Molybdenum (42 Mo):
* group 6 element
* From neo-latin molybdenaum and greek molybdos meaning lead, since its ores were confused with lead ores.
* ground state electron configuration: [Kr].4d⁵.5s¹
* oxidation levels: 6, 5, 4, 3, 2, 1, -1, -2
* First "discovered" (isolated) by Carl Wilhelm Scheele in 1778. Metal was isolated in 1781 by Peter Jacob Hjelm.
* abundance: 54th in the Earth’s crust, 25th in the oceans, 42th in the universe
* Does not occur as a free metal on Earth. The principal ore for its extraction is molybdenite (MoS₂). Molybdenum is also an industrial byproduct of copper and tungstene mining.
* Human abundance: 100 ppb by weight (Mo is a necessary element in all eukaryotes)
* Biological role: at least 50 molybdenum-containing enzymes are now known. 2 main functions: nitrogen fixation (nitrogenase) and redox transformations (xanthine oxidase...)
* Mo forms hard and stable carbide (Mo₂C) in alloys. Around 80% of the Mo world production is used to make steel type alloys.

Molybdenum blue: name given to some polypoxometalate complexes containing Mo(V) and Mo(VI) used in analytical chemistry and also MoO₃.
Phosphomolybdic acid (12 MoO₃ · H₃PO₄) is reduced by unsaturated compounds to molybdenum blue (Seebach staining reagent).

Oxidation processes with heterogeneous Mo catalysts:
* Partial oxidation of methane by nitrous oxide over molybdenum on silica

\[
\begin{align*}
\text{Mo}^V + \text{N}_2\text{O} & \rightarrow \text{Mo}^\text{VI}O^- + \text{N}_2 \\
\text{Mo}^\text{VI}O^- + \text{CH}_4 & \rightarrow \text{Mo}^\text{VII}OH^- + \text{CH}_3 \\
\text{Mo}^\text{VI}O^2^- + \text{CH}_3^- & \rightarrow \text{Mo}^\text{VI}OCH_3^- \\
\text{Mo}^\text{VI}OCH_3^- + \text{H}_2\text{O} & \rightarrow \text{Mo}^\text{V}OH^- + \text{CH}_3\text{OH} \\
\text{Mo}^\text{VI}OH^- + \text{Mo}^\text{V}OH^- & \rightarrow \text{Mo}^V + \text{Mo}^\text{VI}O^2^- + \text{H}_2\text{O}
\end{align*}
\]

Other oxidation products are also formed but good selectivity for CH₃OH and CH₂O (78%) at low conversion (3%). * J. Am. Chem. Soc. 1984, 106, 4117 (kinetics).

* Oxidative dehydrogenation of propane by Mo oxides.

\[
\begin{align*}
\text{C}_3\text{H}_8 + \text{O}^* & \leftrightarrow \text{C}_3\text{H}_6\text{O}^* & (\text{O}^* = \text{lattice oxygen}) \\
\text{C}_3\text{H}_8\text{O}^* + \text{O}^* & \rightarrow \text{C}_3\text{H}_7\text{O}^* + \text{OH}^* \\
\text{C}_3\text{H}_7\text{O}^* & \rightarrow \text{C}_3\text{H}_6 + \text{OH}^*
\end{align*}
\]

* A few prices from Sigma Aldrich catalog 2012:
* Mo(CO)₆ = $361.00/100g
* MoO₃ = $68.00/100g, ≥ 99.5%
* MoCl₅ = $186.30/10g, 99.9900%
* (NH₄)₆Mo₇O₂₄·4H₂O = $25.00/100g (Strem)
* Pd(OAc)₂ = $866.00/25g, ≥ 99.9000%
* PdCl₂ = $917.00/25g, ≥ 99.9000%

PMA is also used in Masson's trichrome stain that enables to distinguishing cells from surrounding connective tissue.
Nitrogenase Enzymes and Analogs:
Nitrogenases are present in certain bacteria and are responsible for nitrogen fixation by reduction of atmospheric dinitrogen to ammonia.

All nitrogenase enzymes possess a iron-sulfur cluster cofactor that generally contains a central Mo atom (sometimes replaced by Va or Fe). For a review on Mo cofactors and enzymes see: Nature 2009, 460, 839.

First nitrogenase analog:


Reduction of dinitrogen to ammonia:
Schrock, Science 2003, 301, 76.

