Aromaticity

Coal as a Source of Benzene

1675 - Bituminous coal is distilled to form tars

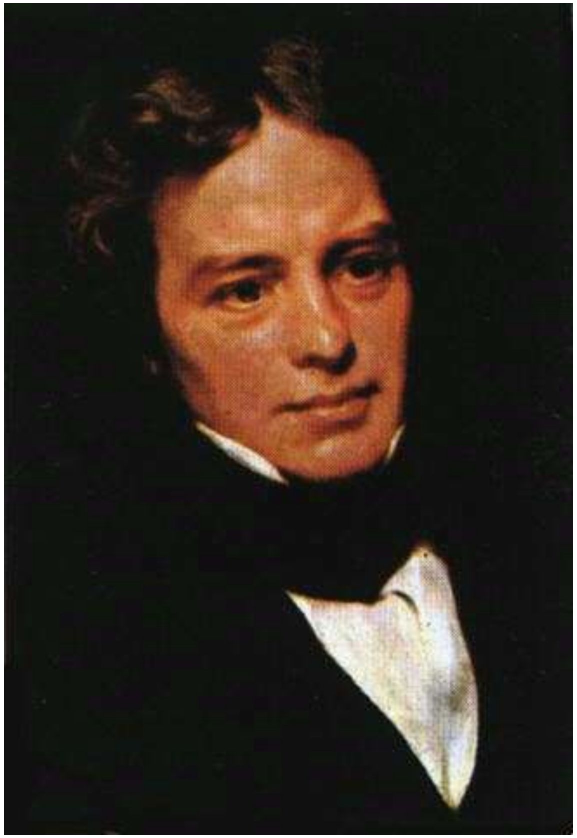
$$\text{Coal} \xrightarrow{1000\ ^{o}\text{C}} \text{gas} + \text{liquid} + \text{tar}$$

illuminating gas
$H_2 + CH_4$

light oil
3.2 gal/ton
60% benzene

tar
pitch
asphalt

Faraday Isolates Bicarburetted Hydrogen



Michael Faraday
(1791-1867)

1825 - Michael Faraday isolates "bicarburetted hydrogen" ($C_{12}H_6$) from liquid residue in a cylinder of illuminating gas. [C = 6, H = 1]

"One Christmas was so much like another, in those years around the sea-town corner now and out of all sound except the distant speaking of the voices I sometimes hear a moment before sleep, that I can never remember whether it snowed for six days and six nights when I was twelve or whether it snowed for twelve days and twelve nights when I was six."

"A Child's Christmas in Wales" --- Dylan Thomas

The Preparation, Naming and Correct Formula of Benzene

Eilhard Mitscherlich
(1794-1863)

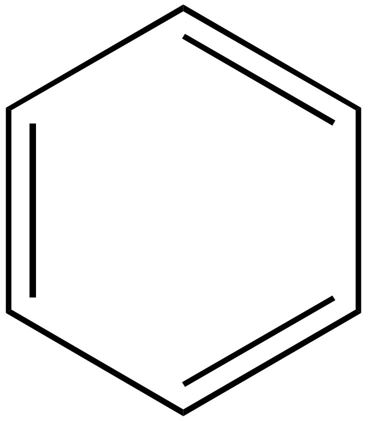
1834 - Mitscherlich prepares benzene (C_6H_6) from benzoic acid by heating with CaO. Benzoic acid was prepared from gum benzoin resin from *Styrax benzoin*.

Kekulé's First Structure of Benzene

August Kekulé

(1829-1896)

1865 - Proposes a cyclic structure for benzene with alternating single and double bonds

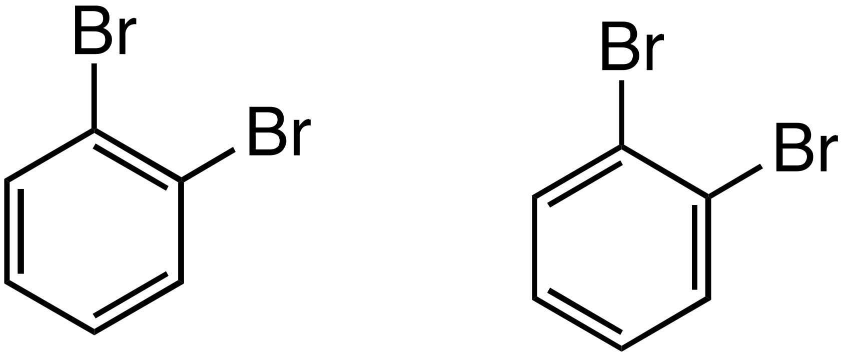


1890- Benzene Fest - Kekulé's Dream

Ladenburg's Riposte

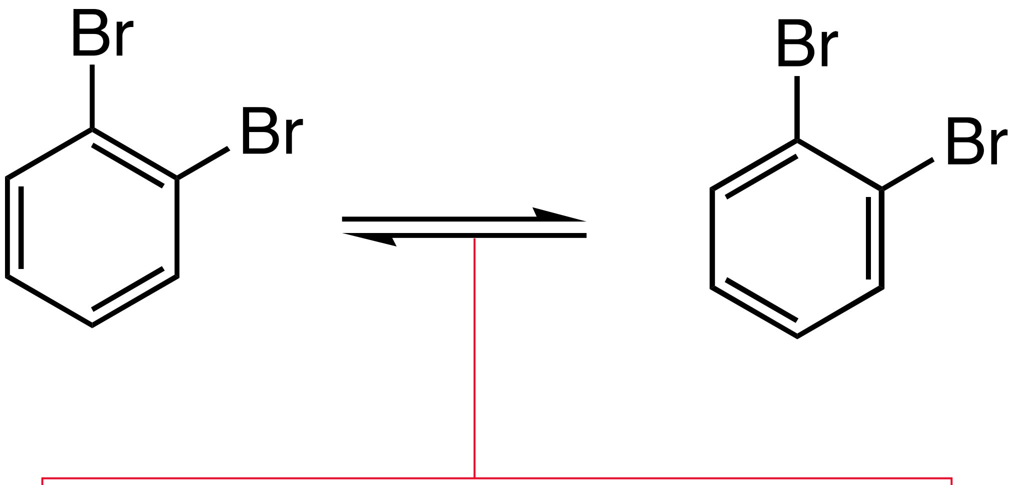
Albert Ladenburg
(1842 - 1911)

Ladenburg, a former student of Kekulé's, objects to his mentor's formula for benzene because only one o-dibromobenzene is known, not two.



Kekule's Response

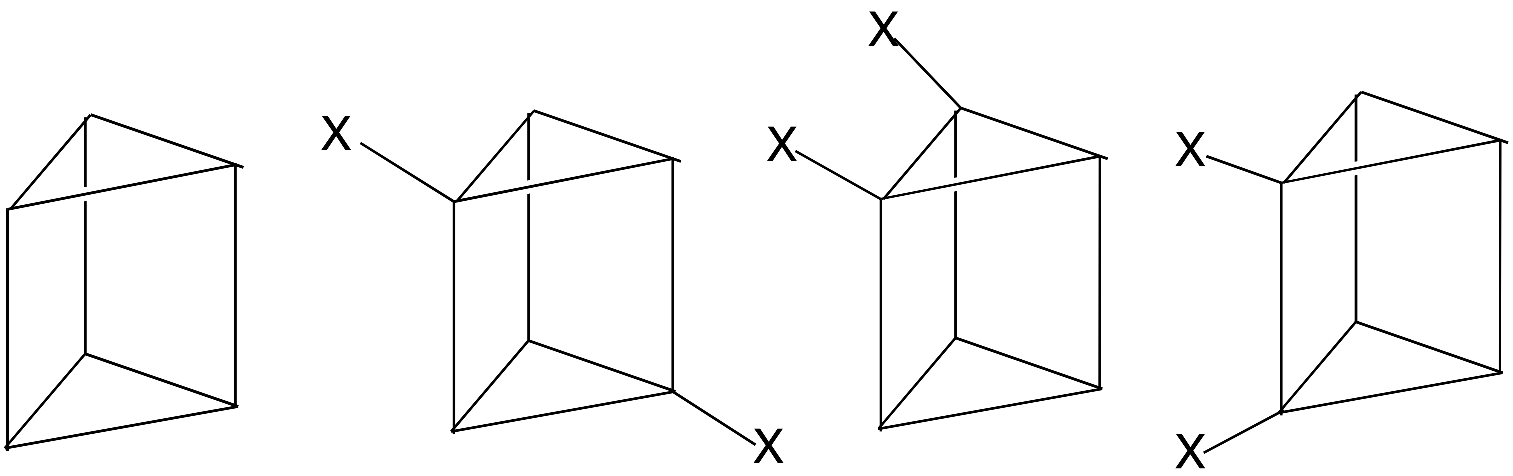
1872 - Kekulé revises his theory, suggesting that the single bonds are changing places with the double bonds.



not resonance - barrier implied

Ladenburg's Prismane Structure

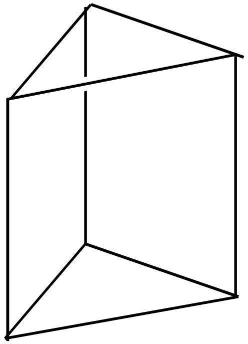
1869 - Ladenburg proposes the prismane structure for benzene.



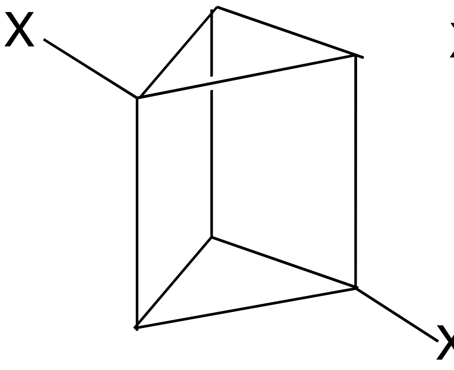
. ortho para meta

Van't Hoff's Objection

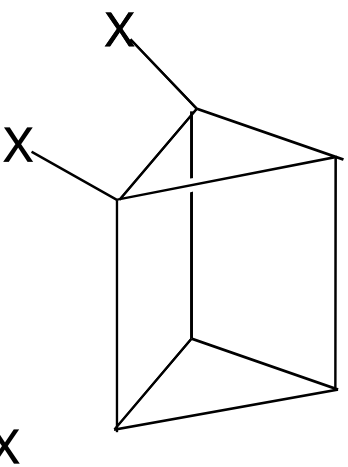
1869 - Ladenburg proposes the prismane structure for benzene.



