Reduction of Organic Compounds with Low-Valent Species of Group IVB, VB, and VIB Metals

Tse-Lok HO

Brookhaven National Laboratory, Upton, New York 11973, U.S.A.

The present article gives a summary of reactions of low-valent species of titanium, vanadium, chromium, molybdenum, and tungsten with organic substrates. Preparations are given for some of the not yet commercially available reagents. The reactions are arranged in terms of the organic reagent. Reactions of chromium(II) and titanium(II)/titanium(III) are treated only briefly as separate reviews on these reagents are available. Mechanistic aspects of the reactions are not discussed in any detail.

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1. Introduction

Transition metals of Group IVB, VB, and VIB are relatively abundant and the chemistry of their various valencies has been fairly well investigated. Work on the reduction of organic molecules by chromium(II) and titanium(III) ions was initiated early this century, but subsequently fell into dormancy and has been largely forgotten by the organic chemist. However, there is good evidence that research in this area is undergoing a revival.

This article surveys reactions of organic compounds with low-valent titanium, vanadium, chromium, molybdenum, and tungsten species. Since reviews on the application of chromium(II)\(^1\) and titanium(II)/titanium(III)\(^2\) ions to preparative chemistry are available, the description of these species is much abbreviated here. Mechanistic aspects of various reductions have also been omitted on account of space limitations. Methods for preparation of several commonly used reagents are described below, while others may be found under relevant experimental procedures. Aqueous titanium(III) chloride solution is commercially available (e.g. from Fisher Scientific Co.).

**Chromium(II) Chloride\(^1\):**

A solution of chromium(II) chloride (12 g) in water (15 mL) and 12 normal hydrochloric acid (25 mL) is reduced with excess granulated zinc under nitrogen. Amalgamated zinc dust, prepared by shaking zinc (10 g) with mercury(I) chloride (0.8 g) in water (10 mL) containing concentrated hydrochloric acid (0.5 mL) for 5 min and then decanting the supernatent liquid, has also been recommended for the reduction. For use as a reducing agent the blue solution is filtered under nitrogen through a plug of glass wool into a solution of the substrate (0.01 mol) in redistilled acetone (50 mL).

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\(^1\) J. R. Hanson, *Synthesis* 1974, 1.

J. R. Hanson, E. Premszaic, *Angew. Chem.* 80, 271 (1968);


Chromium(II) Acetate: 
Powdered chromium metal (9 g) in 6 normal hydrochloric acid (100 ml) is stirred until reaction is complete. A solution of sodium acetate (50 g) in deoxygenated water (100 ml) is added under nitrogen with stirring and cooling. The pink precipitate of chromium(II) acetate (10 g) is washed under nitrogen with air-free water.

Chromium(II) Ethylenediamine Perchlorate: 
A solution of dimethylformamide (40 ml) and ethylenediamine (1 ml) is flushed with nitrogen. 0.8 Normal chromium(II) perchlorate solution (5 ml), prepared from chromium metal and dilute perchloric acid, is added to give a clear blue-purple solution.

2. Alkynic and Alkenic Systems

The reduction of acetylene to ethylene using chromium(II) sulfate in ammoniacal solution was first reported by Berthelot. Under homogeneous conditions [chromium(II) sulfate/water or aqueous dimethylformamide] many alkynes are reduced stereospecifically to (E)-alkenes at room temperature. The presence of a polar function at the propargylic position greatly facilitates the reaction and terminal alkynes are more reactive than their internal counterparts.

Compounds containing conjugated double bonds are also reduced by chromium(II) species. In general, the rate is enhanced by the presence of conjugated coordination sites and electron-withdrawing substituents (COOH, COOR, CN). The (Z)-alkenes are more rapidly reduced than the corresponding (E)-isomers.

With the weaker reducing titanium(III) species, fumaric, maleic, and citraconic acids are converted to the corresponding succinic acids whereas the diesters are untouched. Titanium(III) chloride is also capable of bringing about hydroxylation of enones and eneones esters, cinnamic acid, amide, benzalacetone, and 5-phenylpenta-2,4-dienoic acid. Reactions of the styrenic compounds are carried out at 100° in ammonium hydroxide solution.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Solvent</th>
<th>Product</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂C≡C−CH₂−OH</td>
<td>H₂O</td>
<td>H₂C=CH−CH₂−OH</td>
<td>89</td>
</tr>
<tr>
<td>C₆H₄−C=CH</td>
<td>DMF/H₂O (2:1)</td>
<td>C₆H₄−CH=CH₂</td>
<td>94</td>
</tr>
<tr>
<td>HOOC−C≡C−COOH</td>
<td>H₂O</td>
<td>HOOC−C=CH−COOH</td>
<td>94</td>
</tr>
<tr>
<td>C₆H₄−C≡C−COOH</td>
<td>H₂O</td>
<td>C₆H₄−CH=CH₂</td>
<td>91</td>
</tr>
<tr>
<td>H₂C−C≡C−CH₂−OH</td>
<td>H₂O</td>
<td>H₂C−CH=CH₂−OH</td>
<td>84</td>
</tr>
<tr>
<td>HO−CH₂−C≡C−CH₂−OH</td>
<td>H₂O</td>
<td>HO−CH₂−C=CH−CH₂−OH</td>
<td>92</td>
</tr>
<tr>
<td>C₆H₅−C≡C−C₆H₅</td>
<td>DMF/H₂O (1:2.5)</td>
<td>C₆H₅−CH=CH₂</td>
<td>95</td>
</tr>
<tr>
<td>C₆H₄−COOH</td>
<td>H₂O</td>
<td>C₆H₄−CH=CH₂</td>
<td>86</td>
</tr>
<tr>
<td>HOOC−COOH</td>
<td>H₂O</td>
<td>HOOC−CH=CH₂</td>
<td>91</td>
</tr>
<tr>
<td>HOOC−COOH</td>
<td>DMF/H₂O (1:1)</td>
<td>HOOC−COOH</td>
<td>88</td>
</tr>
<tr>
<td>C₆H₄−COOH</td>
<td>DMF/H₂O (2:1)</td>
<td>C₆H₄−CH=CH₂</td>
<td>84</td>
</tr>
<tr>
<td>C₆H₄−CN</td>
<td>DMF/H₂O (1:1)</td>
<td>C₆H₄−CH=CH₂−CN</td>
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<tr>
<td>C₆H₄−COOCH₃</td>
<td>H₂O</td>
<td>C₆H₄−CH=CH₂−COOCH₃</td>
<td>92</td>
</tr>
<tr>
<td>H₂C=CH−CN</td>
<td>H₂O</td>
<td>HOOC−CH=CH₂−COOCH₃</td>
<td>100</td>
</tr>
</tbody>
</table>
Conant and Lutz obtained 1,4-diphenylbutane-1,4-dione on subjecting halogenated dibenzoylethenes to the action of titanium(III) chloride.

\[
\begin{align*}
C_6H_5\text{CO}\cdot\text{CCl} &= \text{CH} \cdot \text{CO} \cdot C_6H_5
\end{align*}
\]

Molar mixtures of lithium aluminum hydride and transition metal halides (e.g., titanium(III) or chromium(III) chloride) effectively reduce alkenes such as 1-octene. Interestingly, the stoichiometric reagent from lithium aluminum hydride/vanadium(III) chloride is inert towards 1-octene whereas the analogous reaction involving a catalytic amount of vanadium(III) chloride yields 42% of n-octane together with 64% of recovered alkene.

Several steroid enediones have been exposed to the action of chromium(II) chloride. Interestingly, reduction of cholest-4-ene-3,6-dione gives 5β-cholesterol-3,6-dione which is different from the product obtained by titanium(III) chloride-reduction. Reduction of cholest-3,5-diene-2,7-dione affords the non-conjugated 4-ene-2,7-dione.

Hydroquinones have been isolated in fair to good yields after heating the corresponding quinones with a chromium(II) chloride solution. Ring-substituted chlorine atoms can be retained. More variable results emerge from the 1,4-naphthoquinone series. Remarkably, the oxygen function at C-4 of 2-alkyl-3-hydroxy-1,4-naphthoquinones is eliminated when a hydrogen donor (H_3PO_3) is present in the medium. Vanadium(II) chloride effects quinone reduction instantaneously.

1,2-Unsaturated ketones undergo reductive dimerization to give 1,4-diketones under the influence of chromium(II) or vanadium(II) chloride. The chromium bis[ethylenediamine] dichloride [Cr(en)_2(OAc)_2] complex is a more powerful and useful reagent for effecting straightforward reduction of enones, provided that a thiol and acetic acid are present. However, when the enone molecule contains only one β-substituent, Michael addition of the thiol could become a serious side reaction.