Chatt mechanism:

Another system for the reduction of dinitrogen to ammonia:
Nat. Chem. 2011, 3, 120.
Oxotransferase Enzymes and Analogs:
Many different oxotransferase containing Mo have been isolated. Reactions
effected by this family of enzyme is broad, but most of them possess the
molybdopterin moiety in the cofactor:

\[
\text{molybdopterin}
\]

A few examples:

- Mo(VI)
  - xanthine oxidase
  - aldehyde oxidoreductase
- Mo(IV)
  - sulfite oxidase
  - DMSO reductase

Oxotransfer general reaction: \( \text{Mo}^{2+} \text{O}_n \text{L}_m + \text{XO} \leftrightarrow \text{Mo}^{2+\text{O}_n\text{L}_m+1} + \text{X} \)

aldehyde oxidoreductase: \( \text{RCHO} + \text{H}_2\text{O} \leftrightarrow \text{RCOOH} + 2\text{H}^+ + 2\text{e}^- \)

sulfite oxidase: \( \text{SO}_3^{2-} + \text{H}_2\text{O} \leftrightarrow \text{SO}_4^{2-} + 2\text{H}^+ + 2\text{e}^- \)

nitrate reductase: \( \text{NO}_3^- + 2\text{H}^+ + 2\text{e}^- \rightarrow \text{NO}_2^- + \text{H}_2\text{O} \)

DMSO reductase: \( \text{Me}_2\text{SO} + 2\text{H}^+ + 2\text{e}^- \rightarrow \text{Me}_2\text{S} + \text{H}_2\text{O} \)

xanthine oxidase:

\[
\text{xanthine} + \text{H}_2\text{O} \leftrightarrow \text{uric acid} + 2\text{H}^+ + 2\text{e}^-
\]

Water is another potential source of oxygen for the oxotransfer as shown in the
postulated xanthine oxidation mechanism: \( \text{J. Am. Chem. Soc. 2005, 127, 4518} \)

\( \text{J. Am. Chem. Soc. 2008, 130, 55.} \)

\( ^{18}\text{O} \)-labeled transfer experiments with xanthine oxidase: \( \text{J. Biol. Chem. 1966, 241, 4798.} \)
\( \text{J. Biol. Chem. 1966, 241, 3468.} \)

Other mechanisms cannot be ruled out thus far, for a review, see: Hille, R. Chem. Rev. 1996, 96, 2757.
First oxotransferase analog:

\[
\begin{align*}
\text{HNR}_2 & \rightarrow \text{R}_2\text{N} \quad \text{CS}_2, \text{NaOH} \\
& \rightarrow \text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O} \\
\text{then} & \rightarrow \text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}
\end{align*}
\]

\[
\begin{align*}
\text{MoO}_2(\text{S}_2\text{CNR}_2)_2 + \text{O}_2 & \rightarrow \text{MoO}_2(\text{S}_2\text{CNR}_2)_2 + \text{R}_3\text{P} \\
\text{MoO}_2(\text{S}_2\text{CNR}_2)_2 + \text{MoO}_2(\text{S}_2\text{CNR}_2)_2 & \rightarrow \text{MoO}_2(\text{S}_2\text{CNR}_2)_4
\end{align*}
\]

Application of the system to oxidation and reduction reactions: (for a summary, see Holm, J. Am. Chem. Soc. 1986, 108, 6992.)

Oxotransferase analog second generation:

A lot of new oxotransferase analogs have been published then, like these analogs of the sulfite oxidase family using dithiolene ligands:

These complexes can catalyze similar redox reactions as depicted before. For reviews on Mo oxotranferase enzymes and analogs, see Coord. Chem. Rev. 1990, 100, 183. Chem. Rev. 2004, 104, 1175.

Other Oxidations with Mo Complexes:

Episulfidation:

Improvement of the reaction (yield and scope):

MoOPh reagent: (see Newhouse 2007 group meeting)

MoOPh = MoO₅ • Py • HMPA (Vedejs J. Am. Chem. Soc. 1974, 96, 5944.)


Epoxidation with Mo(CO)₆ and 'BuOOH:

Molybdenum in Organic Synthesis

Molybdenum Fisher carbenes:

For a group meeting on Fisher carbenes, see Chen 2007

Fischer carbenes are found with:
* low oxidation state metals;
* middle and late transition metals Fe(0), Mo(0), Cr(0), W(0);
* π-electron acceptor metal ligands;
* π-donor substituents on methylene group such as alkoxy and amino groups.

Fischer carbenes are in the singlet state and the carbene carbonis electrophilic.

Typical synthesis of molybdenum Fisher carbenes:

Molybdenum vs chromium carbene in (Wulff)-Dötz reaction:

Misc:

artemisinin

For other examples, see the synthesis of (+)-azaspiracid-1 (Evans, Angew. Chem. Int. Ed. 2007, 46, 4698.) and C1–C52 fragment of amphidinol 3 (Rychnovsky, Org. Lett. 2007, 9, 4757.)
Molybdenum in Organic Synthesis

**Cyclopropanation:**

\[
\text{(OC)}_5\text{Mo} + \text{Me} + \text{Me} \rightarrow \text{Me} + \text{Me}
\]

The following factors favor indene product over phenol product:
- Aryl complexes > Alkenyl complexes
- Mo > W > Cr
- More coordinating and/or polar solvents
- Higher concentration of alkyne
- Terminal alkynes > Internal alkynes

For a complete study, read Wulff, *Organometallics* 1994, 13, 102.