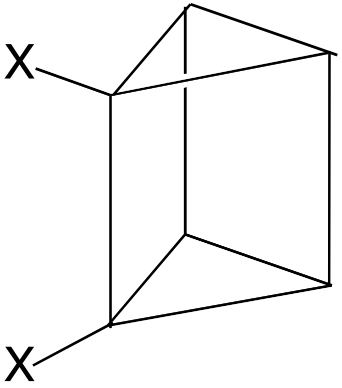
Van't Hoff objects to Ladenburg's prismane structure because the ortho isomer is chiral and should be resolvable.



ortho

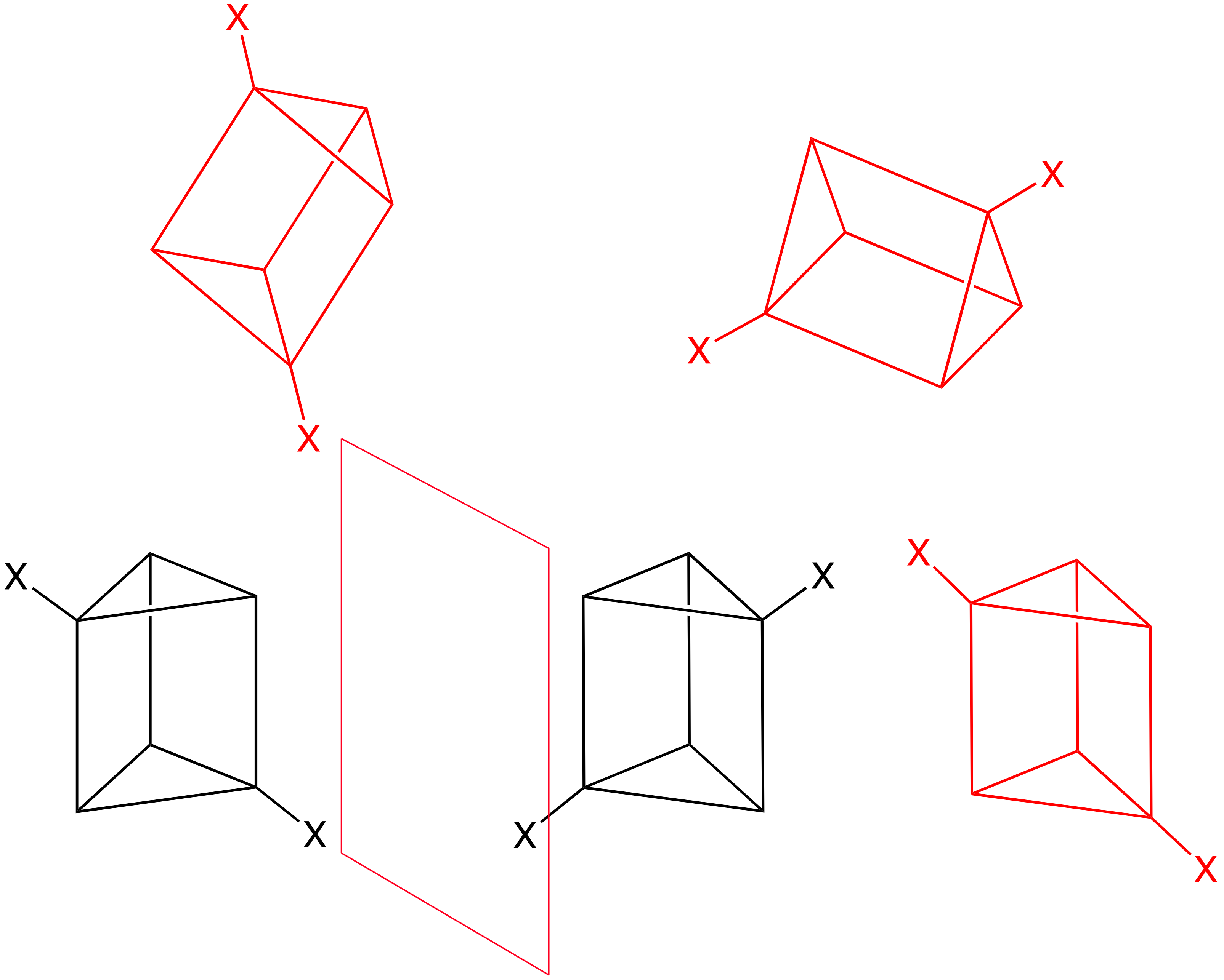


para



meta

The ortho-Isomer

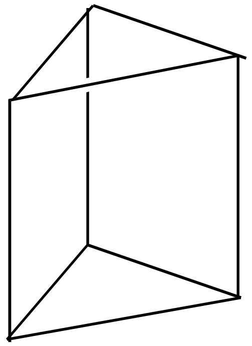


104 Years Later…

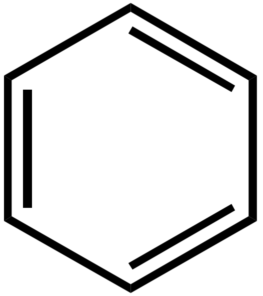
1973 - Acton and Katz synthesize prismane.

.

Prismane



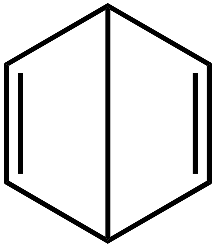
Benzene



^{1}H NMR: δ 2.28, s
^{13}C NMR: 30.6 ppm

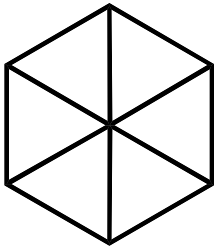
^{1}H NMR: δ 7.34, s
^{13}C NMR: 128.4 ppm

Other Benzenes

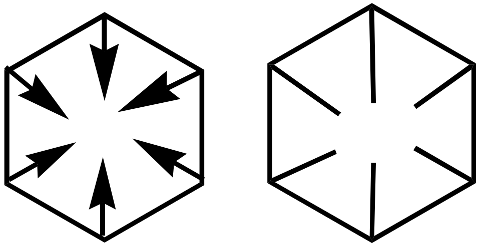


“Dewar benzene”

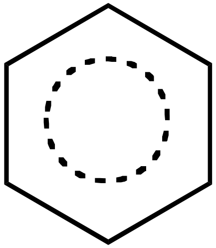
Dewar (1867)
Stadeler (1868)
Wichelhaus (1869)



Claus (1867)

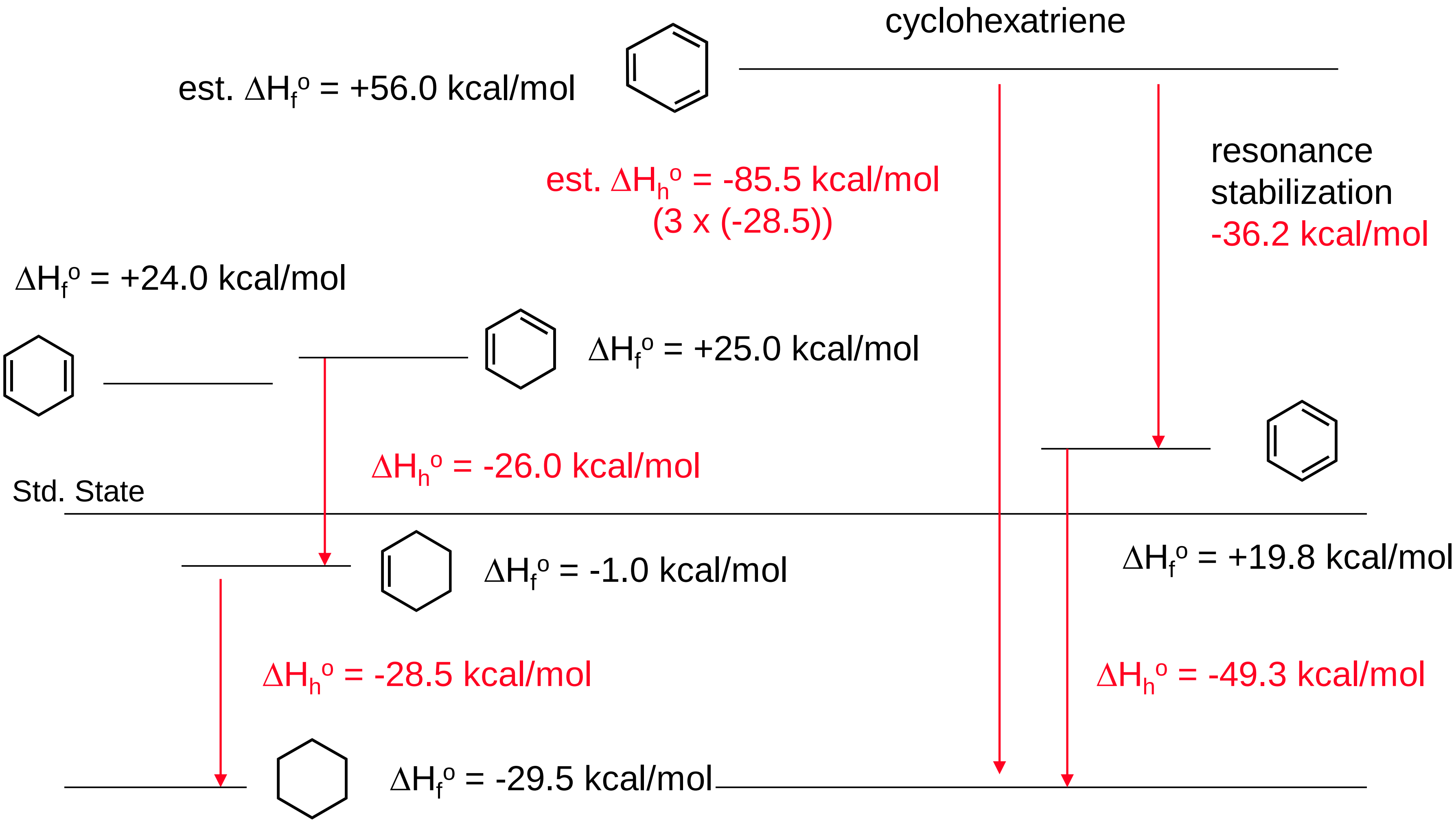


Armstrong-Baeyer (1887)



Thiele (1899)

Cyclohexatriene vs. Benzene



cyclohexatriene

est. ΔH_f^o = +56.0 kcal/mol

est. ΔH_h^o = -85.5 kcal/mol
(3 x (-28.5))

resonance
stabilization
-36.2 kcal/mol

ΔH_f^o = +24.0 kcal/mol

ΔH_f^o = +25.0 kcal/mol

ΔH_h^o = -26.0 kcal/mol

Std. State

ΔH_f^o = +19.8 kcal/mol

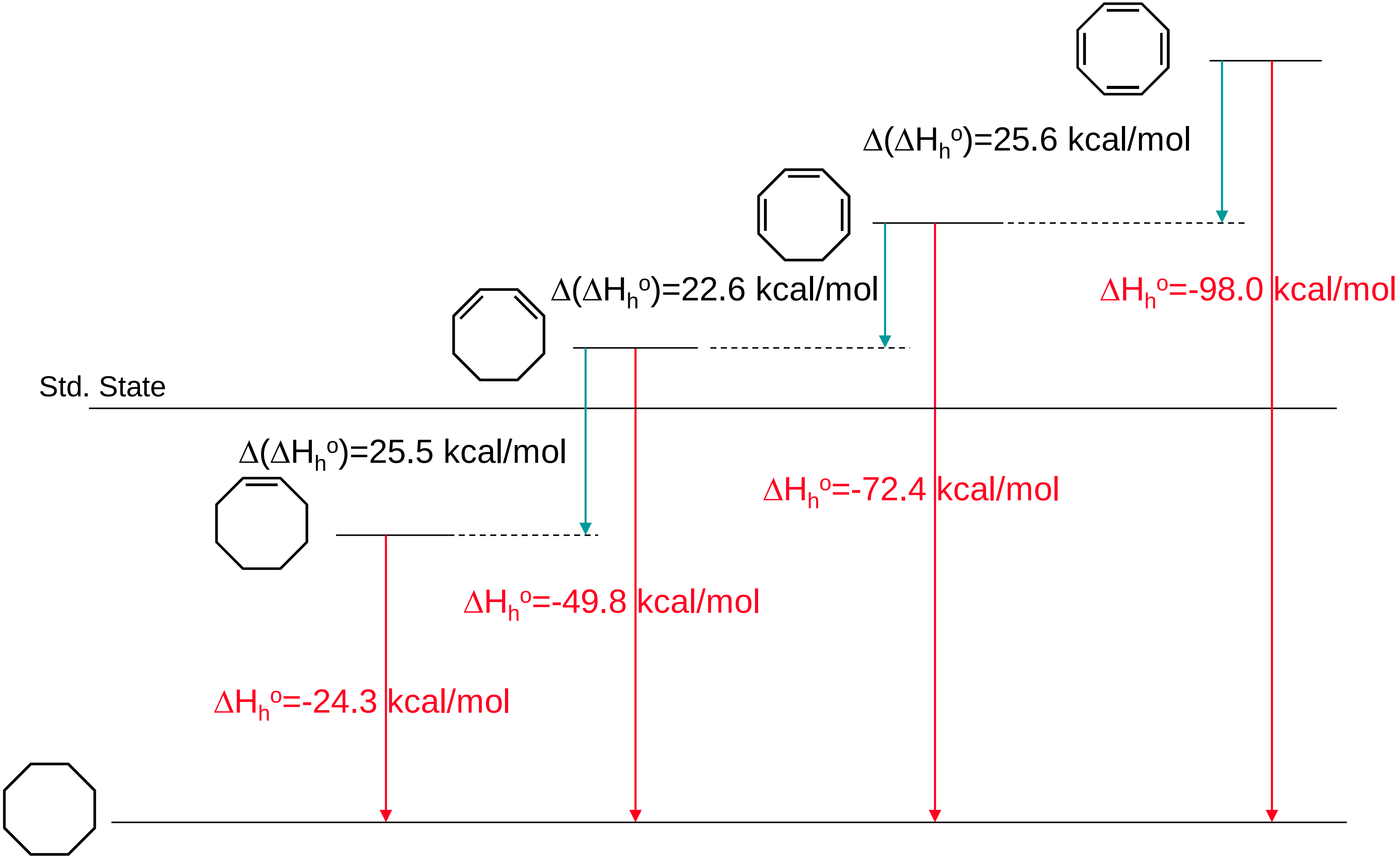
ΔH_f^o = -1.0 kcal/mol

ΔH_h^o = -28.5 kcal/mol

ΔH_h^o = -49.3 kcal/mol

ΔH_f^o = -29.5 kcal/mol

Is Cyclooctatetraene Aromatic?