Alkynes can be reduced to either alkanes (from terminal alkynes) or (Z)-alkenes (from internal alkynes) by the 1:1 lithium aluminum hydride/titanium(IV) chloride reagent. Stearic acid is convertible to oleic acid by the action of the zinc/titanium(III) chloride combination in aqueous acetic acid.

\[
\begin{align*}
H_3C\text{CH}_3 & \quad 79\% \\
\text{O} & \quad \\
\text{O} & \quad 57\% \\
\text{CH}_3\text{CH}_3 & \quad 11\%
\end{align*}
\]

---

3. Halides

Alkyl halides can oxidize acidic chromium(II) solutions\(^{24}\). Aqueous dimethylformamide is a convenient reaction medium owing to its solubilizing capacity for alkyl halides\(^{25}\). The reactivity of monohalides toward chromium(II) falls into the order shown below.

\[
\begin{align*}
\text{Ar}-\text{C}(-\text{X}) & \approx \text{R}-\text{C}(-\text{X}) > \text{H}_2\text{C}(-\text{C})\text{-X} > \text{R}-\text{C}(-\text{X}) > \text{R}-\text{C}(-\text{X}) \\
& > \text{R}-\text{C}(-\text{X}) > \text{R}-\text{C}(-\text{X}) > \text{R}-\text{C}(-\text{X}) > \text{Ar}-\text{X}
\end{align*}
\]

\(\text{x} = \text{j} > \text{Br} > \text{Cl}\)

Depending on the nature of the alkyl group, two types of products may be obtained.

\[
\begin{align*}
\text{R}-\text{X} + 2 \text{Cr(II)} + \text{H}^+ & \longrightarrow \text{R}-\text{H} + \text{XCr(II)} + \text{Cr(III)} \\
\text{R} = \text{alkyl, allyl} \\
\text{R}-\text{X} + \text{Cr(II)} & \longrightarrow \text{1/2 R}-\text{R} + \text{XCr(II)} \\
\text{R} = \text{C}_2\text{H}_5 - \text{CH}_3
\end{align*}
\]

The chromium(II) complexes containing bidentate amino ligands (e.g., ethylenediamine, ethanolamine)\(^{26}\) are substantially more effective. With these species, the least reactive primary alkyl chlorides can be reduced rapidly to alkanes at room temperature. Organochromium complexes are spectroscopically detectable intermediates.

Deciodination of the iodolactone 1 is best accomplished by treatment with chromium(II) acetate in dimethyl sulfoxide in the presence of ethanethiol\(^{27}\). Inversion of the ring juncture carbon configuration in product 2 was noted. Other methods for this conversion, such as catalytic hydrogenolysis and photolysis in cyclohexene, are much inferior.

A systematic study of chromium(II) reduction of 9β-bromo-11β-hydroxy-A^4-3-oxo steroids showed that the nature of the anion associated with chromium(II), the solvent, and the presence or absence of hydrogen atom donors have profound effects on the types of products. The presence of good hydrogen atom donors [butanethiol, triphenylsilyl, triphenylstannane, phosphinic acid H_2P(OiOEt), etc.] directs the normal reaction pathway of A^4-11α-olefin formation to the generation of 11β-hydroxy steroids\(^{28}\).

The exo-chlorine atom of the sulfone 3 is replaceable by hydrogen to give sulfone 4 on being subjected to chromium(II) species in aqueous acetone\(^{29}\).

\[
\text{Cr(II)/aq acetone} \quad \text{H}^\rightarrow
\]

It is also possible to hydrogenolyze selectively one of the geminal chlorine atoms at C-7 of compound 5\(^{10}\). The bridgehead chlorines in a tetrachloronorbornyl acetal are preferentially removed by treatment with an excess of Kochi reagent\(^{31}\).

\[
\text{Cr(II)/Ac} \quad \text{H} \rightarrow
\]

The titanium(IV) chloride/2 lithium aluminum hydride\(^{32}\), titanium(III) chloride/3 tetrahydrofuran/magnesium\(^{33}\), and titanocene dichloride/magnesium\(^{34}\) systems are also useful for replacing halogen atoms in organic molecules by hydrogen atoms. Hydrodehalogenation of alkyl halides\(^{35}\) has been effected also with M^+Mo_2H_4(CO)_{10}. Acetyl chloride is reduced to acetaldehyde under these conditions.

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The anionic vanadium carbonyl hydride \( \eta^2-C_5H_5)VH(CO)_5 \) effects halogen replacement\(^{38} \) with hydrogen in various alkyl (primary, secondary, and tertiary), vinyl, and acyl halides at room temperature. gem-Dihalo cyclopropanes undergo monodehalogenation. Rate, stereochemical, and trapping evidence indicate that short-lived organic radicals are involved in a chain process.

Dichlorocarbene is generated\(^{37} \) by treating carbon tetrachloride with titanium(IV) chloride/lithium aluminum hydride. The adducts with alkenes are obtained in 60–82 % yield.

By a similar mechanism, the chromium(II) species\(^{38} \) obtained from the reaction of chromium(III) chloride and lithium aluminum hydride in tetrahydrofuran readily transforms gem-dibromo cyclopropanes into alkenes.

Phenyllallene\(^{38} \):

The chromium(II) reagent is formed by treatment of anhydrous chromium(III) chloride (834 mg, 5.2 mmol) in tetrahydrofuran (5 ml) with lithium aluminum hydride (98.8 mg, 2.6 mmol) portion-wise at 0 °C. After stirring for 10 min at room temperature, the solvent is replaced with dimethylformamide (5 ml), followed by addition of 1,1-dibromo-2-phenylcyclopropane (289 mg, 1.0 mmol). The mixture is stirred for 4 hr at room temperature to afford, after extractive workup, phenylallene; yield: 75 mg (62%); b.p. 80–95 °C/20 torr (Kugelrohr).

Vicinal dibromides are readily converted into oleins on treatment with chromium(II)\(^{38} \). A potentially useful result is indicated in the debromination of stigmasteryl acetate tetra bromide to furnish stigmasteryl acetate 22,23-dibromide even in the presence of excess reducing agent.

Stigmasteryl Acetate 22,23-Dibromide\(^{39} \):

A suspension of stigmasteryl acetate tetrabromide (8 g) in acetone (500 ml) at 34 °C under carbon dioxide is treated with 1 normal chromium(II) chloride solution (140 ml) for 5 hr at 25–30 °C. Diluting with water (200 ml) and filtering gives a white powder (5.9 g) which is redissolved in benzene (30 ml), filtered, and then diluted with 95 % ethanol (80 ml) to afford the product; yield: 3.9 g, m.p. 211–213 °C. A second crop weighing 0.2 g (m.p. 207–210 °C) is also obtained; total yield: 95 %.

The homogeneous reaction of vic-dihalides with chromium(II) sulfate in aqueous dimethylformamide is rapid\(^{40} \). Allenes and appropriately substituted alkynes which are inert to chromium(II) can thus be secured.

Other \( \beta \)-haloethyl derivatives are also fragmented under the influence of bis[ethylenediamine]chromium(II) at room temperature to afford ethene quantitatively.

The elimination has been employed in a synthesis of precalciiferol-3\(^{42} \) and A\(^{211} \)-steroids\(^{43} \) from the corresponding halohydrins, and 2,3-anhydroribo nucleosides\(^{44} \) from \( \beta \)-halo-2\(_2\)-O-acetoxy precursors.

Bis[\( \eta^2 \)-cyclopentadienyl]dinitrosylchromium] \( [\eta^2-C_5H_5Cr(NO)\_2] \) converts vic-dihaloalkanes to alkenes in refluxing tetrahydrofuran\(^{45} \). Low-valent titanium species generated by mixing titanium(III) chloride and lithium aluminum hydride efficiently removes halogen atoms from vic-dihalides\(^{46} \) and converts bromo hydrides to oleins\(^{47} \). The reaction is nonstereospecific.

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Cyclopropane formation can be effected by chromium(II) reduction of 1,3-diodopropanes. This reagent shows higher specificity than tributylstannane or lithium aluminum hydride.

\[
\text{H}_2\text{C} = \text{CH}_2 \xrightarrow{\text{Cr(II)}} \text{H}_2\text{C} - \text{CH}_3 + \text{H}_2\text{C} - \text{CH}_3 + \text{Br} - \text{CH}_2
\]

A chromium(II)-induced stereospecific fragmentation of a 1,4-bromomesylate has been observed.

\[
\begin{align*}
\text{Br} & \quad \text{MesO} \\
\text{MesO} & \quad \text{[en]Cl}_2\text{CrIII}_2\text{H}_2\text{C} - \text{C} - \text{O} - \text{NCH}_2 \text{H}_2 \text{H}_2
\end{align*}
\]

Benzyl halides undergo reductive dimerization on reaction with the following reagents: (1) chromium(III) chloride/lithium aluminum hydride, (2) bis[η-cyclopentadienyldinitrolylchromium] [η-C,5H2Cr(NO2)3], (3) vanadium(III) chloride/lithium aluminum hydride, (4) vanadium(III) chloride/lithium hexacarbonyl, (5) vanadocene, and (6) molybdenum hexacarbonyl. Similar coupling of allylic halides may be accomplished with reagents (1), (3), and (4), but not with (2).

