borane•morpholine has been used in a correction fluid for removing errors on a master used in a spirit duplicating process.[26] An interesting report was that borane•pyridine effectively removes subsurface stains from plasticized polymeric materials without swelling or marring the surface.[27] Finally, a potentially important use of borane•amines has been reported for the bleaching of wood pulp.[28] Mechanically disintegrated wood pulp slurries are effectively bleached when contacted with borane•amines under a wide range of conditions. [28]

BORANE•AMINES AS FUEL ADDITIVES

Liquid borane•amine complexes possess ideal properties as fuel additives in hydrocarbon diesel fuel.[29] The borane•amines are useful as ignition improvers in hydrocarbon fuels for compression ignition engines and can be utilized as additives in other hydrocarbon compositions.[30] For example, minor proportions of borane•amines, when blended with burner fuels, improves their combustion characteristics, and the borane•amines can be used as additives in natural and synthetic lubricating oils and greases. Also, various borane•amines, in combination with tetraethyllead, have been claimed to be highly effective co-antiknock gasoline additives.[31]

BORANE•AMINES IN PHOTOGRAPHIC PROCESSING

The ability of borane•amines to reduce silver salts to free silver [32] has naturally resulted in the application of these borane complexes in the field of photographic processing. Silver halide emulsions have been treated with various borane•amines as fogging agents to give high-contrast positives.[33] The reduction of a silver salt solution with borane•amines in the presence of a protective colloid gave a colloidal dispersion of free silver with blue light absorbing characteristics that were useful in the preparation of trilayer color film.[34]

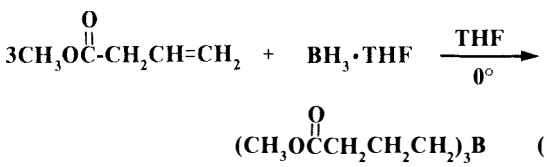
BORANE•AMINES AS POLYMERIZATION CATALYSTS

Borane•amines are reported to be effective catalysts for the formation of polyesters from a polyhydric alcohol and a diester of a dibasic carboxylic acid.[35] The flexural modulus of polyolefins is improved by formation of the polymer in the presence of a catalyst system containing a borane•amine, such as borane•trimethylamine or borane•pyridine.[36] Also, borane•amines have been used as catalysts for the formation of epoxy foams,[37] as curing agents for epoxy resins,[38] and as vulcanizing agents for natural and synthetic rubbers.[39]

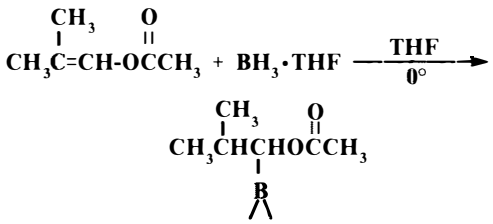
The cold flow of polybutadiene prepared in toluene in the presence of an organometallic catalyst, is improved by deactivating the catalyst with borane•triethylamine.[40] Minor amounts of borane•dimethylamine or borane•pyridine are also reported to inhibit a vigorous exothermic reaction in the emulsion polymerization of mixtures of butadiene and vinylidene monomers to form synthetic rubbers of good color, improved softness and low gel content.[41]

BORANE•AMINES AS HYDROBORATING AGENTS

The most powerful hydroborating agent currently available is the borane•tetrahydrofuran complex in tetrahydrofuran. This reagent rapidly and quantitatively converts olefins into the corresponding trialkylboranes under exceptionally mild conditions, *e.g.*, equations 15-17.[42]



$$3CH_3OC(=O)\text{-}CH_2CH{=}CH_2 + BH_3\cdot THF \xrightarrow[0^\circ]{THF} (CH_3OC(=O)CH_2CH_2CH_2)_3B \qquad (15)^{43}$$