$\Delta(\Delta H_h^o)=25.6$ kcal/mol

$\Delta(\Delta H_h^o)=22.6$ kcal/mol

$\Delta H_h^o=-98.0$ kcal/mol

Std. State

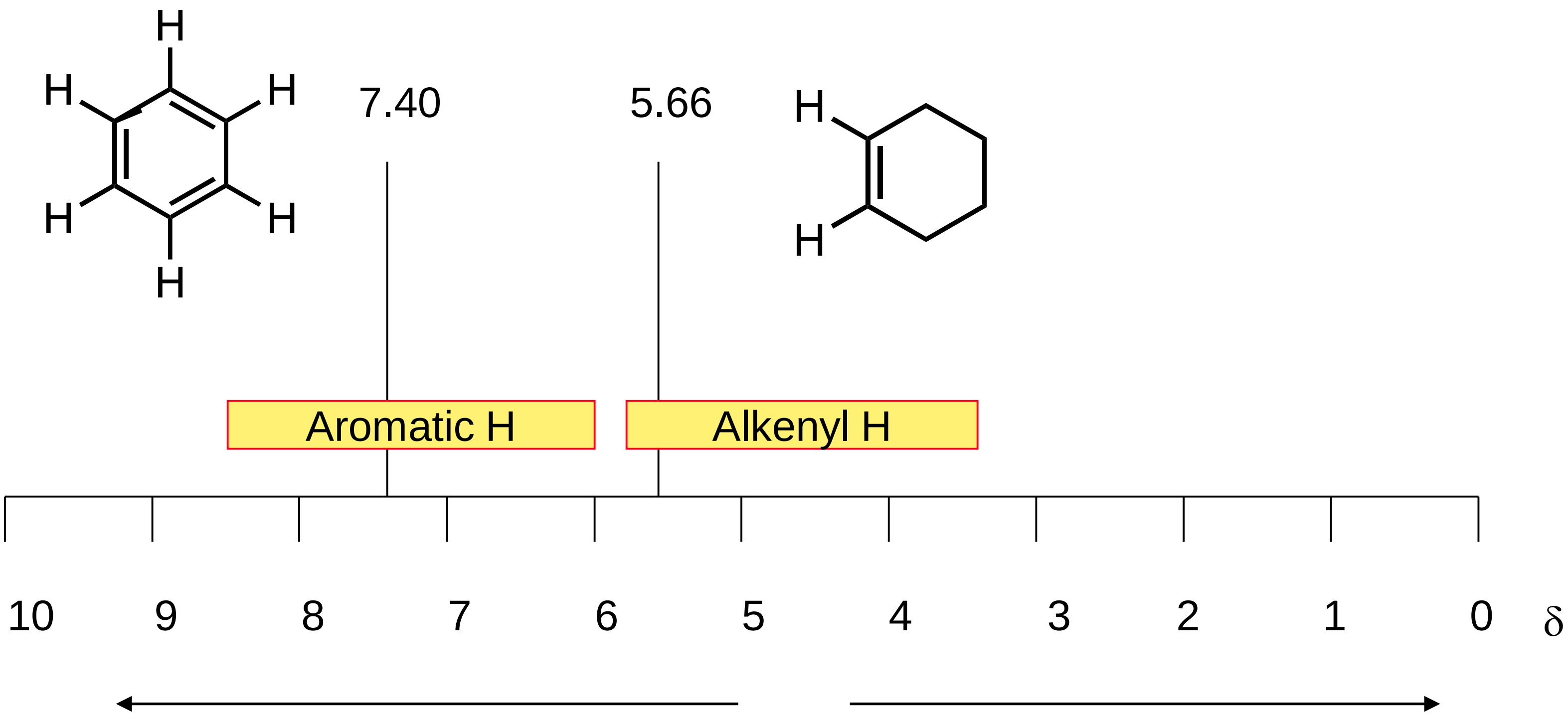
$\Delta(\Delta H_h^o)=25.5$ kcal/mol

$\Delta H_h^o=-72.4$ kcal/mol

$\Delta H_h^o=-49.8$ kcal/mol

$\Delta H_h^o=-24.3$ kcal/mol

^{1}H NMR: Aromatic vs. Alkenyl Hydrogens



7.40

5.66

Aromatic H

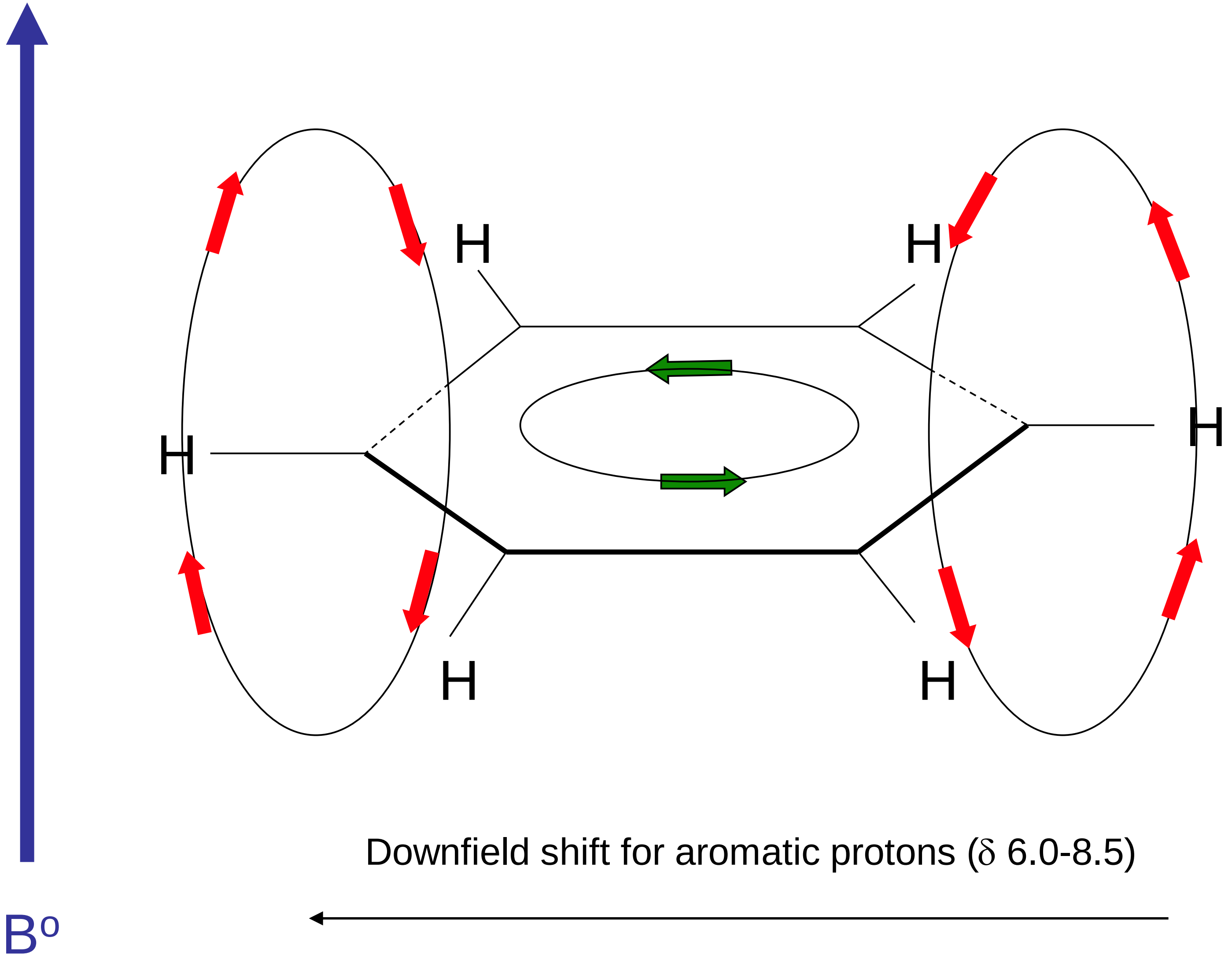
Alkenyl H

10 9 8 7 6 5 4 3 2 1 0 δ

deshielding / downfield

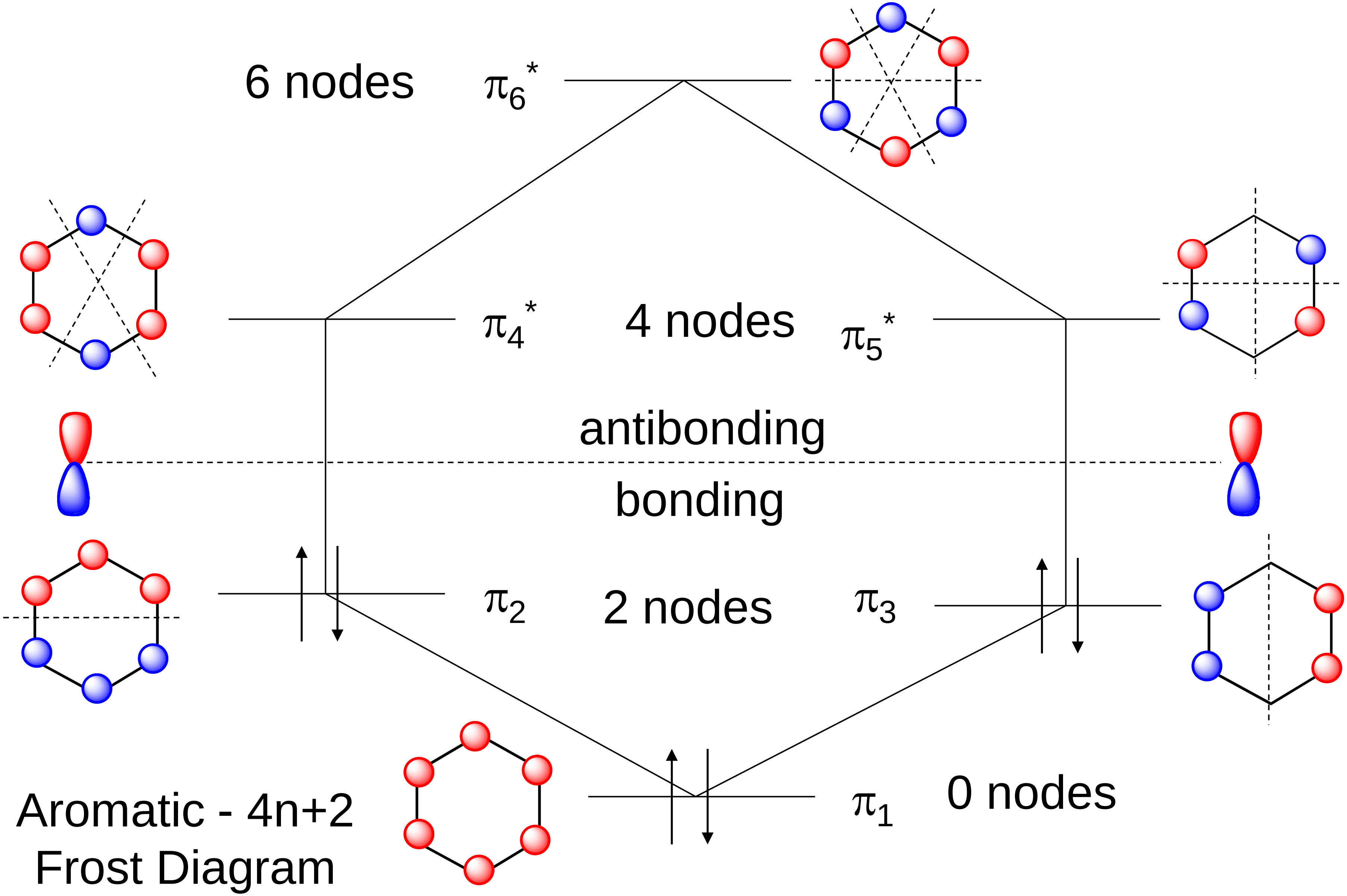
shielding / upfield

Magnetic Anisotropy



Downfield shift for aromatic protons (δ 6.0-8.5)