The allylicromium species, formed in situ, attack aldehydes and ketones in the presence of ester and cyano groups. The high stereoselectivity and chemoselectivity are synthetically valuable. The more highly substituted carbon atoms of unsymmetrical allyl units would become attached to the carbonyl. Since allyl halides are more reactive toward chromium(II), allyl, aryl, and vinyl halogen atoms may be retained if they are present in the same molecules.

* A kinetic study of the coupling with dichlorотетракис[пирidine]-
  vanadium has been reported.


Artemisia Alcohol

Chromium(III) chloride (4.28 g; 27 mmol) is reduced with lithium aluminum hydride (0.513 g, 13.5 mmol) in tetrahydrofuran (20 ml). After stirring at room temperature for 10 min, 3-methyl-2-butenal (0.56 g, 6.1 mmol) and then prenyl bromide (2.01 g, 13.5 mmol) in tetrahydrofuran are added dropwise during 20 min. Workup after 3 h gives an oil which is identified as artemisia alcohol; yield: 0.90 g (88%); b.p. 97-100°/4 torr (Kugelrohr).

Concerning the stereoselectivity of the reaction, it has been subsequently determined that the threo product is formed. Maintenance of minimal non-bonded interactions in the transition state is the governing factor.

z-Bromoketones are convertible to the parent ketones using chromium(III) chloride/lithium aluminum hydride, simple chromium(II) salts (2,4,6-trimethylpropionophenone 93%); 3,12-diacetoxynor-
cholanyl phenyl ketone 80%, titanium(III) chloride,9,56, and vanadium(II) chloride.7 The final step of a muscone synthesis58 involves removal of a chlorine alpha to the ketone group with chromium(II).

Methyl ketones are produced together with varying amounts of the aldol condensation products53 from treatment of 2-halomethyl ketones with molybdenum hexacarbonyl in dimethoxyethane. Chromium and tungsten hexacarbonyls are less effective reagents.

\[
R - CO - CH_2 - X \xrightarrow{\text{Me,COD/toluene}} R - CO - CH_3 + R - CO - CH = C \sim \text{CH}_3
\]

\[\beta\]-Phorone is the major product from the reduction of 4-bromoisothisporone.59 Such allylic bromine atoms can be selectively removed in the presence of an alkyl iodide.60

\[
\begin{array}{c}
\text{H}_3\text{C} - \text{Br} \\
\text{O} - \text{CH}_3
\end{array}
\xrightarrow{\text{CrCl}_2} \begin{array}{c}
\text{H}_3\text{C} - \text{CH}_3 \\
\text{O} - \text{CH}_3
\end{array}
\]

5,9-Cyclosteroids may be formed by treatment of 9β-bromo-4α,3-oxo steroids with chromium(II) ion.61

Quantitative yields of hydrocarbons are obtained from bisethyleneamine chromium(II) reaction with vinyl and aryl halides.44 In the case of α-diodo-benzene, the intermediacy of benzene has been excluded by the fact that iodo-benzene is produced efficiently when less than stoichiometric amounts of the reagent are added. Interestingly, 9-chloroaurocine has been coupled by chromium(II) salts in acetic acid to give 9,9-biaceclidine.62

Recently it has been found that the mixture of sodium hydride, sodium t-pentoxide and a heavy metal salt is a convenient dehalogenating agent.51 Low-valent metal species may be involved. Typical yields of naphthalene from reduction of 1-bromonaphthalene in dimethoxyethane at 60° are: 75% [chromium(II) chloride], 70% [molybdenum(V) chloride], 72% [bis(cyclopentadienyl)titanium(II) chloride], and 80% [tungsten(VI) chloride], with respect to the added metal salts.

Reaction of N-arylhydroxyl chlorides with chromium(II) chloride in ether leads to \(\alpha,\beta\)-unsaturated aldehydes.64

\[
\begin{array}{c}
\text{C}_6\text{H}_5\text{CH} = \text{CHO} > 80% \\
\text{C}_6\text{H}_5\text{CH} = \text{CH} = \text{CHO} > 80% \\
\text{C}_6\text{H}_5\text{CH} = \text{CH} = \text{CHO} 50% \\
\text{C}_6\text{H}_5\text{CH} = \text{CH} = \text{CHO} > 50% \\
\text{C}_6\text{H}_5\text{CH} = \text{CH} = \text{CHO} \text{ CHO} 30% \\
\text{C}_6\text{H}_5\text{CH} = \text{CH} = \text{CHO} \text{ CHO} 25-30% \\
\end{array}
\]

R - CH = CH - C = N - Ar \xrightarrow{\text{CrCl}_2/\text{ether}} R - CH = CH - CHO

Saturated aldehydes cannot be prepared in this fashion.

N-Haloamides are readily reduced by chromium(II), vanadium(II), and titanium(III) chlorides. In the presence of an alkene, adducts are formed. The addition proceeds in the anti-Markownikoff sense, as expected from a free radical pathway. Products with cis stereochemistry generally predominate. In certain cases, adducts devoid of halogen are also obtained.

[Diagram]

\[
\begin{array}{c}
\text{H} \\
\text{CH}_3
\end{array} + \text{Cl} - \text{NH} - \text{CO} - \text{C}_2\text{H}_5 \xrightarrow{\text{CrCl}_2} \begin{array}{c}
\text{H} \\
\text{CH}_3
\end{array} + \text{Cl} - \text{NH} - \text{CO} - \text{C}_2\text{H}_5
\]

Intramolecular addition of N-chloramine to a proximate alkenic linkage has been studied. An application of this cyclization to complex molecule synthesis is illustrated in the work related to dendrobine.65,66
found to be identical with those species prepared by the Gomberg procedure. Furthermore, dimers were isolated after storage.

Table 2. Hydrohalogenation of $\alpha$-Haloketones $^{55,56}$

<table>
<thead>
<tr>
<th>$\alpha$-Haloketone</th>
<th>Product</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-bromooxocetophene</td>
<td>acetophenone</td>
<td>100</td>
</tr>
<tr>
<td>2,4-dibromooxocetophene</td>
<td>oxocetophenone</td>
<td>98</td>
</tr>
<tr>
<td>desyl chloride</td>
<td>oxocetophenone</td>
<td>98</td>
</tr>
<tr>
<td>2-bromocycloheptanone</td>
<td>cycloheptanone</td>
<td>95</td>
</tr>
<tr>
<td>2-bromocyclocodecanone</td>
<td>cyclooctadecanone</td>
<td>90</td>
</tr>
<tr>
<td>(-)-$\pm$-bromocamphor</td>
<td>(-)-camphor</td>
<td>84</td>
</tr>
<tr>
<td>2-chlorocamphor</td>
<td>noncamphor</td>
<td>84</td>
</tr>
<tr>
<td>3-bromo-4-heptanone</td>
<td>-4-heptanone</td>
<td>88</td>
</tr>
</tbody>
</table>

4. Carbocations

Stable carbocations which are in the isolated salt form or generated by ionization of alcohol precursors undergo one-electron reduction by chromium(II) and vanadium(II) ions $^{69}$. For practical reasons, vanadium(II) ion has proved to be the reagent of choice.

The persistent free radical products from such reductions have been fully characterized and were

\[ \text{C}_6\text{H}_5-\text{CH}_2-\text{N}^{\ominus} \overset{\text{Cl}^{-}}{\longrightarrow} \text{C}_6\text{H}_5-\text{CH}_2-N^{\ominus} \]

**sym-Tetraphenylethane and "hexaphenylethane"** are produced by exposing benzhydryl and trityl alcohol, respectively, to acidic vanadium(II) chloride $^{70}$.

\[ 2 \text{C}_6\text{H}_5\text{CH}-\text{OH} \rightarrow \text{C}_6\text{H}_5\text{CH}-\text{CH}(\text{C}_6\text{H}_5)_2 \]

Isocyclic carbocation $^{71}$ indicates that "free" cations are reduced by chromium(II) by an outer-sphere mechanism with rate constants directly dependent on free energy differences between the cations and the free radicals. On the other hand, covalent halides are reduced via an inner-sphere process, with halide transfer from carbon to chromium. Second-order rate constants of $N$-methylacridinium, 2,4,6-triphenylpyrylium, sesquixanthylum, tropylidium, flavylium, 9-phenylxanthylum, and 9-phenylthioxanthylum reduction span a range of $10^4$.

---

The reducibility of N-alkylpyridinium ions by chromium(II) species is an apparent anomaly according to their one-electron reversible polarographic reduction potential in aqueous solution.