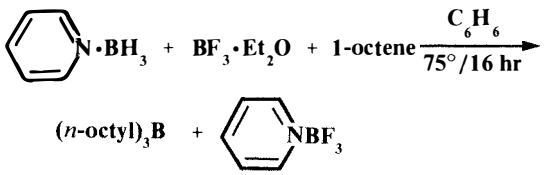
$$CH_3C(CH_3){=}CH\text{-}OC(=O)CH_3 + BH_3\cdot THF \xrightarrow[0^\circ]{THF} CH_3CH(CH_3)CH(B<)OC(=O)CH_3 \qquad (16)^{44}$$

$$+ BH_3\cdot THF \xrightarrow[0^\circ]{THF} \qquad (17)^{45}$$

As a laboratory reagent borane•THF has a number of disadvantages, the most serious being its rapid decomposition on exposure to moisture in the atmosphere. Also, borane•THF can only be used as a relatively dilute solution in THF. The borane•amines do not possess these disadvantages and are available in pure form as air-stable solids or liquids which readily dissolve in a variety of solvents. However, the increased strength of these coordination complexes greatly reduces the reactivity of borane•amines. For example, temperatures of 100° and higher are required for the hydroboration of olefins with borane•triethylamine,[46] for the hydroboration of terminal olefins in diglyme with borane•pyridine,[5] and for the deuterioboration of olefins with borane-d_3•trimethylamine.[6] Various borane•amines are also reported to react with terminal olefins in the absence of a solvent at 200° to produce the corresponding trialkylboranes.[47]

The drastic conditions that were used in the early studies on the use of borane•amines as hydroborating agents results in extensive thermal isomerization and none of these procedures could possibly be used for the hydroboration of functionally substituted olefins, as shown in equations 15-17. Thus, hydroboration of 2-hexene with $(C_2H_5)_3N\cdot BH_3$ at 200° produces only the isomerized product, tri-*n*-hexylborane,[47] and substantial isomerization was noted in the hydroboration of 2-methyl-2-pentene with $(C_2H_5)_3N\cdot BH_3$ at 80-165°.[48] Consequently, lower reaction temperatures are a necessity if the borane•amines are ever to become useful hydroborating agents.

A slight measure of success in lowering the reaction temperature is achieved by adding boron trifluoride etherate.[49] However, a temperature of 75° for 16 hr is required to obtain a 90% yield for the hydroboration of 1-octene (eq 18).[49]



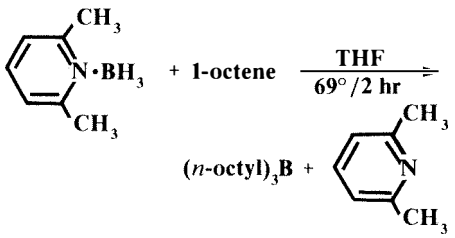
$$N\cdot BH_3 + BF_3\cdot Et_2O + \text{1-octene} \xrightarrow[75^\circ/16\ hr]{C_6H_6} (n\text{-octyl})_3B + NBF_3 \qquad (18)$$

The rate determining step in the hydroboration of olefins with borane complexes is presumably the dissociation of the complex into free borane (eq 19).

$$R_3N\cdot BH_3 \rightleftharpoons R_3N + BH_3 \qquad (19)$$

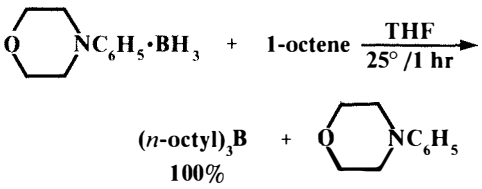
Consequently, modifying the electronic effects to lower the Lewis basicity of the amine and increasing the steric effects should increase the rate of dissociation of the complex and thereby increase the rate of hydroboration. Both effects have been noted. Thus, in contrast to the reaction of borane•trimethylamine with olefins, *tert*-butylborane•trimethylamine reacts readily with terminal olefins at 60° to give the corresponding *tert*-butyldialkylboranes with no detectable isomerization of the *tert*-butyl group.[50] This could be the result of a combination of both an electronic (lower Lewis acidity of an alkylborane) and a steric effect.

A steric effect becomes apparent when borane•pyridine is compared with borane•2,6-lutidine. In refluxing THF, the hydroboration of 1-octene with borane•pyridine is only 25% complete after 2 hr, while with borane•2,6-lutidine, the hydroboration is quantitative (eq 20).[2]

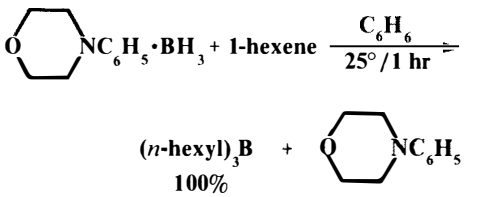


(20)