Molecular Orbitals of Benzene



6 nodes π_6^*

π_4^* 4 nodes π_5^*

antibonding

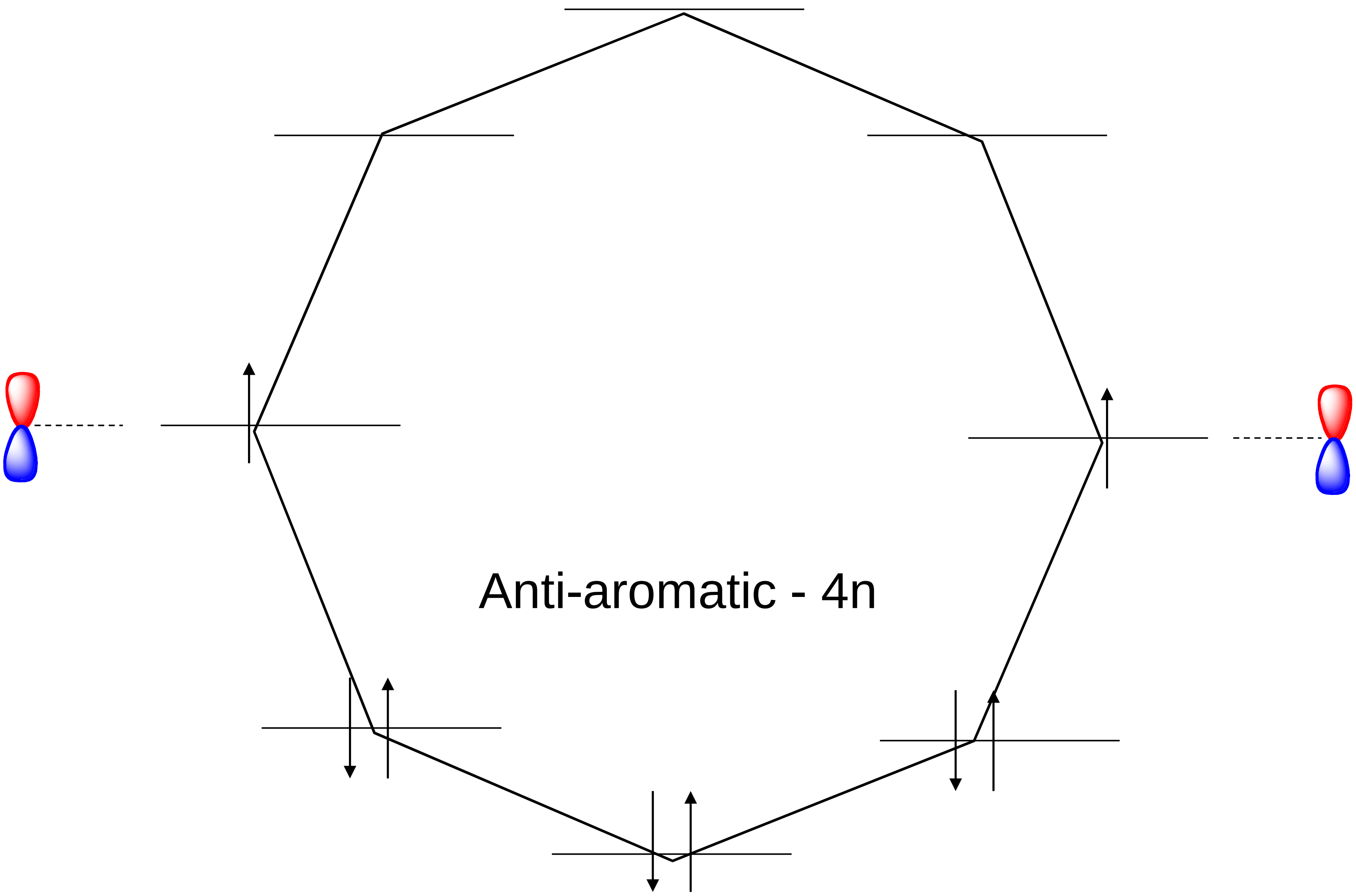
bonding

π_2 2 nodes π_3

π_1 0 nodes

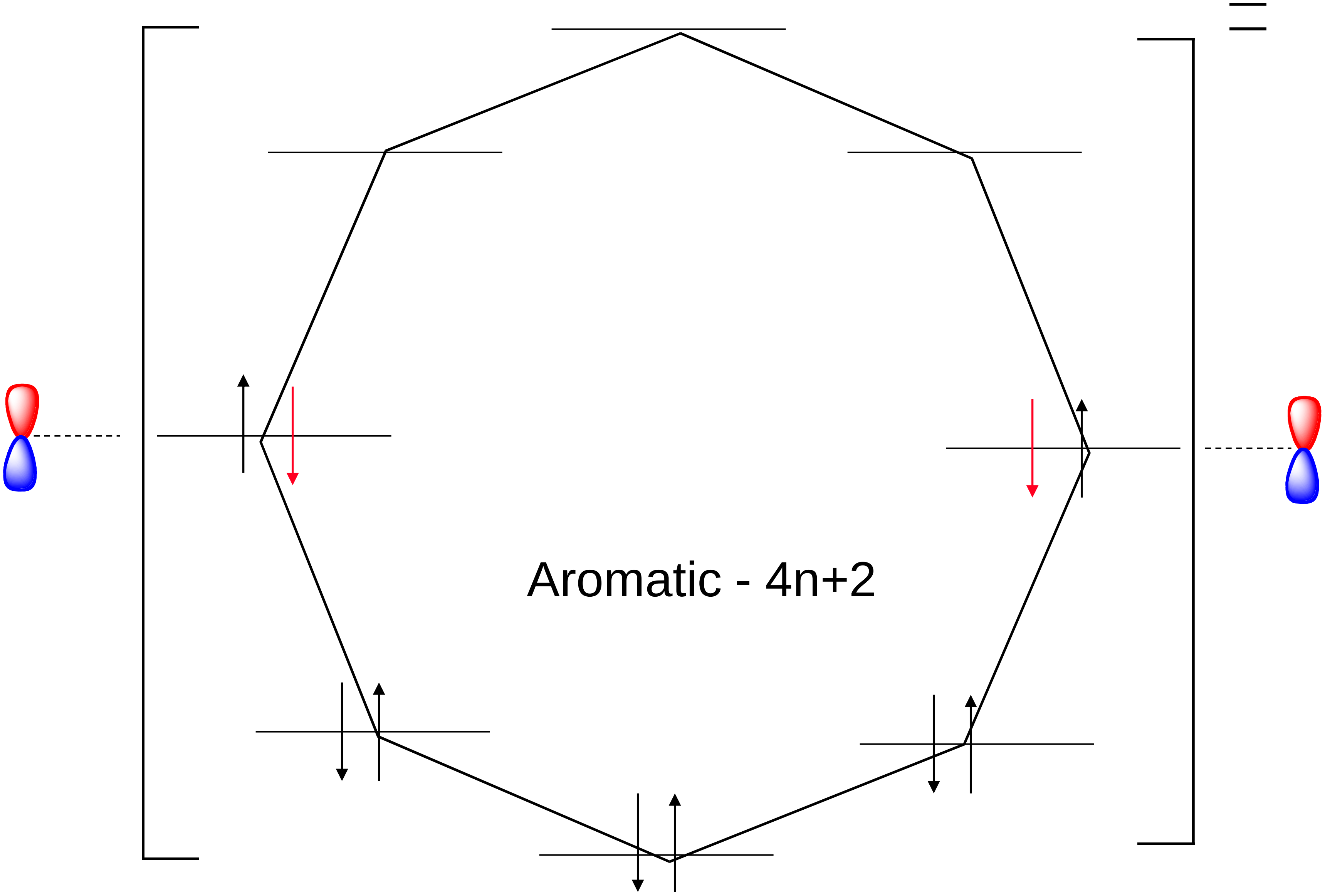
Aromatic - 4n+2
Frost Diagram

Molecular Orbitals of Cyclooctatetraene



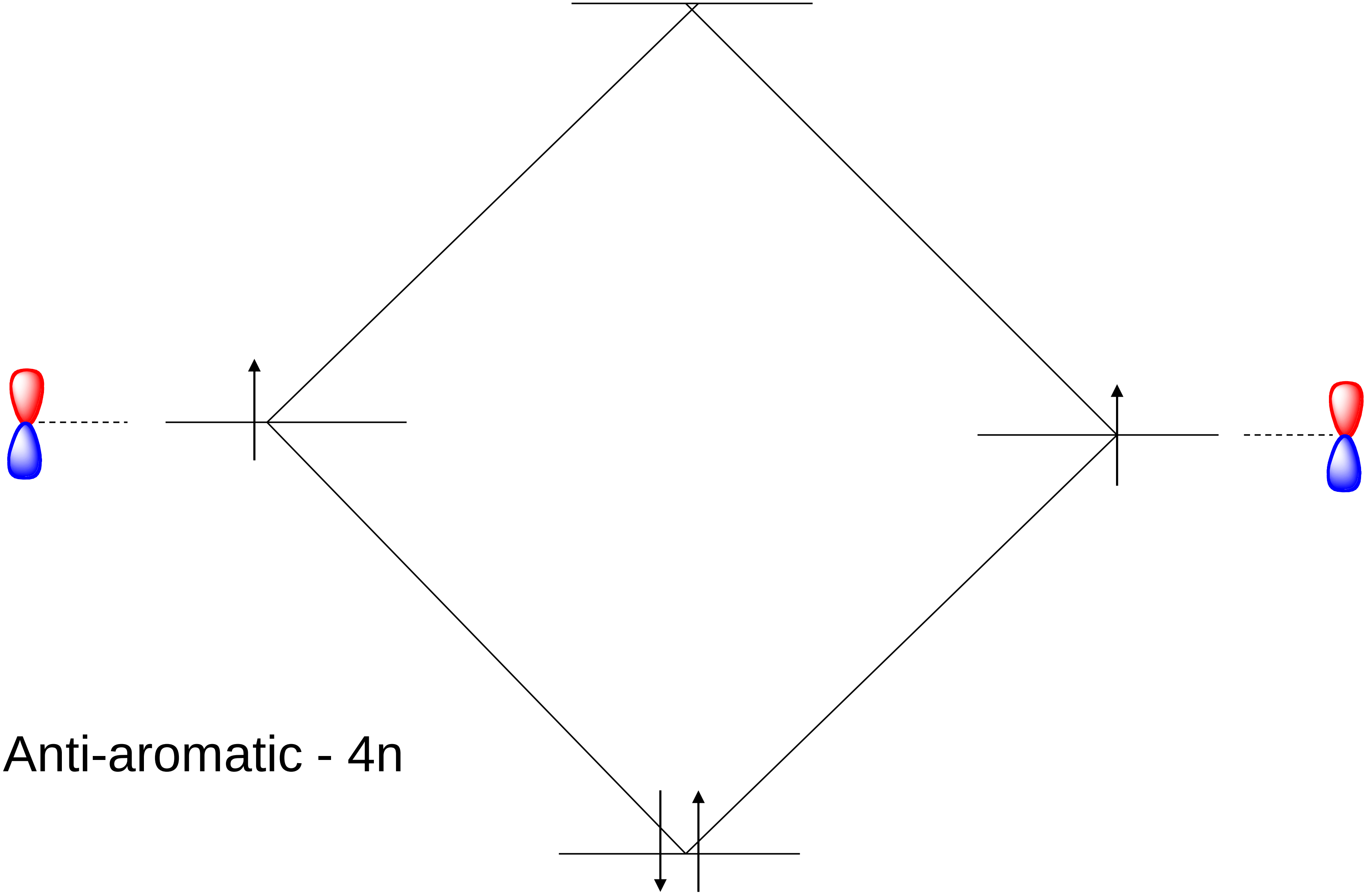
Anti-aromatic - 4n

Molecular Orbitals of Cyclooctatetraene Dianion



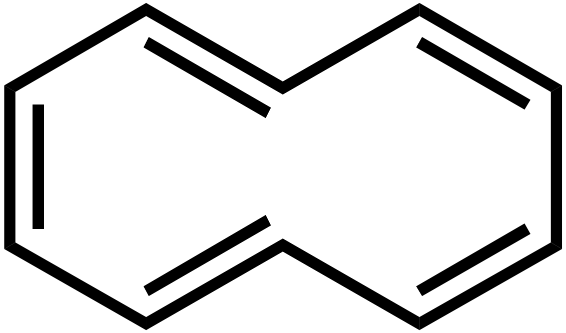
Aromatic - 4n+2

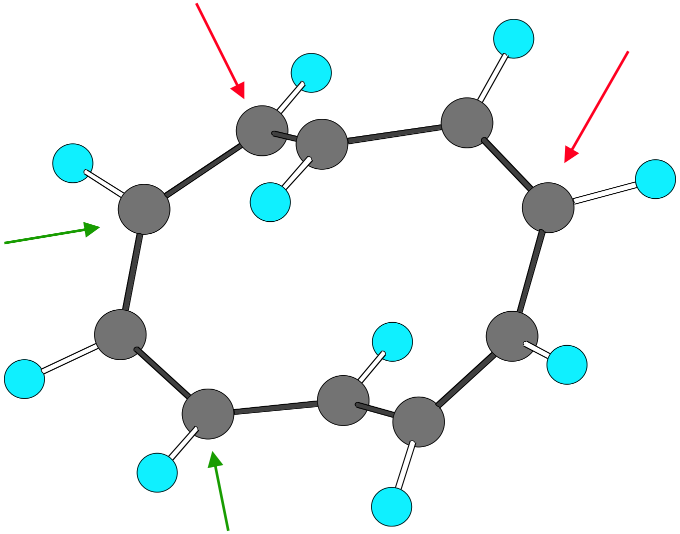
Molecular Orbitals of Cyclobutadiene



Anti-aromatic - 4n

4n + 2 (E,Z,Z,E,Z)-Cyclodecapentaene



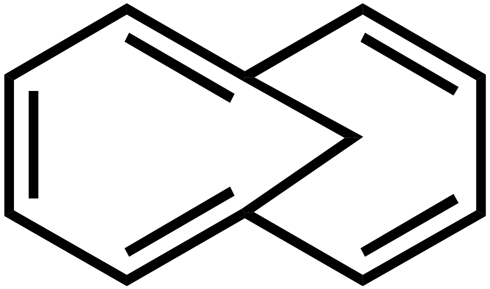


(E,Z)-Dihedral angle = 48º

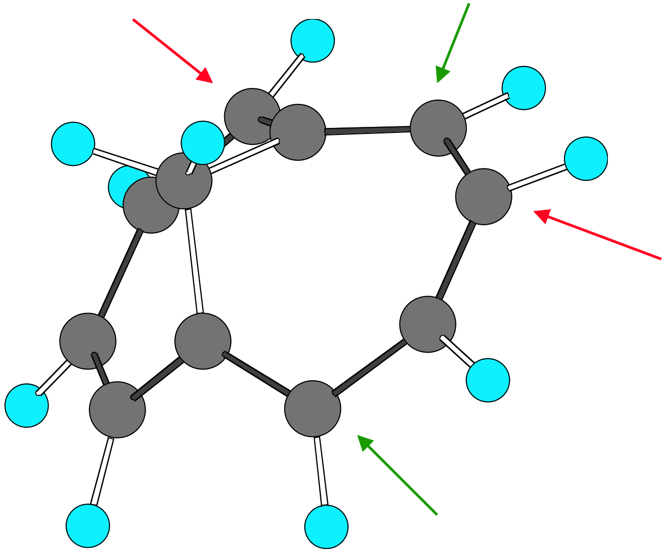
(Z,Z)-Dihedral angle = 31º

4n + 2, non-planar; non-aromatic!