Preparatively, bitropyl and sym-tetrazenoibitorpypyl are conveniently synthesized by mixing aqueous tropylum solutions with vanadium(II) chloride or chromium(II) chloride. A series of substituted cyclopropenium ions have been converted to the dimers. Tri-n-propylcyclopropenium ion is resistant to chromium(II) reduction even at 125°, however.

\[
\begin{array}{ccc}
\text{R}^1 & \text{R}^2 & \text{Reaction} \\
\text{Ch}_{3} & \text{C}_6\text{H}_5 & 25° \quad 100 \quad 0 \\
\text{C}_6\text{H}_5 & \text{n-C}_3\text{H}_7 & 75° \quad 100 \quad 0 \\
\text{n-C}_3\text{H}_7 & \text{n-C}_3\text{H}_7 & 125° \quad 50 \quad 50 \\
\end{array}
\]

Bitropyl:
To a solution of tropylum tetrabutylborate (1.0 g) in water (10 ml) ~1 molar vanadium(II) chloride (20 ml) is added with stirring. The mixture is immediately filtered, the solid washed with water, and recrystallized from pentane to give bitropyl; yield: 0.5 g (98%); m.p. 60°.

Sodium bis[diglyme]hexacarbonylvandate(1-) reduces 1,3-dithiole compounds to 2,2'-bi(1,3-dithioly).  

5. Alcohols
Deoxygenating coupling of an alcohol to a hydrocarbon is a synthetically valuable process. A scheme has been devised in which metallic potassium is used to dechlorinate dialkoxytitanium dichlorides [from titanium(IV) chloride + 2 sodium alkoxide] and the resultant titanium(II) alkoxides are then decomposed by heating (100-140°) to yield the hydrocarbons. In this manner the following substances have been prepared: bibenzyl 51%, biallyl 38%, squalene 38%.

A milder and more efficient procedure was developed later. The coupling reagent is formed by mixing titanium(III) chloride with 3 mol of an organolithium compound at ~78° in dimethoxyethane. Treatment of an allyl alcohol (2 equiv.) with the reagent for a few minutes, raising the temperature to room temperature, and eventually to reflux, serve to accomplish the dimerization. By employing one of the alcohols in large excess, preparatively useful yields of the cross-coupling products may be attained.

The Ti(II) reagent developed by McMurry [titanium(III) chloride/lithium aluminum hydride] brings about coupling of benzyl and allylic alcohols very efficiently. The degree of substitution at the carbinoic carbon does not seem to affect the reaction. An intramolecular version of this reaction is observed in the formation of a mixture of cis- and trans-1,2-diphenylicyclopropane.

An unusual hydrogenolysis of the propargylic hydroxy group in 2-methyl-3-hexyne-2,5-diol has been observed. Chromium(II) sulfate reduction of this compound leads to three products in a combined yield of 70%.
On the other hand, the double bond of the $\alpha$-hydroxyallene shown below suffers reduction on treatment with chromium(II) sulfate$^{83}$.

![Chemical structure]

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{C}<em>8\text{H}</em>{14}-\text{CH}_2-\text{OH}$</td>
<td>$\text{C}<em>8\text{H}</em>{14}-\text{CH}_2-\text{CH}_2-\text{C}_6\text{H}_5$</td>
<td>78</td>
</tr>
<tr>
<td>$\text{C}<em>8\text{H}</em>{14}-\text{CH}_2-\text{OH}$</td>
<td>$\text{C}<em>8\text{H}</em>{14}-\text{CH}_2-\text{CH}_2-\text{C}_6\text{H}_5$</td>
<td>68</td>
</tr>
<tr>
<td>$\text{C}<em>8\text{H}</em>{14}-\text{C}_6\text{H}_5$</td>
<td>$\text{C}<em>8\text{H}</em>{14}-\text{C}_6\text{H}_5$</td>
<td>87</td>
</tr>
</tbody>
</table>

Table 3. Reductive Coupling of Alcohols with the Titanium(III) Chloride/Lithium Aluminum Hydride Reagent$^{83}$

Deoxygenative Coupling of Alcohols$^{85}$:
A suspension formed by mixing titanium(III) chloride (2.3 g, 15 mmol) and lithium aluminum hydride (0.19 g, 5 mmol) in dry glyme (70 ml) under nitrogen is treated with the substrate alcohol (5 mmol) in several ml of glyme. After being heated under reflux for 16 h, the mixture is cooled, quenched with dilute acid, and extracted with ether. The ether extract is washed with sodium chloride solution and worked up; yield: 68 - 95\%.

$\beta$-Hydroxyethyl phenyl sulfides and benzoates are defunctionalized to afford alkenes$^{84,85,86}$ by the action of low-valent titanium species in the presence of a tertiary amine.

![Chemical structure]

Tertiary alkyl hydroperoxides are reduced$^{87}$ instantaneously by two equivalents of chromium(II) salts in aqueous solution to a mixture of alcohols, ketones, and alkenes; the latter compounds are formed in equimolar amounts. Aliphatic diacyl peroxides are also readily converted to alkenes, carbon dioxide, and carboxylatochromium(II) salts.

$$(\text{R-COO})_2 + 2 \text{Cr(II)} \rightarrow \text{R-H} + \text{R-COOCr(III)} + \text{CO}_2$$

6. Ethers

Active oxiranes such as styrene oxide and $\alpha,\beta$-epoxyketones are deoxygenated on treatment with chromium(II) chloride$^{88}$. The reaction has found practical uses in the steroid field$^{89}$ and during structural elucidation of limonoid triterpenes$^{90}$. Under milder conditions [e.g. with chromium(II) acetate/aqueous acetic acid], $\beta$-hydroxy ketones may be isolated$^{91}$.

When unactivated oxiranes are exposed to chromium(II) solutions side reactions may become serious. Thus, cyclohexene oxide yields the corresponding chlorohydrin on treatment with chromium(II) chloride. However, the use of Kochi's reagent obviates this difficulty, although the reduction rate is still quite slow. Generation of ethene, cyclohexene, and styrene in good yield has been reported$^{92}$.

The McMurry complex is capable of transforming oxiranes into alkenes$^{92}$. The non-stereospecificity of the reaction suggests that a free radical mechanism operates.

Table 4. Conversion of Oxiranes to Alkenes using 4 Titanium(III) Chloride/Lithium Aluminum Hydride Reagent$^{92}$

<table>
<thead>
<tr>
<th>Oxirane</th>
<th>Yield [%] of Alkene</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-methylstyrone oxide</td>
<td>36</td>
</tr>
<tr>
<td>cyclooctene oxide</td>
<td>53</td>
</tr>
<tr>
<td>1-dodecene oxide</td>
<td>69</td>
</tr>
<tr>
<td>1-decene oxide</td>
<td>65</td>
</tr>
<tr>
<td>cholesterol oxide</td>
<td>75</td>
</tr>
<tr>
<td>(Z)-5-decene oxide</td>
<td>70 (4: 1: E: Z)</td>
</tr>
<tr>
<td>(E)-5-decene oxide</td>
<td>70 (4: 1: E: Z)</td>
</tr>
</tbody>
</table>


Oxiranes are also deoxygenated by treatment with titanocene\textsuperscript{8a}. It should be noted that the alkenes suffer further reduction to afford the alkanes, e.g., 1-decene oxide → n-decane 68-81%; (E)-2-decene oxide → n-decane 58-8%; 2-methyl-1-undecene oxide → 2-methylundecane 52%; x-pinene oxide → cis-pinane 10-5%.

Low-valent tungsten species generated by reacting tungsten(VI) chloride with either alkylithium, lithium metal dispersion, or lithium iodide, are efficient deoxygenating agents for oxiranes\textsuperscript{84}. Note that this is a two-electron process giving rise to products with a high degree of stereoretention.

**Reaction of (E)-Cyclooctadecene Oxide with Low-Valent Tungsten Reagents\textsuperscript{86}:**

To a suspension of tungsten(VI) chloride (60 g) in dry tetrahydrofuran (420 ml), under stirring at \(-62^\circ\)C is slowly added an n-butylithium solution (0.3 mol/l in hexane) over 5 min. After gradual warming to room temperature (E)-cyclooctadecene oxide (14.8 g) is added. After 0.5 h the mixture is poured into an aqueous solution, 1.5 mol in sodium tetratrate and 2 mol in sodium hydroxide (600 ml) and extracted with hexane. The organic layer is dried, concentrated, and the residue distilled to afford cyclooctadecene: yield: 12.7 g (94%).