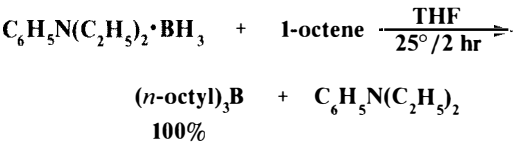
An even more striking electronic effect is exhibited by the borane•*N*-arylamine complexes which are capable of hydroborating terminal olefins at 25° in THF or benzene, *e.g.*, equations 21-23.[2] The other borane•amines show no evidence of reaction after 2 hr at 25°C.[2]



(21)



(22)



(23)

Consequently, borane•*N*-phenylmorpholine and borane•*N,N*-diethylaniline show great promise as convenient, stable hydroborating agents.

In view of the increasing importance of trialkylboranes in synthetic organic chemistry,[42] a systematic study of the use of borane•2,6-lutidine, borane•*N,N*-diethylaniline, and borane•*N*-phenylmorpholine as hydroborating agents is currently in progress in the laboratories of Aldrich-Boranes, Inc. and will be reported shortly.

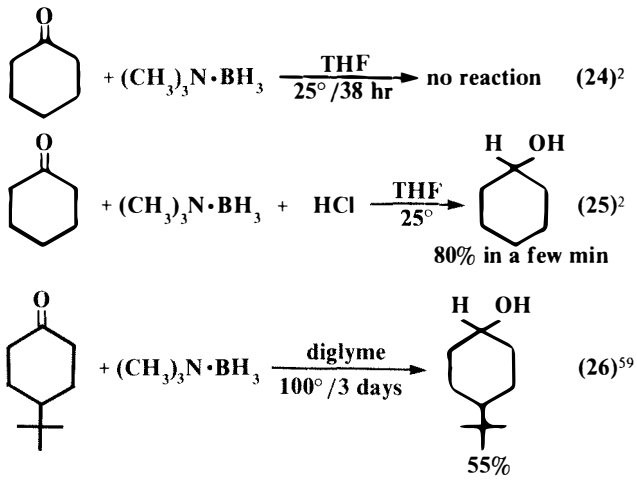
BORANE•AMINES AS REDUCING AGENTS

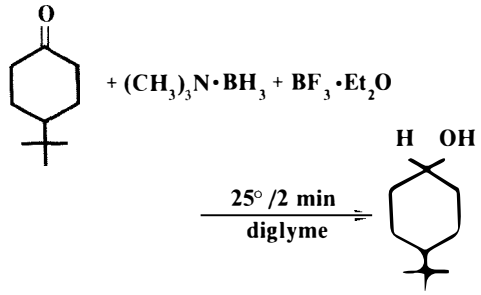
Various borane•amines are soluble in and unreactive toward water, alcohols, lower alkylamines, liquid ammonia, chlorinated hydrocarbons, ethers, and aliphatic and aromatic hydrocarbons. Thus, the borane•amines may be used to carry out organic reductions in solvents toward which aluminohydrides and borohydrides are reactive or in which they are insoluble. For example, certain aralkyl halides have been reduced to hydrocarbons using borane•triethylamine in liquid sulfur dioxide,[51] and in a process which may involve hydroboration, borane•amines were reported to be effective soluble catalysts for catalytic hydrogenation of alkenes.[52]

The borane•*N*-arylamine complexes reduce cyclohexanone in less than 3 hr at 25° in THF.[2] However, only two of the three hydrides on boron are available for reaction, *i.e.*, the intermediate $(RO)_2BH$ must have failed to react with the ketone as has been observed for BH_3•THF reductions.[53] Borane•pyridine and borane•trimethylamine in THF give no detectable reduction of a carbonyl compound after 38 hr at 25°.[2] Under more vigorous conditions (refluxing benzene or toluene), borane•pyridine reduces aldehydes, ketones and acid chlorides to the corresponding alcohols.[54]

Other workers have reported the reduction of carbonyl compounds with borane•amines in neutral, non-aqueous solvents, but again the reactions are usually quite slow and the yields usually unsatisfactory. For example, the reduction of benzaldehyde with borane•pyridine in pyridine was carried out at 100°,[55] the reduction of benzaldehyde with borane•*tert*-butylamine was carried out in refluxing benzene,[56] and the reduction of carbonyl compounds with various borane•amines in neutral water, benzene, or methanol gave only 30-60% reduction.[57]