1,6-Methano-(E,Z,Z,E,Z)-Cyclodecapentaene



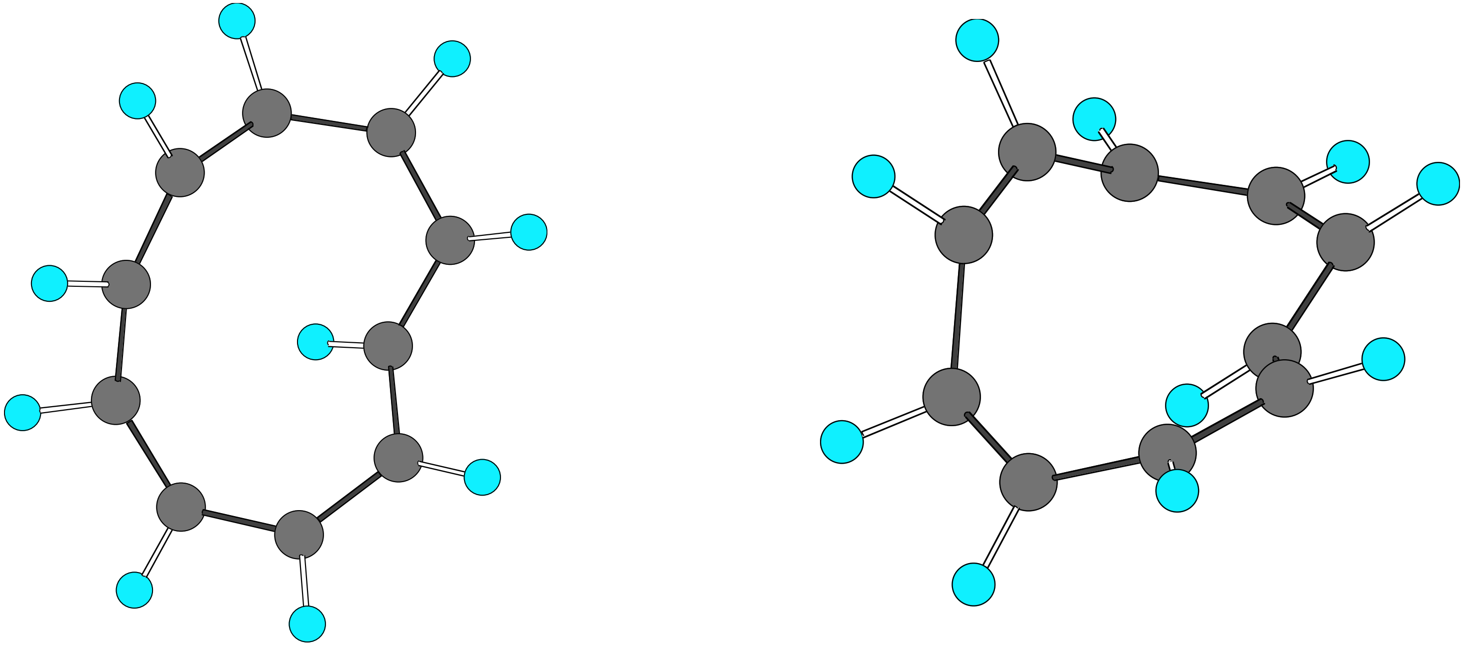
(E,Z)-Dihedral angle = 24º



(Z,Z)-Dihedral angle = 0.5º

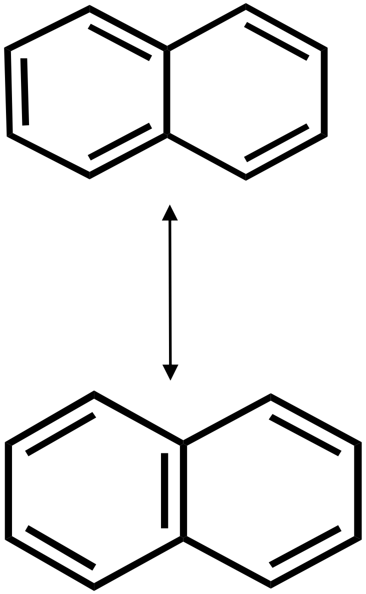
4n + 2, “planar”; aromatic

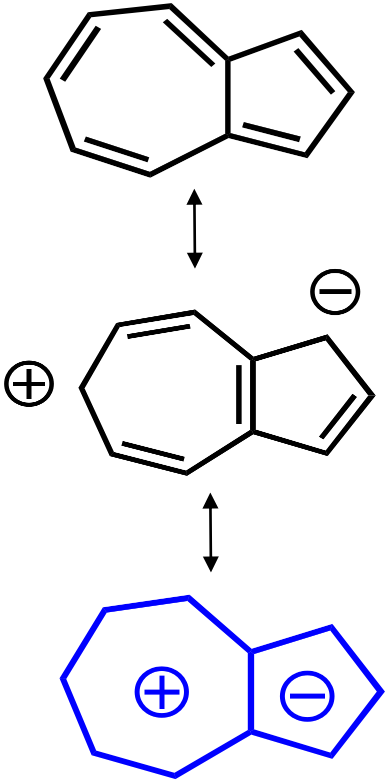
(E,Z,Z,Z,Z,Z)-Cyclodecapentaene



4n + 2, non-planar; non-aromatic

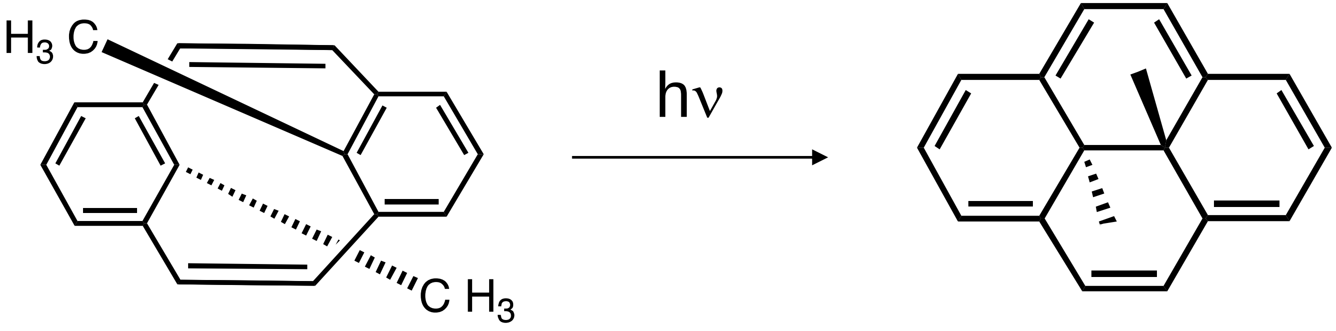
Naphthalene and Azulene



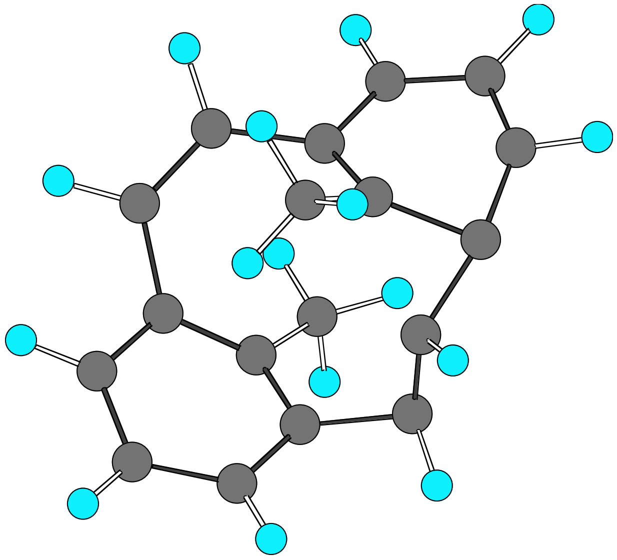


4n + 2, planar; aromatic

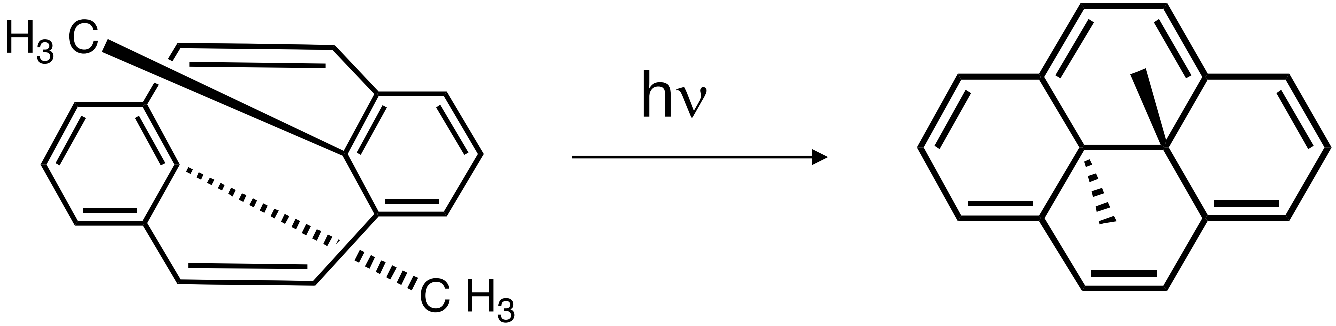
Pyrenes