Oxiranes undergo molybdenum hexacarbonyl-catalyzed rearrangement\textsuperscript{95} to carbonyl compounds. Frequently alkenes are obtained as by-products.

\[ \text{C}_8\text{H}_{16} \rightarrow \text{C}_8\text{H}_{16} + \text{CH}_2 = \text{CH}_2 + \text{CO}_2 + \text{Mo(CO)}_5 \]

Upon cocondensation in a metal atom reactor with first row transition elements including titanium, vanadium, and chromium, oxiranes are deoxygenated\textsuperscript{96}. Under similar conditions, dibenzyl ether forms the bis[arene]chromium complex, and dibenzyl sulfide undergoes mainly desulfurization\textsuperscript{97}.

\[ \text{C}_6\text{H}_{12} - \text{O} - \text{CH}_2 - \text{C}_6\text{H}_{15} + \text{Cr}(I) \]

\[ \text{CH}_2 - \text{O} - \text{CH}_2 - \text{C}_6\text{H}_{15} \]

\[ \text{C}_6\text{H}_{12} - \text{S} - \text{CH}_2 - \text{C}_6\text{H}_{15} + \text{Cr}(I) \]

\[ \text{C}_6\text{H}_{12} - \text{CH}_2 - \text{C}_6\text{H}_{12} - \text{C}_6\text{H}_{15} + \text{Cr}(I) \]

**7. Carbonyl Compounds**

Aromatic aldehydes give hydrobenzoins on reaction with acidic chromium(II) or vanadium(II) chlorides\textsuperscript{13}, whereas aliphatic \(\alpha,\beta\)-unsaturated aldehydes are dimerized to glycols. Non-conjugated aldehydes are stable toward these reagents.

\[ 2 \text{R} = \text{CH} = \text{CH} = \text{CHO} \rightarrow \text{R} = \text{CH} = \text{CH} = \text{CH} = \text{OH} \]

A mechanism involving initial ligand transfer reduction of a halohydrin or a protonated hydrate of benzaldehyde has been proposed\textsuperscript{99}. The dimers arise from organochromium intermediates. It appears that formation of dimers depends on the acidity of the medium, for benzaldehyde and acetophenone undergo simple reduction to the corresponding alcohols by the action of chromium(II) sulfate in aqueous dimethylformamide\textsuperscript{100} or in aqueous ammonia\textsuperscript{101}.

It has been observed\textsuperscript{8} that ammonical titanium(III) chloride causes the production of a pinacol from flavone, but a straight-forward reduction at the carbonyl takes place in flavonones.

Corey et al.\textsuperscript{102} have developed several titanium(II) reagents for inter- and intramolecular pinacolic coupling of aldehydes and ketones. These are prepared by reaction of (a) magnesium amalgam with titanium(IV) chloride, (b) cyclopentadienyltitanium trichloride with lithium aluminium hydride, and (c) hexamethylbenzene with titanium(II) tetrachloroaluminate. Unsymmetrical pinacols can be readily synthesized using an excess of the low molecular weight carbonyl substrate.


\textsuperscript{86} T. Mukaiyama, Y. Watanabe, M. Shiono, Chem. Lett. 1974, 1523.


Using the titanium(IV) chloride/magnesium amalgam system diols have been produced from benzaldehyde (84%), n-octanal (80%), cyclohexanone (93%), cyclopentanone (95%). The yields of diols obtained from cross-coupling between acetone and various ketones (cyclopentanone 65%, cyclohexanone 76%, cycloheptanone 75%) attest to the effectiveness of the method. The following compounds have been isolated in the yields indicated by the intramolecular cyclization.

Earlier, deoxygenative condensations of carbonyl compounds to symmetrical alkynes have been reported using the different low-valent titanium reagents generated from TiCl₃/Zn₁₀₉, TiCl₃/LiAlH₄/R₃N₁₀₄, TiCl₃/THF/Mg₁⁰₅, and TiCl₃/LiAlH₄₁⁰₆. The last system has been employed to synthesize β-carotene, and some highly hindered alkynes such as tetraisopropyl₁⁰₇,₁⁰₈ and tetracosenopentylethene₁⁰₉. Typical yields of the symmetrical alkynes from the McMurry reaction are: 95% (from benzophenone), 95% (from cycloheptanone), 85% (from benzaldehyde), 85% (from adamantanone), 80% (from cyclooctadecanone), 95% (from fluorone), 85% (from p-methoxypropiofenone), 85% (from retinal).

Tetraphenylethane₁⁰₈:
Lithium aluminum hydride (1 equiv) is added to a stirred slurry of titanium(III) chloride (2 equiv) under nitrogen in dry tetrahydrofuran. After a few minutes, a solution of benzophenone (1 equiv) in tetrahydrofuran is introduced. At the end of 4 h reflux, tetraphenylethane is isolated by crystallization; yield: 95%; m.p. 220°-221°.

Reductive dimerization of 1,1'-diformylferrocene₁¹₀ using Mukaiyama's procedure₁⁰₄ furnished the dimeric dialdehyde and [2,2]-ferrocenophane-1,13-diene. Resubmitting the former adduct to the same reaction led to the ferrocenophane in fair yield (43%).

<table>
<thead>
<tr>
<th>Carbonyl Compounds</th>
<th>Yield [%] of cross-coupled alkyne</th>
</tr>
</thead>
<tbody>
<tr>
<td>adamantane + acetone (4:1)</td>
<td>63</td>
</tr>
<tr>
<td>cycloheptanone + acetone (4:1)</td>
<td>50</td>
</tr>
<tr>
<td>1-indanone + acetone (4:1)</td>
<td>71</td>
</tr>
<tr>
<td>benzophenone + acetone (4:1)</td>
<td>94</td>
</tr>
<tr>
<td>benzophenone + acetone (1:1)</td>
<td>81</td>
</tr>
<tr>
<td>benzophenone + cholestane (1:1)</td>
<td>82</td>
</tr>
<tr>
<td>benzophenone + hexanal (1:1)</td>
<td>84</td>
</tr>
<tr>
<td>benzophenone + di-tert-butyl ketone (1:1)</td>
<td>90</td>
</tr>
<tr>
<td>fluorenone + acetone (4:1)</td>
<td>84</td>
</tr>
<tr>
<td>fluorenone + acetone (1:1)</td>
<td>74</td>
</tr>
<tr>
<td>fluorenone + cycloheptanone (1:1)</td>
<td>77</td>
</tr>
<tr>
<td>fluorenone + acetophenone (1:1)</td>
<td>70</td>
</tr>
<tr>
<td>pulegone + acetone (4:1)</td>
<td>55</td>
</tr>
<tr>
<td>isophorone + acetone (4:1)</td>
<td>63</td>
</tr>
</tbody>
</table>

Table 6. Cycloalkene Formation by Carbonyl Coupling

<table>
<thead>
<tr>
<th>Cycloalkene</th>
<th>Yield [%]</th>
<th>Cycloalkene</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>C₂H₅</td>
<td>67</td>
<td>C₅H₇-n</td>
<td>68</td>
</tr>
<tr>
<td>C₃H₅</td>
<td>70</td>
<td>C₅H₇-n</td>
<td>75</td>
</tr>
<tr>
<td>C₄H₇</td>
<td>79</td>
<td>C₅H₇-n</td>
<td>76</td>
</tr>
<tr>
<td>C₅H₇</td>
<td>95</td>
<td>C₆H₈</td>
<td>76</td>
</tr>
<tr>
<td>C₆H₈</td>
<td>52</td>
<td>C₆H₈-n</td>
<td>80</td>
</tr>
<tr>
<td>C₇H₈</td>
<td>80</td>
<td>C₆H₈-n</td>
<td>80</td>
</tr>
<tr>
<td>C₈H₉</td>
<td>67</td>
<td>C₆H₈-n</td>
<td>85</td>
</tr>
</tbody>
</table>

R-CHO → R-CH₃

R¹-COOR² → R¹-CH₃ + R²-ÖH

Analogous reactions of ketones afford much lower yields of the hydrocarbons (7-25%) and correspondingly larger quantities of alcohols (up to 74%), together with recovered starting materials.

Evidence indicates that the sequence of events is: ester → aldehyde → olefin → alkane. Aromatic aldehydes and esters without z-hydrogen atoms do not give alkane products. A variety of other systems [(C₆H₅)₃C=M(OC₂H₅), (C₆H₅)₃C=O, (C₆H₅)₂C=O, C₆H₅CO₂H, (C₆H₅)₂C=O, (C₆H₅)₂Cl] have been found to be useless.

The Mo₂H(CO)₁₀ molecule is capable of reducing carbonyl compounds to alcohols, e.g. heptan-1-ol to heptanol, cyclohexene to cyclohexanol.

When carboxylic acids, an alkylithium, and titanium(III) chloride are mixed, vic-glycols are obtained in moderate yields. These products are most likely generated by coupling of the ketone hydrates.

\[ 2 \text{R}^1-\text{COOH} + 4 \text{R}²-\text{Li} \rightarrow 2 \text{R}^1-\text{C}=\text{OLi} \]

Metallic titanium prepared by dechlorination of titanium(III) chloride with potassium reduces enol phosphates to alkenes. The method is superior to that using lithium/ethyamine, and it permits regioselective synthesis of dienes from Z,β-unsaturated ketones. Generally, no over-reduction is observed, although the enol phosphate derived from isobutyrophenone is converted to isobutylibenzene very rapidly.

References:
The gas-phase chemistry of chlorotitanium ions (ClTICl) in the presence of oxygen-containing organic compounds has been examined \(^{117}\).

8. Carbonyl Derivatives

Acetals derived from aromatic aldehydes and ketones are reductively coupled on exposure to titanium(IV) chloride-lithium aluminum hydride. However, the aliphatic counterparts undergo hydrodealkoxylation \(^{118}\).