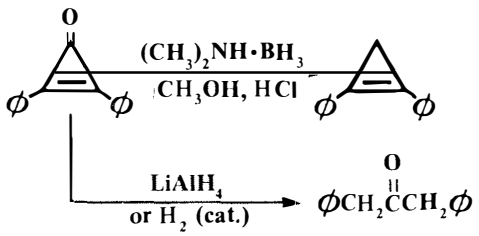
Interestingly, the borane•amines are much more effective reducing agents in strong aqueous acid, and their rates of reaction with carbonyl compounds actually increase with increasing acidity of the medium.[58] For example, a tremendous increase in rate occurs upon addition of a mineral acid or a Lewis acid (eq 24-27).





(27)[59]

The above pronounced effect of added boron trifluoride etherate is most remarkable and has been used for the reduction of ketones with borane-d_3•trimethylamine to give α-deuterio alcohols.[6] Also, borane•amine reduction in the presence of hydrogen chloride was used effectively in the preparation of a cyclopropene in a case where both aluminohydride and catalytic reduction had failed (eq 28).[60]



(28)

Borane•morpholine is reported to be a highly effective reducing agent in strong aqueous acid.[58] Both water and water/alcohol solvents can be used, and these reductions occur under conditions where a relatively rapid rate of hydrolysis of sodium borohydride occurs.[58] The kinetics and mechanism of this acid-catalyzed borane•morpholine reduction of carbonyl compounds have been investigated.[61,62]

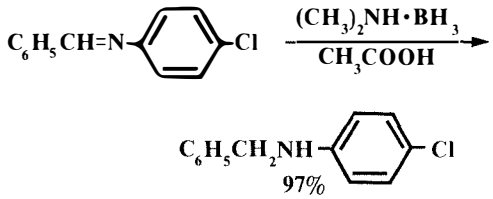
The borane•amine reduction of carbonyl compounds can even be carried out under mild conditions in glacial acetic acid as shown by the results given in Table IV.[2]

Table IV. Reduction of Cyclohexanone by Borane•amines in Glacial Acetic Acid at 25°

Borane•amine Complex	Reduction, %	Time, hr
Borane•2,6-lutidine	85	1
	87	2
Borane•pyridine	85	1
	87	2
	94	14
Borane•morpholine	77	1
	83	2
	87	4
	95	20

Borane•amines can also be used for the reductive amination of ketones.[63] Reduction of ketones with a borane•amine in the presence of an excess of ammonia, methylamine, or dimethylamine (pH ~ 9-10) at room temperature gives reasonable yields of the corresponding amines. An interesting modification of this reductive amination reaction has been used to prepare α-amino acids. Thus, several substituted pyruvic acids were reduced at room temperature with a borane•amine in the presence of a 5-fold excess of ammonia to give the corresponding α-amino acids in 66-72% yield.[63]

A very useful application of borane•amines that appears to have been overlooked by most synthetic organic chemists is the reduction of Schiff bases. Borane•dimethylamine selectively reduces the imino linkage in the presence of the chloro, nitro, alkoxy, hydroxy, carboxy, carbethoxy, and sulfonamido groups.[64] This reduction proceeds rapidly and smoothly in glacial acetic acid to give excellent yields of secondary amines (eq 29-31).



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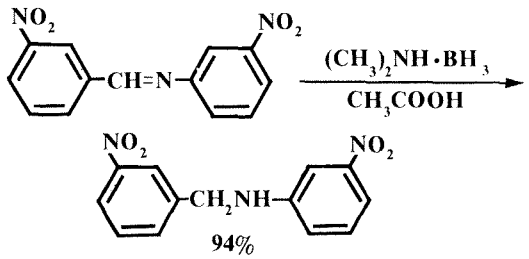