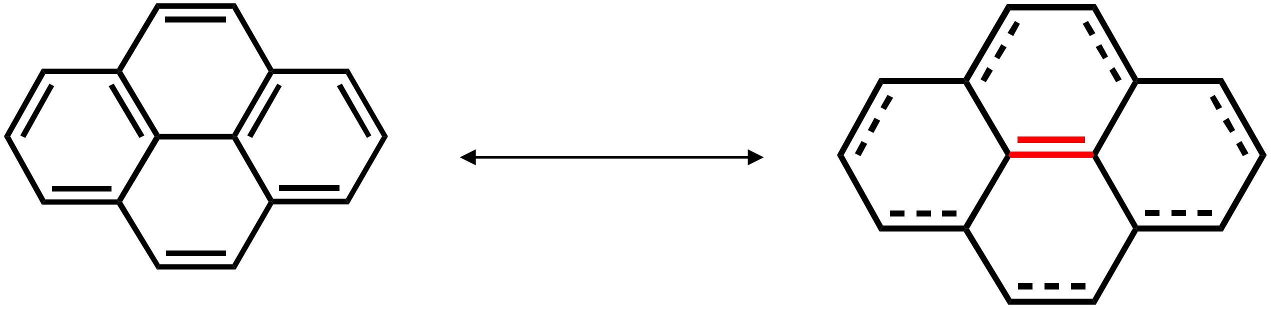
14e: aromatic



Pyrenes



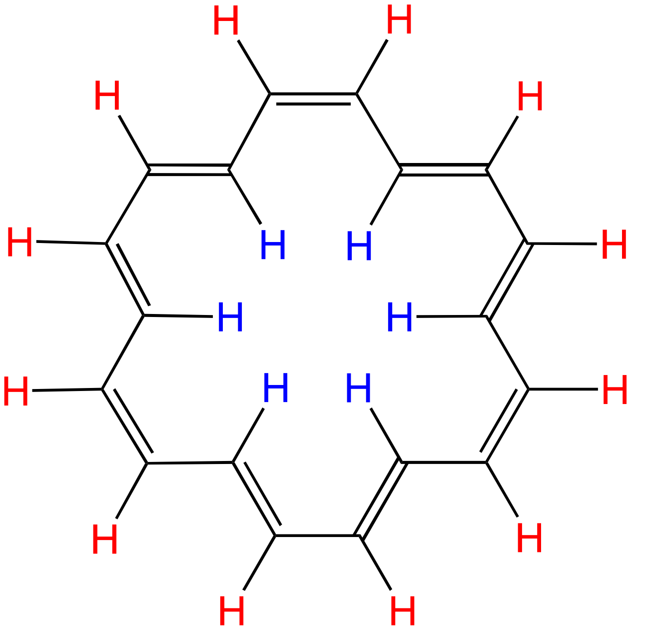
14e: aromatic

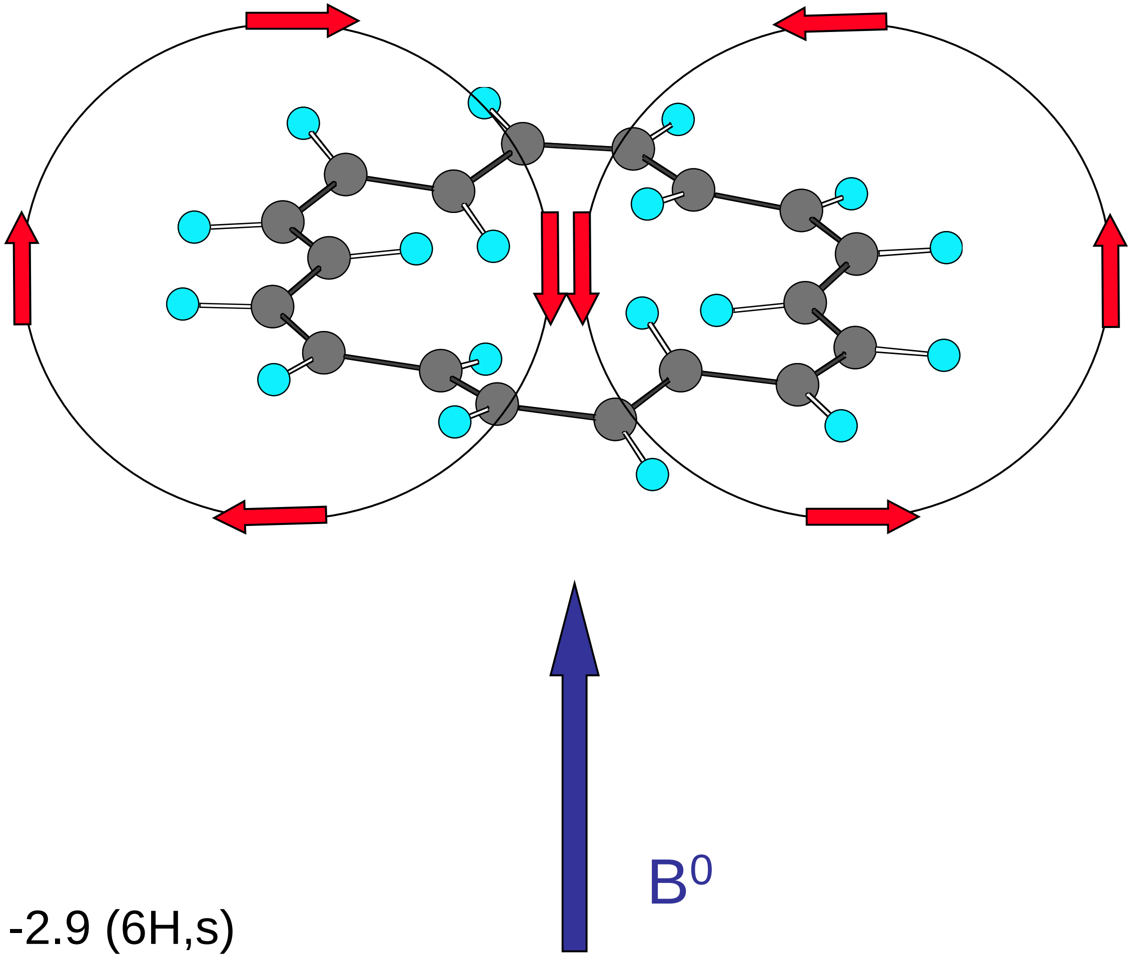


16e: anti-aromatic?

14e: aromatic!

[18]-Annulene



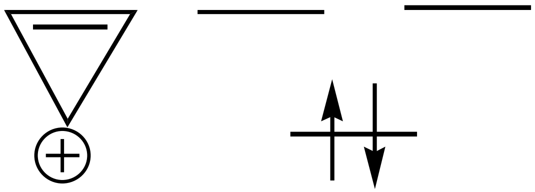


^{1}H NMR:

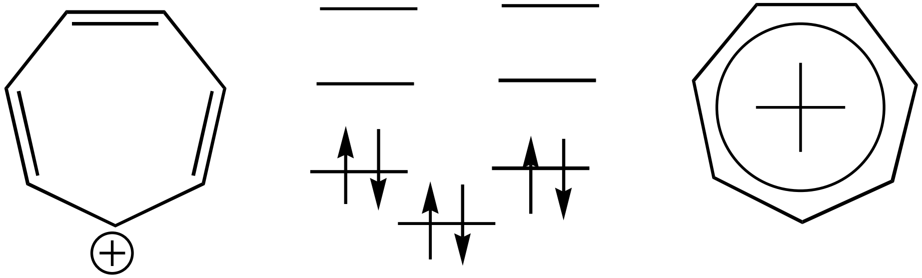
120^{O}C; δ5.45 (18H,s)

-60^{o}C; δ9.25 (12H,s), -2.9 (6H,s)

Aromatic Cations

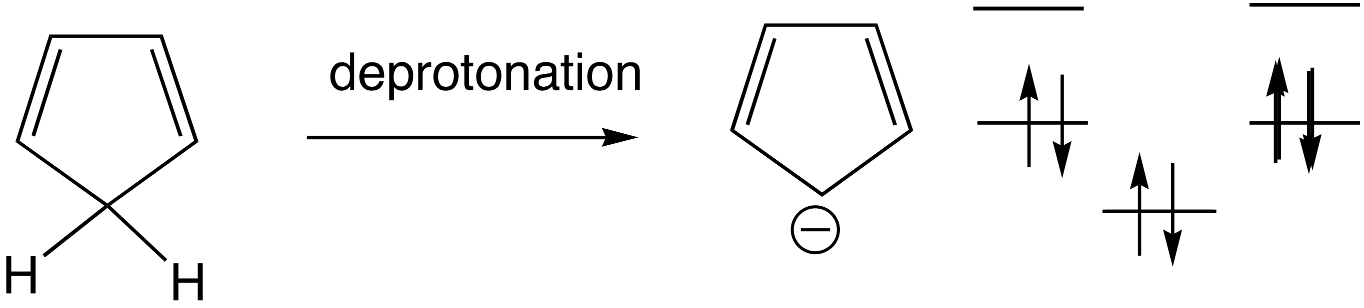


Cyclopropenium cation



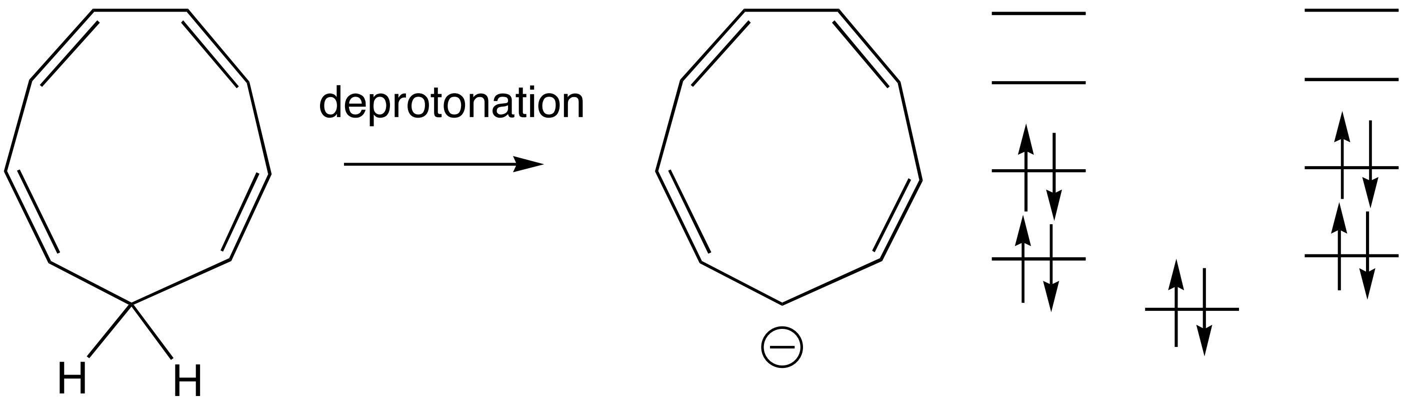
Tropylium cation
^{1}H NMR: δ9.17, singlet