Dithioacetals are desulfurized \(^{112}\) by the reagent.

\[
\begin{align*}
\text{SCH}_2\text{CH}_2\text{S} & \xrightarrow{\text{Ti(II)} / \text{LiAlH}_4} \text{C}_6\text{H}_5\text{S} - \text{CH}_2\text{SH} - \text{C}_6\text{H}_5 \\
\end{align*}
\]

Common nitrogenous derivatives of carbonyl compounds are subject to cleavage by chromium(II) and titanium(III) ions. Chromium(II) chloride in dilute hydrochloric acid is useful for severing 2,4-dinitrophenylhydrazones of 3-oxo-steroids \(^{119}\) such as cortisone 21-acetate. The reaction fails in the cases of cholesta-1,4-diene-3-one and prednisone 21-acetate 2,4-dinitrophenylhydrazones.

Aqueous titanium(III) chloride is a more convenient reagent owing to its commercial availability. A variety of ketones have been regenerated in excellent yield from their 2,4-dinitrophenylhydrazones \(^{120}\) using glyme as solvent. It has been postulated that reductive cleavage of the 2,4-diaminophenylhydrazone intermediates to the imines is involved. The isolation of 1,2,4-triaminobenzene supports the contention.

Steroidal tosylhydrazones \(^{121}\) oximes, semicarbazones, and thiosemicarbazones \(^{122}\) are also cleaved by titanium(III) chloride at room temperature. Yields of the ketones are in the range of 80–99\%.

Oximes can be converted to the parent ketones by successive acetylation and reaction with chromium(II) acetate in aqueous tetrahydrofuran \(^{123}\). Deoxygenation of acetoximes of conjugated enones and aryl alkyl ketones occurs much more easily than that of nonconjugated ketones, in contrast to that of acid-catalyzed hydrolysis.

Since electronegative substituents alpha to a carbonyl group are removable by chromium(II) (e.g., 2-acetoxycarbonyl ketones \(^{124}\)), extension of the method makes possible the facile conversion of alkenes to ketones and the transposition of a carbonyl function.

\[
\begin{align*}
\text{CH}_3 & \xrightarrow{\text{AcO} / \text{Cr(II)}} \text{N}=\text{O} \\
\text{C}_6\text{H}_5-\text{CO}-\text{CH}_2-\text{CH}_3 & \xrightarrow{\text{R} \rightarrow \text{NO/CH}_2\text{NH} / \text{Ac-O} / \text{Cr(II)}} \text{C}_6\text{H}_5-\text{CH}_2-\text{C}=\text{CH}_3 \\
\end{align*}
\]


Table 8. Conversion of Oxime Acetates to Ketones using Chromium(II) Acetate\(^{123}\)

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Reaction conditions (time/temperature)</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclohexanone</td>
<td>4.5 h, 65(^\circ)</td>
<td>84</td>
</tr>
<tr>
<td>phenylacetone</td>
<td>16 h, 65(^\circ)</td>
<td>74</td>
</tr>
<tr>
<td>camphor</td>
<td>11 h, 65(^\circ)</td>
<td>88</td>
</tr>
<tr>
<td>propiophenone</td>
<td>24 h, 65(^\circ)</td>
<td>80</td>
</tr>
<tr>
<td>2-methyl-2-cyclohexenone</td>
<td>48 h, 25(^\circ)</td>
<td>80</td>
</tr>
<tr>
<td>progesterone 20-monooxime</td>
<td>24 h, 25(^\circ)</td>
<td>84</td>
</tr>
</tbody>
</table>

\(^{123}\) Propiophenone oxime \(\text{O-acetate (193 mg, 1.0 mmol)}\) and excess chromium(II) acetate (1 g) are stirred in 9:1 tetrahydrofuran:water (10 ml) at 25\(^\circ\) for 24 h. The reaction mixture is then exposed to air to oxidize the excess reagent. Evaporation of most of the solvent under reduced pressure, washing with dilute acid and base, and concentration affords after distillation 80-90\% pure propiophenone; yield: 80%.

It is possible to deoxygenate oximes to imines with aqueous titanium(III) chloride. Sterically unhindered imines suffer rapid hydrolysis in situ to give ketones\(^{125}\). \(\alpha\)-Halo oximes afford halogen-free ketones directly on treatment with the reagent\(^{55}\).

In an asymmetric synthesis of 19-norsteroids, cleavage of oxime derivatives\(^{126}\) with chromium(II) or titanium(III) chlorides proceeds in good yields. The free carboxyl group in these derivatives is essential, for the corresponding methyl esters are not reduced.

\[\text{H3C} \quad \text{C} \quad \text{N} \quad \text{O} \quad \text{CH} \quad \text{COOH} \quad \text{CrCl}_2 \text{ or TiCl}_3 \]

In a recent investigation, deoximation was achieved by a molybdenum(III) reagent\(^{127}\) generated from the reaction of molybdenyl chloride with zinc dust. Both aldehydes and ketones have been obtained in high yield using this reagent.

Treatment of oximes with chromium(II) or titanium(III) acetate in acetic anhydride/dimethylformamide leads to enamides\(^{128}\). This transformation may be more conveniently performed in an acetic anhydride/pyridine mixture under reflux.


Table 9. Formation of Enamides from Oximes\(^{128}\)

<table>
<thead>
<tr>
<th>Oxime of</th>
<th>Reagent</th>
<th>Temp.</th>
<th>Time</th>
<th>Yield [%] of Enamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>5α-cholestan-3-one</td>
<td>Cr(OAc)(_2)</td>
<td>80(^\circ)</td>
<td>20 h</td>
<td>74</td>
</tr>
<tr>
<td>cyclohexanone</td>
<td>Cr(OAc)(_2)</td>
<td>22(^\circ)</td>
<td>20 h</td>
<td>82</td>
</tr>
<tr>
<td>butan-2-one</td>
<td>Ti(OAc)(_2)</td>
<td>32(^\circ)</td>
<td>5 h</td>
<td>80</td>
</tr>
<tr>
<td>5α-lanost-8-en-3-one</td>
<td>Cr(OAc)(_2)</td>
<td>50(^\circ)</td>
<td>7 h</td>
<td>64</td>
</tr>
<tr>
<td>isopent-2-one</td>
<td>Cr(OAc)(_2)</td>
<td>22(^\circ)</td>
<td>25 h</td>
<td>66</td>
</tr>
<tr>
<td>isoazopirone</td>
<td>Cr(OAc)(_2)</td>
<td>22(^\circ)</td>
<td>17 h</td>
<td>70</td>
</tr>
<tr>
<td>2-methylcyclohexanone</td>
<td>Cr(OAc)(_2)</td>
<td>22(^\circ)</td>
<td>18 h</td>
<td>58 + 26(^a)</td>
</tr>
<tr>
<td>2,2-dimethylcyclohexanone</td>
<td>Cr(OAc)(_2)</td>
<td>80(^\circ)</td>
<td>50 h</td>
<td>57</td>
</tr>
</tbody>
</table>

\(^{a}\) Mixture of 3 products.

\(^{b}\) Trisubstituted enamide predominant.

9. Nitro Compounds

The report of oxime deoxygenation\(^{125}\) by titanium(III) chloride apparently spurred the investigation of McMurtry and Melton\(^{129}\) in realizing a nitro to carbonyl transformation. The high efficiency of this mild procedure opened up new vistas in the synthetic utility of aliphatic nitro compounds, which, on the basis of the reaction, could serve as acyl anion equivalents. The following equations illustrate an application to the synthesis of cis-jasmonate\(^{129}\).

\[
\text{O}_2\text{N} + \text{C}_3\text{H}_7\text{CH} = \text{C} = \text{CH}_2 + \text{H}_2\text{C} = \text{CH} = \text{C} = \text{CH}_3 \rightarrow \text{C}_3\text{H}_7\text{CH} = \text{C} = \text{C} = \text{C} = \text{CH}_3 + \text{H}_3\text{C} \text{CHO} \\
\text{CH}_3 \text{CH} = \text{C} = \text{CH}_3 + \text{Ti}^{III} \rightarrow \text{CH}_3 \text{CH} = \text{C} = \text{C} = \text{CH}_3 + \text{H}_2
\]

Cyclohexenones are easily obtained by a sequence of Diels-Alder reaction and titanium(III) reduction/
hydrolysis. If cyclohex-3-enones are desired, or other acid sensitive functions are present, the reduction is best carried out by treatment of the nitronate anions with buffered titan(III) chloride.

The reduction mechanism is outlined in the accompanying scheme.

Reduction of Non-Aromatic Nitro Compounds with Titan(III) Chloride; General Procedures:
Method A: Reduction with aqueous titan(III) chloride at pH 1: A 0.2 molar solution of the alkyl nitro compound in tetrahydrofuran or dimethylformamide is treated with a 20% aqueous commercial titan(III) chloride solution (4 equiv) and stirred under nitrogen at room temperature. The reaction mixture is then poured into ether and separated into phases. The aqueous phase is extracted several times with ether; the organic extracts are combined, washed with 5% sodium hydrogen carbonate and with sodium chloride, then dried, concentrated, and distilled.