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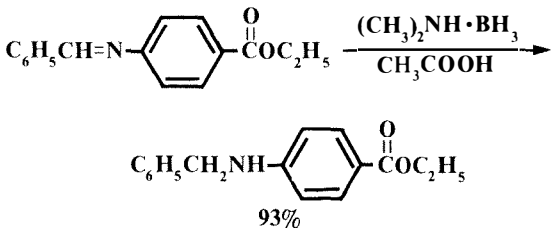
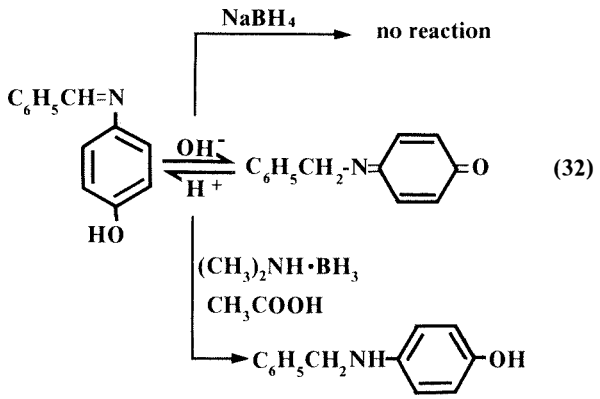


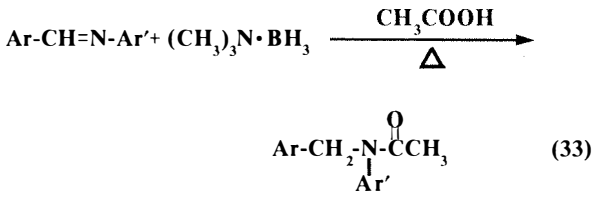
(31)

The ease and speed of the reduction of Schiff bases by borane•amines are comparable to or better than the reductions using sodium borohydride or lithium aluminum hydride. The fact that Schiff base reductions can now be carried out in a mildly acid medium is important in cases where the Schiff base is unstable or undergoes tautomerization in an alkaline medium, *e.g.*, *N*-benzylidene-*p*-aminophenol fails to react with sodium borohydride but undergoes a rapid borane•amine reduction in glacial acetic acid. (eq 32)[64]

When the reduction of Schiff bases is carried out under more vigorous conditions using an excess of borane•trimethylamine, reductive acylation is observed (eq 33).[65]



(32)



(33)

In addition to the reduction of carbonyl compounds and Schiff bases, the borane•amines are highly effective reducing agents for inorganic compounds. For example, mercuric chloride is reduced to mercurous chloride (eq 13),[12] iron to the ferrous state,[32] silver nitrate to free silver,[32] and iodine to iodide.[32] The reduction of silver nitrate and cupric nitrate with borane•amines gives the pure metals with no boride formation and no contamination by oxides or other materials.[66] This ability of borane•amines to reduce metal salts to the pure metal is being used in the chemical plating industry as discussed in the following section.

BORANE•AMINES AS CHEMICAL PLATING AGENTS

The original chemical plating solutions employed sodium hypophosphite as the reducing agent for formation of the nickel, cobalt, nickel-cobalt, or nickel-iron coatings. Certain inherent disadvantages in the use of hypophosphite have prompted interest in the development of alternative reducing agents for use in electroless plating. The borane complexes, borane•dimethylamine and borane•diethylamine, appear to be the most promising and their use as reducing agents in chemical plating baths has been discussed in detail elsewhere.[67-69] The application of borane•amines in electroless plating has also been the subject of numerous patents.[15,70-76]

The chemical plating solutions using a borane•amine as the reducing agent have the following important advantages:

1) Lower total operating costs because of improved bath stability.

2) Lower operating temperatures allow temperature-sensitive thermoplastics to be plated with a conductive metal film for subsequent electroplating.

3) The coatings have good corrosion resistance, generally better than conventional nickel electrodeposits.

4) The nickel coatings have low electrical resistance making them particularly important in the electronics field.

5) Relatively pure deposits (as high as 99.9% nickel) are obtainable.

6) The nickel coatings have high melting points which approach that of electrodeposited nickel.

Recently, it was reported that borane•dimethylamine can be used as the reducing agent for the electroless deposition of gold[77] or silver.[78] This electroless silver deposition is particularly noteworthy because all previous attempts to use hypophosphite solutions for silver plating had failed.[78]

CONCLUSIONS

It should now be readily apparent that the borane•amine complexes are very useful reagents which have many important laboratory and industrial applications. The air stability, availability as both solids and liquids, excellent solubility characteristics, and interesting chemical properties should facilitate the development of numerous other interesting uses.