Aromatic Anions



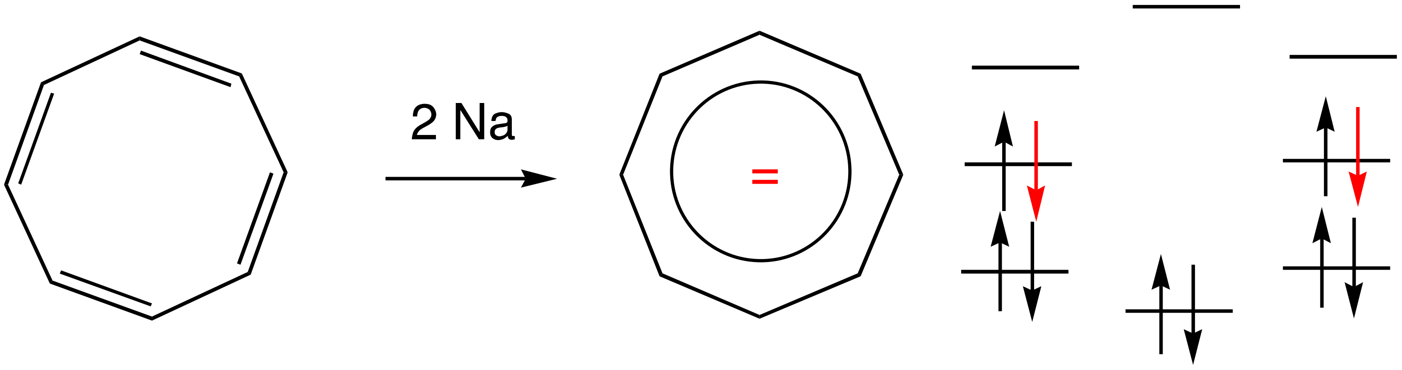
pKa = 16

Cyclopentadienyl anion



Cyclononatetraenyl anion

Aromatic Dianions I



Cyclooctatetraene

anti-aromatic

tub-shaped

^{1}H NMR: δ6.75, singlet

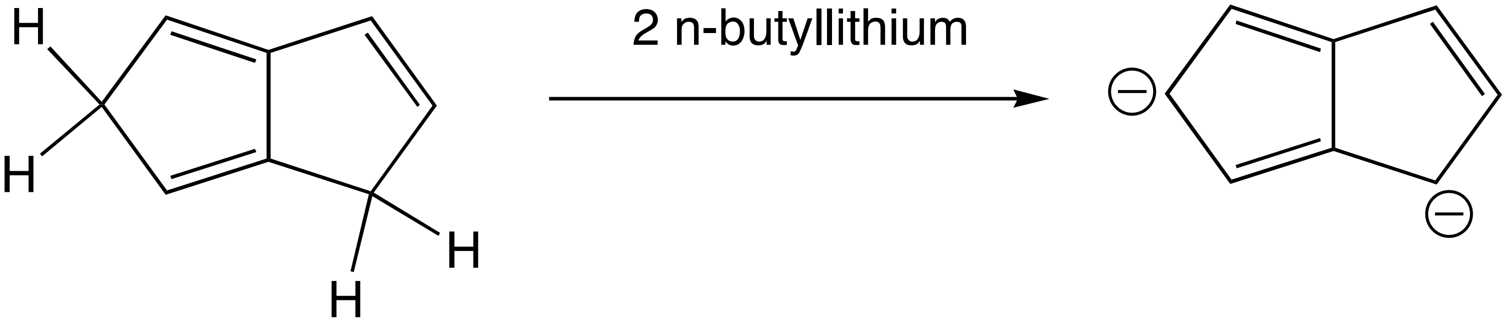
Cyclooctatetraenyl anion

aromatic

planar

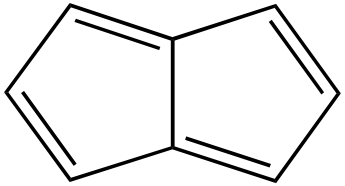
^{1}H NMR: δ5.56, singlet

Aromatic Dianions II

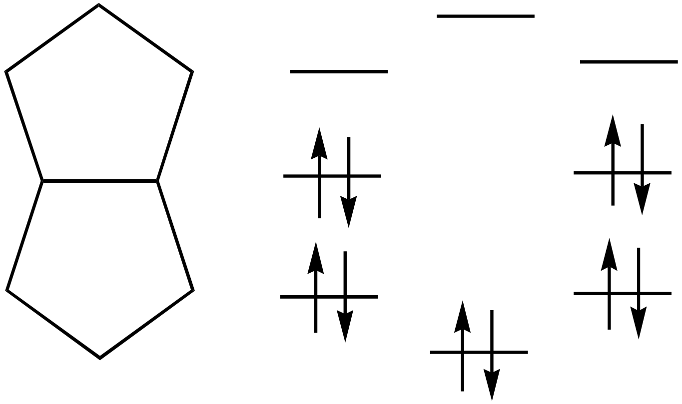


Dihydropentalene

Pentalene dianion



Pentalene



The End

Various experimental conditions have been used for oxidations of alcohols by Cr(VI) on a laboratory scale, and several examples are shown in Scheme 12.1. Entry 1 is an example of oxidation of a primary alcohol to an aldehyde. The propanal is distilled from the reaction mixture as oxidation proceeds, which minimizes overoxidation. For secondary alcohols, oxidation can be done by addition of an acidic aqueous solution containing chromic acid (known as *Jones' reagent*) to an acetone solution of the alcohol. Oxidation normally occurs rapidly, and overoxidation is minimal. In acetone solution, the reduced chromium salts precipitate and the reaction solution can be decanted. Entries 2 to 4 in Scheme 12.1 are examples of this method.

The chromium trioxide-pyridine complex is useful in situations when other functional groups might be susceptible to oxidation or the molecule is sensitive to acid.[4] A procedure for utilizing the CrO_3-pyridine complex, which was developed by Collins,[5] has been widely adopted. The CrO_3-pyridine complex is isolated and dissolved in dichloromethane. With an excess of the reagent, oxidation of simple alcohols is complete in a few minutes, giving the aldehyde or ketone in good yield. A procedure that avoids isolation of the complex can further simplify the experimental operations.[6] Chromium trioxide is added to pyridine in dichloromethane. Subsequent addition of the alcohol to this solution results in oxidation in high yield. Other modifications for use of the CrO_3-pyridine complex have been developed.[7] Entries 5 to 9 in Scheme 12.1 demonstrate the excellent results that have been reported using the CrO_3-pyridine complex in dichloromethane. Entries 5 and 6 involve conversion of primary alcohols to aldehydes, Entry 7 describes preparation of the reagent in situ, and Entry 8 is an example of application of these conditions to a primary alcohol. The conditions described in Entry 9 were developed to optimize the oxidation of sensitive carbohydrates. It was found that inclusion of 4A molecular sieves and a small amount of acetic acid accelerated the reaction.

Another very useful Cr(VI) reagent is pyridinium chlorochromate (PCC), which is prepared by dissolving CrO_3 in hydrochloric acid and adding pyridine to obtain a solid reagent having the composition $CrO_3Cl{\cdot}pyrH$.[8] This reagent can be used in amounts close to the stoichiometric ratio. Entries 10 and 11 are examples of the use of PCC. Reaction of pyridine with CrO_3 in a small amount of water gives pyridinium dichromate (PDC), which is also a useful oxidant.[9] As a solution in DMF or a suspension in dichloromethane, this reagent oxidizes secondary alcohols to ketones. Allylic primary alcohols give the corresponding aldehydes. Depending upon the conditions, saturated primary alcohols give either an aldehyde or the corresponding carboxylic acid.

$$CH_3(CH_2)_8CH_2OH \xrightarrow[\text{DMF, 25°C}]{\text{PDC}} \underset{98\%}{CH_3(CH_2)_8CH{=}O}$$

---

[4] G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953); W. S. Johnson, W. A. Vredenburgh, and J. E. Pike, *J. Am. Chem. Soc.*, **82**, 3409 (1960); W. S. Allen, S. Bernstein, and R. Little, *J. Am. Chem. Soc.*, **76**, 6116 (1954).

[5] J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).

[6] R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).

[7] J. Herscovici, M.-J. Egron, and K. Antonakis, *J. Chem. Soc., Perkin Trans. 1*, 1967 (1982); E. J. Corey and G. Schmidt, *Tetrahedron Lett.*, 399 (1979); S. Czernecki, C. Georgoulis, C. L. Stevens, and K. Vijayakumaran, *Tetrahedron Lett.*, **26**, 1699 (1985).

[8] E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975); G. Piancatelli, A. Scettri, and M. D'Auria, *Synthesis*, 245 (1982).

[9] E. J. Corey and G. Schmidt, *Tetrahedron Lett.*, 399 (1979).

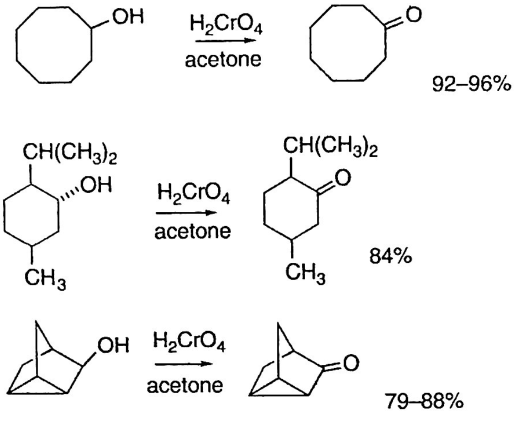
PDC

Scheme 12.1. Oxidation with Chromium(VI) Reagents

A. Chromic acid solutions

1[a] $CH_3CH_2CH_2OH \xrightarrow[H_2O]{H_2CrO_4} CH_3CH_2CH{=}O$ 45–49%

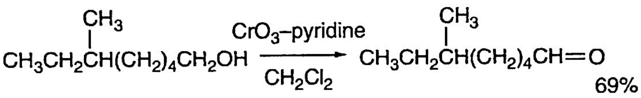
2[b] 3[c] 4[d]



B. Chromium trioxide–pyridine

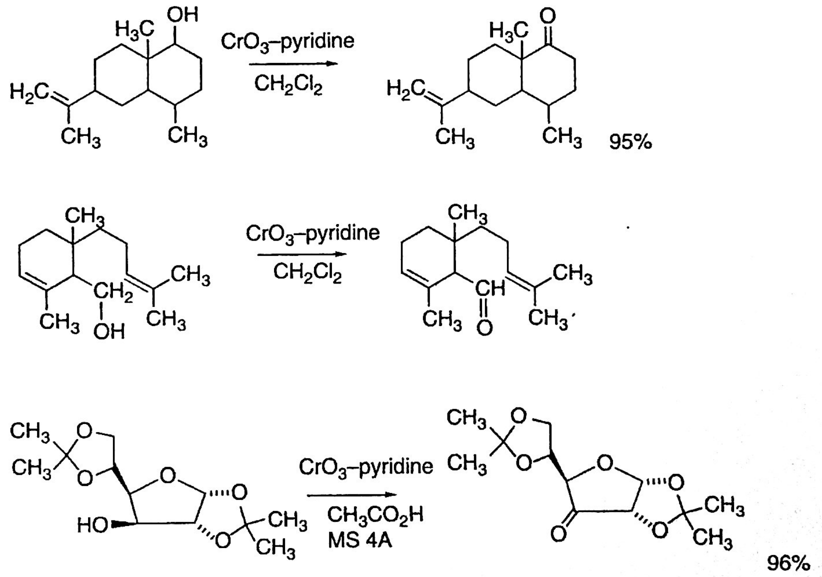
5[e] $CH_3(CH_2)_5CH_2OH \xrightarrow[CH_2Cl_2]{CrO_3\text{–pyridine}} CH_3(CH_2)_5CH{=}O$ 70–84%