Method B: Reduction with aqueous titan(III) chloride at pH 5: A buffered titan(III) chloride solution is prepared by adding ammonium acetate (46g, 60mmol) in water (15ml) to 20% aqueous titan(III) chloride (10mmol) under nitrogen. The nitro compound in an appropriate solvent is rapidly added and the mixture is stirred at room temperature. Product isolation is carried out described above.

Method C: Reduction of sodium nitronates with aqueous titan(III) chloride at pH 5: The nitro compound is dissolved in methanol to give a 0.5 molar solution and treated with sodium

Table 10. Reaction of Nitro Compound with Aqueous Titan-um(II) Chloride at pH < 1

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂CNO₂CH₃</td>
<td>H₂CCONO₂CH₃</td>
<td>85</td>
</tr>
<tr>
<td>C₆H₅CHO.NO₂</td>
<td>C₆H₅CHO</td>
<td>80</td>
</tr>
<tr>
<td>NO₂</td>
<td></td>
<td>55</td>
</tr>
<tr>
<td>H₂CNO₂CH₂CN</td>
<td>H₂CCONCN</td>
<td>55</td>
</tr>
<tr>
<td>H₂CNO₂CH₂COOH</td>
<td>H₂CCONH₂COOH</td>
<td>40</td>
</tr>
<tr>
<td>H₂CNO₂CH₂COOCH₃</td>
<td>H₂CCONH₂COOCH₃</td>
<td>40</td>
</tr>
<tr>
<td>n-C₃H₇CHO.NO₂</td>
<td>n-C₃H₇CHO</td>
<td>35</td>
</tr>
<tr>
<td>n-C₃H₇CHO.CH₂CH₂n</td>
<td>n-C₃H₇CHO.CH₂CH₂n</td>
<td>74</td>
</tr>
</tbody>
</table>

Table 11. Reaction of Nitronates with Titan(III) Chloride/Ammonium Acetate at pH 6

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂CNO₂CH₃</td>
<td>H₂CCONO₂CH₃</td>
<td>70</td>
</tr>
<tr>
<td>H₂CNO₂CH₂COOH</td>
<td>H₂CCONH₂COOH</td>
<td>90</td>
</tr>
<tr>
<td>H₂CNO₂CH₂COOCH₃</td>
<td>H₂CCONH₂COOCH₃</td>
<td>90</td>
</tr>
<tr>
<td>n-C₃H₇CHO.NO₂</td>
<td>n-C₃H₇CHO</td>
<td>45</td>
</tr>
<tr>
<td>C₆H₅CHO.CH₂CH₂NO₂</td>
<td>C₆H₅CHO.CH₂CH₂NO₂</td>
<td>70</td>
</tr>
</tbody>
</table>

132 J. R. Hanson, E. Premuzic, Tetrahedron 23, 4105 (1967).
methoxide (1 equiv). A buffered titanium(II) chloride/ammonium acetate solution prepared as in Method B is then added in one portion to the sodium nitrate solution at room temperature under nitrogen atmosphere. After an appropriate period, the reaction is worked up.

Reduction of conjugated nitroolefins such as 1-nitrocyclooctene in the presence of an alkoxide base (RO"\textsuperscript{−}) leads to \(\gamma\)-alkoxy ketones.

\[
\begin{array}{c}
\text{NO}_2^- \quad \text{RO}^\text{−} \quad \text{TiCl}_4 \\
\text{slow} \quad \text{fast} \quad \text{fast}
\end{array}
\]

The titanium(III) reduction can be utilized in the preparation of certain \(\alpha,\beta\)-unsaturated aldehydes\(^{136}\).

\[
\begin{array}{c}
\text{CHO} \quad \text{NO}_2^- \quad \text{TiCl}_4 \\
\end{array}
\]

At low pH values, vanadium(II) chloride also converts primary and secondary nitro groups to carbonyls\(^{131}\) in moderate yield.

Only a few examples of chromium(II) reduction of aliphatic nitro compounds have been studied. 6-Nitrocholesteryl acetate has been reduced to 5a-hydroxy-6-oximinocholesteryl acetate in 80% yield with chromium(II) chloride in refluxing tetrahydrofuran; the 5a-chloro-6\(\beta\)-nitro derivative gives the same type of product\(^{132}\).

\(\omega\)-Nitrocamphene undergoes ring expansion to afford the \(\gamma\)-ketol in 78% yield\(^{133}\). It is likely that the nitroso intermediate is hydrated in situ, and the hydroxy oxime then undergoes further reduction of hydrolysis to the corresponding hydroxy aldehyde. Finally, ring enlargement and isomerization ensues.

Previously, it has been shown that zinc dust reduction of \(\omega\)-nitrocamphene gives rise to tricyclencaldehyde\(^{134}\).

The long delay in the study of reduction of aliphatic nitro compounds by low-valent metal ions is due mainly to the relative inaccessibility of the substrates. On the other hand, nitroaromatics had been subjected to reaction with titanium(III) chloride\(^{135}\), chromium(II) chloride\(^{136}\), and vanadium sulfate\(^{137}\) much earlier and more thoroughly. All three metal ions effect total transformation of nitroarones to amines.

\[
\begin{array}{c}
\text{Ar}=\text{NO}_2^- + 6 \text{M}^\times + 6 \text{H}^\text{+} \\
\end{array}
\]

The kinetics of titanium(III) reduction of aromatic nitro compounds have been examined\(^{138}\). The active species were thought to be ArNO\(_3\)H\(^{+}\) and a hydrolyzed form of titanium(III).

There has been a report on the use of molybdenum(III) ion to reduce aromatic nitro compounds such as trinitrophenol\(^{139}\). More recently, a convenient procedure for converting nitroaromatics directly to anilides has been developed\(^{140}\).

\[
\begin{array}{c}
\text{Ar}=\text{NO}_2^- + \text{HO}^- + \text{Co(CO)}_\text{II} \\
\end{array}
\]

Reductive Acylation of Nitroarones\(^{140}\): A mixture of a nitroarene (5 mmol) and molybdenum hexacarbonyl (2.64 g, 10 mmol) in a carboxylic acid (5 ml) is heated under nitrogen at 120° for 20 h. The sublime molybdenum hexacarbonyl is returned to the liquid phase during the reaction by occasional swirling. The cooled reaction mixture is neutralized with dilute ammonia, extracted with ether, and the extracts are dried, evaporated to give a solid product. Recrystallization of the solid affords the anilide; yield: 46−85%.

Aniline is obtainable from the reaction of nitrobenzene\(^{35}\) with either M\(_2\)Mo\(_2\)(CO)\(_{10}\) or M\(_2\)Mo\(_3\)(CO)\(_{14}\). The latter reagent is generated by reaction of molybdenum hexacarbonyl with a metal borohydride.

Oxygen abstraction\(^{141}\) from nitro- and nitrosoarenes has also been observed upon condensation with atomic chromium.

\[^{137}\text{B. C. Banerjee, J. Ind. Chem. Soc. 19, 30 (1942).}
\[^{138}\text{S. A. Newton, Jr., F. J. Stubbins, C. Hinselwood, J. Chem. Soc. 1953, 3384.}
\[^{139}\text{M. V. Gapchenko, Zavodsk. Lab. 10, 245 (1941); C. A. 35, 7312 (1941).}
\[^{140}\text{T.-L. Ho, J. Org. Chem. 42, 3755 (1977).}
\[^{142}\text{E. Knecht, E. Hibbert, Ber. Disch. Chem. Soc. 40, 3819 (1907).}
\[^{144}\text{S. Verbel, Can. J. Chem. 32, 638 (1954).}
\]
10. Other Nitrogen Compounds

Knecht observed that azo dyes decolorize titanium(III) chloride solutions immediately on contact. The stoichiometric relationship portrayed by the following equation is, however, applicable to ideal situations only.

\[ R^1-N=N-R^2 + 4 \text{Ti}^{3+} + 4 \text{H}^+ \rightarrow R^1-NH_2 + R^2-NH_2 + 4 \text{Ti}^{4+} \]

Complications arise as a consequence of the strongly acidic medium which is conductive to benzidine/semidine rearrangement. While 4,4'-dichlorobenzidine undergoes reduction normally, the 2,2'- and 3,3'-isomers consume only two mol of the reagent. In fact, benzidine/semidine rearrangement occurs even in nearly neutral solutions. The hydrazobenzene intermediates hardly have a chance to be further reduced.

Azobenzene gives anilides on reaction with molybdenum hexacarbonyl in carboxylic acid solvents. Simple reduction to hydrazobenzene is possible with the titanocene dichloride/magnesium system.