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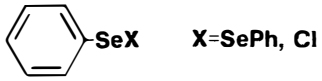
New Reagents for Olefin Synthesis



We have produced several new organoselenium reagents for the mild and convenient preparation of olefins, α,β-unsaturated esters and ketones, etc. Olefins are formed *via syn*-elimination from the alkyl phenyl selenoxide intermediate.

1) K.B. Sharpless and R.F. Lauer, *J. Amer. Chem. Soc.*, **94**, 7154 (1972); *ibid.*, **95**, 2697 (1973).
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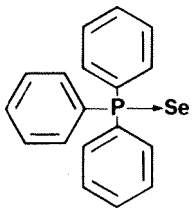
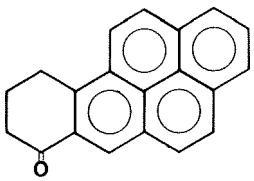


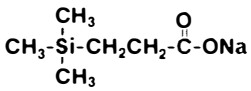
It was recently demonstrated that Ph_3PSe and CF_3COOH provide a highly effective combination for the stereospecific conversion of epoxides to olefins in good yield. The addition of CF_3COOH (1 equiv.) to a solution of epoxide and Ph_3PSe in CH_2Cl_2 resulted in a 53-75% conversion after 1 to 2.5 hours.

D.L.J. Clive and C.V. Denyer, *J. Chem. Soc., Chem. Commun.*, 253 (1973).

Benzopyrene Precursor

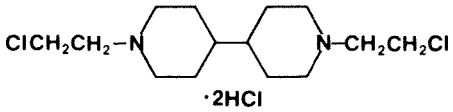


Water-Soluble 'TMS'



NEW BIOCHEMICALS

Obesity in Mice



When BPM is incubated in 0.1*M* borate buffer (pH 9) for 1 hr at 37° and injected intraperitoneally into female mice, it causes obesity to a degree of 3-4 times normal weight within 3-4 months after injection.

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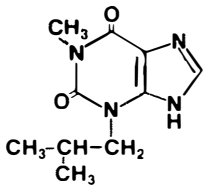
Cyclic AMP Phosphodiesterase Inhibitor



3-Isobutyl-1-methylxanthine exhibits potent lipolytic activity[1] (15 times more potent than theophylline), an action probably resulting from its inhibitory effects on cyclic AMP phosphodiesterase.[1] In the presence of glucose the level of cyclic AMP and insulin release are increased.[2,3]

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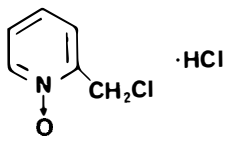
Novel Protecting Group



2-Picolyl-*N*-oxide is a new *N*-protecting group quite stable to alkaline and acid treatment and readily removed by acetic anhydride at room temperature. It is especially useful in cases where the benzyl protecting group cannot be used. It has been used in the synthesis of 3-benzyluracil, 7-benzylhypoxanthine and 7-α-D-arabinofuranosylhypoxanthine.

Y. Mizuno *et al., J. Org. Chem.,* **37**, 39 (1972).

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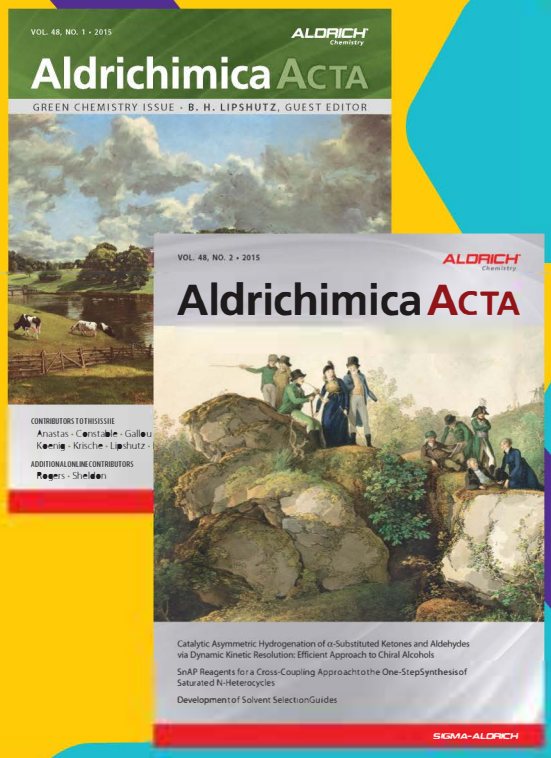

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