Mo carbene reacts faster for cyclopropanations than Cr and W.

With Mo carbene cyclopropanation is faster than CO insertion. For a study on the effect of tether length and composition on the cascade see: *J. Am. Chem. Soc.* 1992, 114, 8424.

Misc Mo carbenes reaction:

\[
\text{(OC)}_5\text{Mo} + \text{Me} + \text{Me} \rightarrow \text{Me} + \text{Me}
\]

van Halban-White type cyclization

1. H_2O
2. CH_2(O)Me
3. PPTS


Molybdenum and metathesis at a glance:

**Alkene metathesis**: early reports of olefin disproportionation by the Phillips Petroleum Company R&D department used heterogeneous catalysts like CoO–MoO$_3$–Al$_2$O$_3$ (Industrial & Engineering Chemistry Product Research and Development, 1964, 3, 170.) First homogeneous catalysts were also based on Mo complexes:

$\text{H}_2\text{C} = \text{CH}_2$ (20 atm)

$\text{rt, 19 h, 91 wt \%} 


Schrock alkylidene catalysts: highly reactive but air and water sensitive (glove box use only). Generally favor E-alkene formation.


$\text{Ph} \rightarrow \text{Me} \text{(cat. A)}$ or $\text{iPr} \text{(cat. B)}$

$\text{R} = \text{Me}$

$\text{R'} = \text{Me}$ (cat. A) or $\text{iPr}$ (cat. B)

Alkyne metathesis: first report of alkyne disproportionation in 1968 with heterogeneous catalysts (Chem. Commun. 1968, 1548.)


$\text{PhTol}_2\text{Mo(CO)}_6\text{resorcinol}$

$\text{160°C, 3 h} 

\text{Ph} \rightarrow \text{Me}$

$\text{Ph} \rightarrow \text{Me}$

$\text{Tol} \rightarrow \text{Tol}$

$\text{55\%} 

\text{23.5\%} 

\text{21.5\%} 

(\text{tBuO})_3\text{W}$

W alkylidyne: highly reactive but does not tolerate several functional groups. Air and water sensitive.

For a review on alkyne metathesis, see Fürstner, Chem. Commun. 2005, 2307.

New catalysts, more reactive and user friendly (Fürstner, J. Am. Chem. Soc. 2010, 132, 11045.)

Indefinitively stable on benchtop.

Air and water sensitive.

Precatalyst, stable in air for hours.
Asymmetric Allylic Alkilations (Trost):

1. Boc₂O, DCM, Et₃N, DMAP, rt, 98%
2. 10 mol % Mo(CO)₃(C₇H₈), 15 mol % (R,R)-L, dimethyl sodiomalonate,
   THF, reflux, 94%, 96% ee.
3. NaCl, 150 °C, 20:1 DMSO/H₂O, 100%.

Tipranavir

See Michaudel 2011 group meeting for the full synthesis.

Model for enantiodiscrimination:

Isoxazoles are good surrogates for 1,3 diketones: see Michaudel 2011 Poly(β-carbonyl)s group meeting.

Other Reductions:

Reaction temperature can be decreased to rt to 45 °C by using Mo(CO)₆ supported on SiO₂. J. Chem. Soc., Chem. Commun. 1980, 169.

See also the synthesis of 35–deoxy amphotericin B methyl ester, Carreira, Angew. Chem. Int. Ed. 2008, 47, 4335.
Miscellaneous Reactions:

MoCl₅ is a strong Lewis acid and oxidizing reagent, often used for the Scholl reaction:

\[
\text{MoCl}_5 + \text{PPh}_3 \quad \text{(cat.)} \quad \text{CO}_2 (1 \text{ atm}) \quad \text{rt}, 7 \text{ d}, 78 \%
\]

MoF₆ is a fluorinating reagent (similar reactivity to SF₅): mp 17.5 °C; bp 35 °C

It can be used in normal glassware at room temperature or below.

Br \rightarrow \text{CO}_2 \text{H} \rightarrow \text{Br} \rightarrow \text{CF}_3 \quad \text{(DAST generally stops at RCO}_2\text{F)}

MoF₆ is a fluorinating reagent (similar reactivity to SF₅): mp 17.5 °C; bp 35 °C

It can be used in normal glassware at room temperature or below.

MoF₆ + \text{PPh}_3 (1:5) (cat.) \quad \text{CO}_2 (1 \text{ atm}) \quad \text{rt}, 7 \text{ d}, 78 \%

Mo(CO)₆(CN)₃(Bu)₃ (MoBI₃) is a catalyst for hydrostannations of alkyne

Mo(CO)₆(CN)₃(Bu)₃ \rightarrow \text{Bu}_3\text{SnH} \quad \text{THF, 55 °C, 48 h} \quad 86 \%

In brackets are yield and selectivity of the reaction using PdCl₂(PPh)₃ instead of MoBI₃.