Saturation of the N≡N-multiple bonds in diazonium salts by the action of chromium(II) chloride has been described.

\[ \text{Ar}-\text{N}=\text{N} + 4 \text{CrCl}_2 + 4 \text{HCl} \rightarrow \text{Ar}-\text{NH}_2 + \text{NH}_3 + 4 \text{CrCl}_3 \]

By titration, it has been shown that benzenediazonium chloride reacts with two equivalents of titanium(III) chloride. The initially formed phenylhydrazine attacks the starting material in situ.

The diazotized product of picramic acid suffers reduction at both the nitro functions and the diazonium site when exposed to titanium(III) chloride. The structure of the product was not specified, however.

It has been claimed that phenylhydrazine can be analyzed by titanometry, despite an earlier indication of incomplete reduction of the same compound. Halogen substituents on the benzene ring also render aryldiazines resistant to titanium(III) reduction. On the other hand, nitro groups facilitate reductive cleavage of hydrazines.

\[ \text{O}_2N-\text{NH}_2 + 8 \text{TiCl}_3 + 9 \text{HCl} \rightarrow \text{H}_2\text{N}-\text{NH}_2 + 8 \text{TiCl}_4 + \text{NH}_2\text{Cl} + 2 \text{H}_2\text{O} \]

Rathsburg also claimed that picryl azide is reduced by titanium(III) chloride to 2,4,6-triaminophenyltriazine. Heterocyclic amines are obtained by treating the corresponding azides with the same reagent. Vanadium(II) chloride effects clean reduction of aryldiazides to amines (aniline 70%, p-toluidine 85%, 2,4-xylidine 76%, 4-chloroaniline 78%, 4-fluoroaniline 95%, 2-trifluoromethylaniline 78%). Reactions of aliphatic azides do not afford substantial amounts of amines.

Red-Hydro azides can be conveniently reduced to amino alcohols with chromium(II) species in acidic media. This reaction constitutes a crucial step in the conversion of 17-oxo steroids to D-homosteroids via oxiranes, hydrazine azides, and amino alcohols. This route is superior to that involving cyano hydrid formation and lithium aluminum hydride reduction.

**Arylamines from Aryl Azides**

To a solution of an aryl azide (10 g) in tetrahydrofuran (10 ml) a 1 molar aqueous solution of vanadium(II) chloride (10 ml) is added with stirring. After effervescence subsides, the mixture is poured onto aqueous ammonia (50 ml). The resultant slurry is mixed with benzene, filtered, and the filter cake washed with more benzene. The filtrate is separated into layers, and the aqueous phase further extracted. Drying, evaporation and distillation provide the amine product; yield: 70–95%.

The amino radical produced by the action of titanium(III) chloride on hydroxylamine in acid solution mediates additive dimerization with alkynes. The titanium(III) ion may be recycled through electrochemical reduction.

---

Reduction of Organic Compounds with Low-Valent Species of Group IVB, VB, and VIB Metals

\[
\begin{align*}
\text{Tl}^{\text{III}} + \text{NH}_2\text{OH} + \text{H}^\text{+} & \rightarrow \text{Tl}^{\text{IV}} + \cdot\text{NH}_2 + \text{H}_2\text{O} \\
2 \cdot\text{NH}_2 + 2\text{H}_2\text{C} & \rightarrow \\
\text{H}_2\text{N} & \rightarrow \text{H}_2\text{N} \\
\text{H}_2\text{NH}_2 & \rightarrow \text{H}_2\text{N} \cdot\text{CH}_2
\end{align*}
\]

Chemical fixation of molecular nitrogen has been a subject of intense studies. The system of van Tamelen works reasonably well and is illustrated by the following equation.

\[
\begin{align*}
\text{C}_2\text{H}_5\text{Cl} + \text{Mg} + \text{N}_2 & \rightarrow \text{C}_2\text{H}_5\text{N} \cdot\text{H}_2 \\
(0.01 \text{ mol}) & \rightarrow (80 \text{ ml} \text{ absorbed}) \\
\text{ICl}_{2}\text{C}=\text{O} & \rightarrow \text{C}_2\text{H}_5\text{N}=\text{H}_2 + \cdot[\text{C}_2\text{H}_5\text{C}]\text{NH} \\
(25-50\% \text{ based on fixed N})
\end{align*}
\]

Vol'pin et al. claimed that 1-naphthylamine is produced (2% yield) by the reaction of naphthalene, lithium, and titanium(IV) chloride in tetrahydrofuran under 100 atm nitrogen pressure. Another Russian report indicates that titanium(IV) chloride, aluminum powder, and aluminum bromide in benzene react with nitrogen (90 atm) to give 300 mmol of ammonia per mol of titanium(IV) chloride.

The V(OH)$_2$/Mg(OH)$_2$ coprecipitate shows activity for nitrogen reduction.

11. Sulfoxides

The appreciable affinity of titanium for oxygen has already been demonstrated in the facile deoxygenation of nitro and nitroso (oxime) groups. Sulfoxides are similarly reduced to sulfides by titanium(II) chloride, titanium(IV) chloride/zinc, and titanium(IV) chloride/lithium aluminum hydride.

As have often been observed in other areas, titanium(III) reactions can be effected equally well with vanadium(II) ion, sulfoxides undergo deoxygenation under the influence of vanadium(II) chloride. Several molybdenum reagents have also proven useful for the sulfoxide → sulfide transformation. These include MoOCl$_3$/Zn, MoO$_3$/H$_2$OAc, K$_2$MoCl$_6$, Cs$_3$Mo$_2$Cl$_8$H, (NH$_4$)$_6$Mo$_2$Cl$_8$·NH$_2$Cl, and also the tungsten salt K$_3$W$_5$Cl$_8$.

Refluxing a sulfoxide with molybdenum hexacarbonyl in glyme gives approximately 50% yield of the sulfide. Thioacetal is produced when 2-bromo sulfoxides are submitted to the same conditions.

\[
\begin{align*}
R^1\text{S-CH-R}^2 & \xrightarrow{\text{Mo(CO)}_6} R^1\text{S-CH-S-R}^1 + R^2\text{Br}
\end{align*}
\]

**Table 12. Reaction of 2-Bromoalkyl Sulfoxides with Molybdenum Hexacarbonyl**

<table>
<thead>
<tr>
<th>R$^1$</th>
<th>R$^2$</th>
<th>Yield [%] of S,S-Acetal</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_4$H$_8$</td>
<td>H</td>
<td>56</td>
</tr>
<tr>
<td>C$_4$H$_9$</td>
<td>C$_2$H$_5$</td>
<td>44</td>
</tr>
<tr>
<td>4-H$_2$C-C$_6$H$_5$</td>
<td>H</td>
<td>64</td>
</tr>
<tr>
<td>4-Br-C$_6$H$_5$</td>
<td>H</td>
<td>75</td>
</tr>
<tr>
<td>3-H$_2$C-C$_6$H$_5$</td>
<td>H</td>
<td>67</td>
</tr>
<tr>
<td>3-H$_2$C-C$_6$H$_5$</td>
<td>CH$_3$</td>
<td>38</td>
</tr>
<tr>
<td>2-naphthyl</td>
<td>H</td>
<td>81</td>
</tr>
<tr>
<td>n-C$_2$H$_5$</td>
<td>C$_2$H$_5$</td>
<td>48</td>
</tr>
</tbody>
</table>

The facile, quantitative reduction of heterocyclic N-oxides has been adapted to a titrometric method for determination of these substances. An interesting observation was made pertaining to the extent of reaction of bis[2-pyridyl] disulfide N-oxide. In the presence of citrate or thiocyanate anion, complete reduction leading to 2-pyridinethiol results.

\[
\begin{align*}
\text{N=S-S=N} & \xrightarrow{\text{Tl}^\text{III}/\text{H}^\text{+}} 2 \cdot\text{N=S-SH} \\
\text{citrate}
\end{align*}
\]

A few examples demonstrating the preparative value of this method have been given.

**Reduction of Dimethyl Sulfoxide with K$_2$MoCl$_6$**

To a flask containing K$_2$MoCl$_6$ (1.29 g, 3.22 mmol) and a 5:1 water/methanol mixture (30 ml), purged with nitrogen, is injected via a rubber septum dimethy1 sulfoxide (155 mg, 2.0 mmol). The mixture is stirred and heated at 60° while a slow stream of nitrogen is passed over. The exiting gas is scrubbed with aqueous mercu-ri(I) chloride. After 2h, the solid collected is dried, and from its weight the yield of dimethyl sulfide is estimated to be 47%.

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12. Addendum

Reductive removal of one of the three phenylthio groups from tris[phenylthio] alkanes can be achieved in 94–99% yield by chromium(II) chloride\(^{189}\). Notable recent applications of the chromium(II) ion in natural product chemistry are found in the elaboration of terrein into a prostanoid synthon\(^{170}\), during a synthesis of erythronolide B\(^{171}\), and in structural elucidation of maneoneses\(^{172}\) from marine algae.

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