6[f]



$$CH_3CH_2\overset{CH_3}{\overset{|}{C}}H(CH_2)_4CH_2OH \xrightarrow[CH_2Cl_2]{CrO_3\text{–pyridine}} CH_3CH_2\overset{CH_3}{\overset{|}{C}}H(CH_2)_4CH{=}O$$ 69%

7[g] 8[h] 9[i]

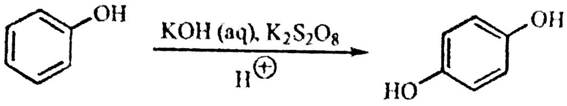


(*Continued*)

See the similarity in the:

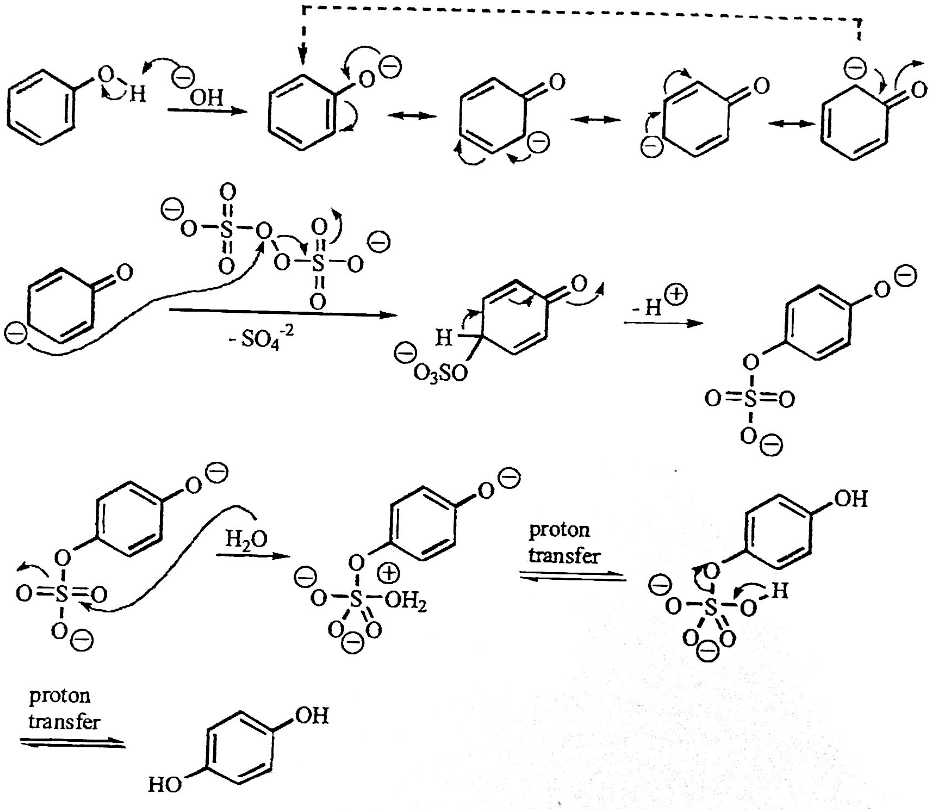
Elbs Persulfate Oxidation (Elbs Reaction)

The Reaction:



Proposed Mechanism:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 92-93; V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International, Ltd., Pangbourne, U.K., 2002, pp 320-321.

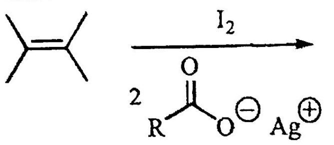


Notes:

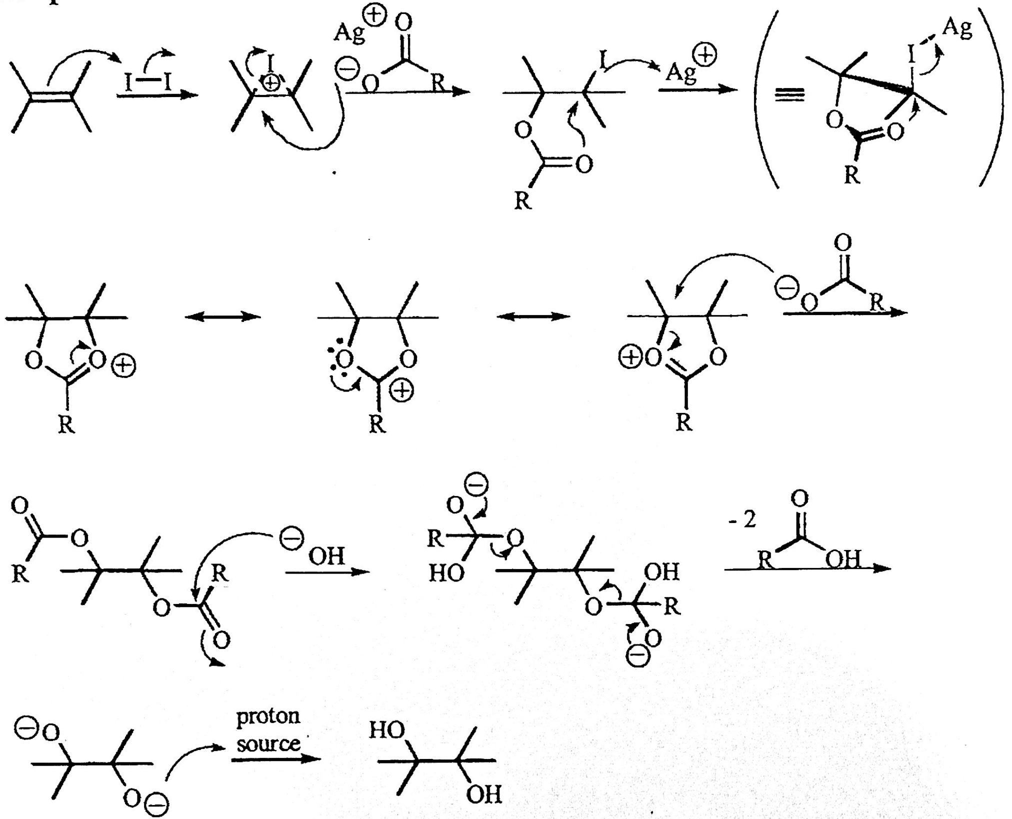
Oxidation usually occurs at the *para* position. If the *para* position is occupied, the *ortho* position is the next likely site for reaction.

Prévost Reaction (Glycolization)

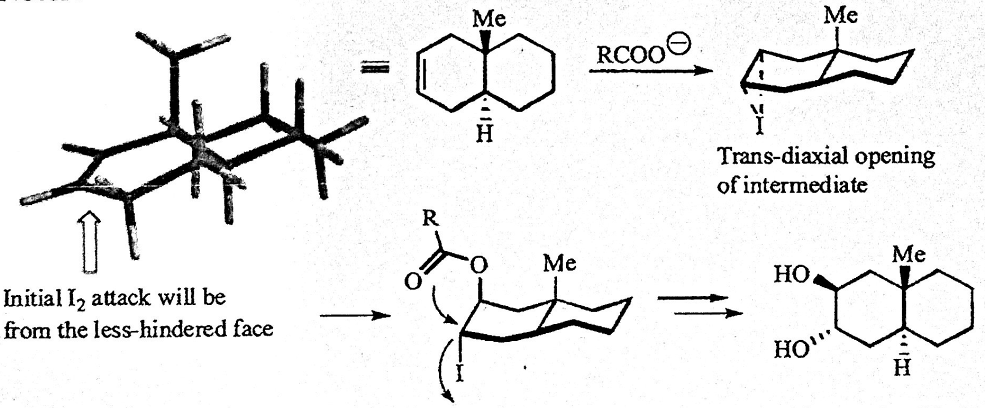
The Reaction:



Proposed Mechanism:



Notes:



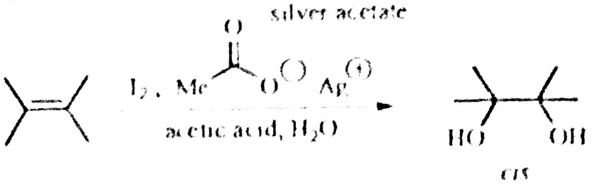
Trans-diaxial opening of intermediate

Initial I_2 attack will be from the less-hindered face

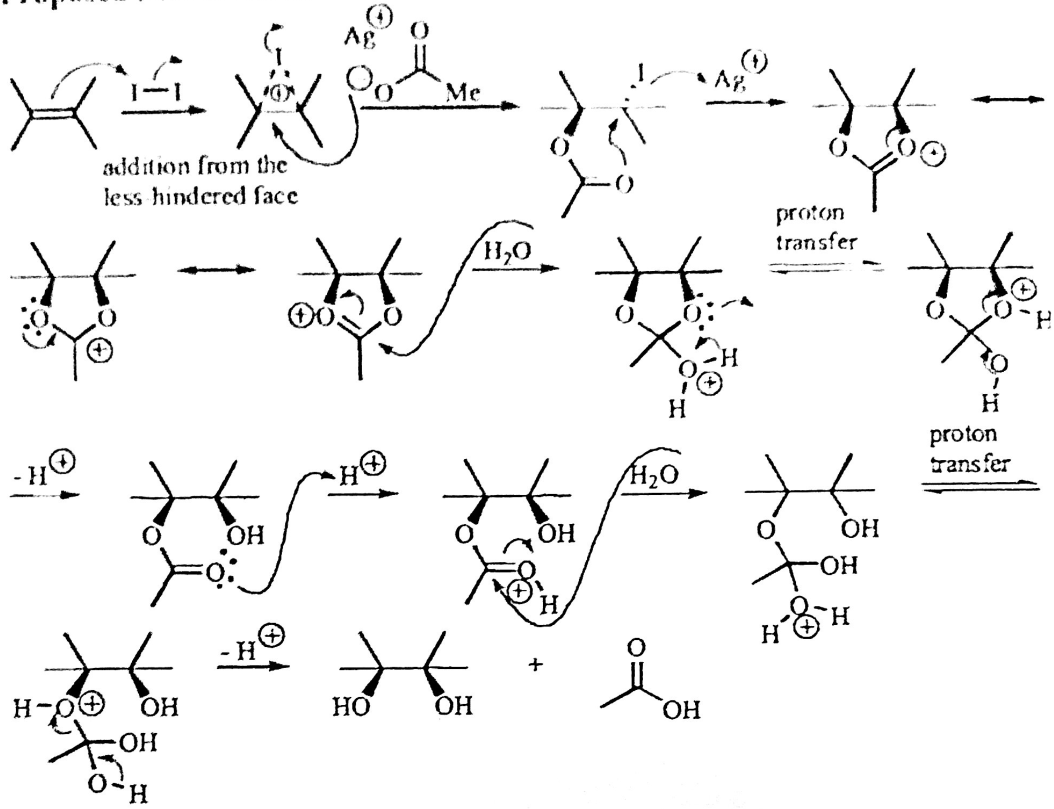
V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms,* Alpha Science International Ltd., Pangbourne, U.K., 2002, pp. 189-191; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1049-1050

Woodward Modification of the Prevost Reaction

The Reaction:

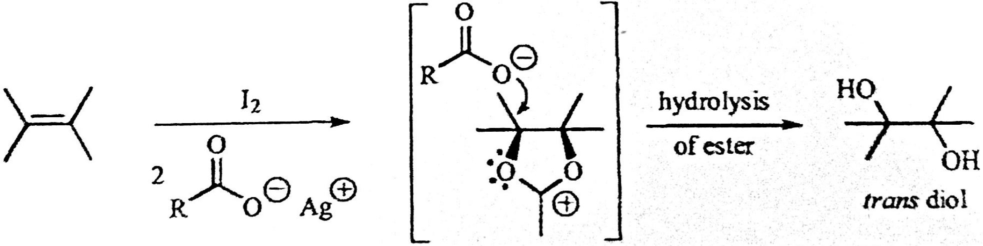


Proposed Mechanism:



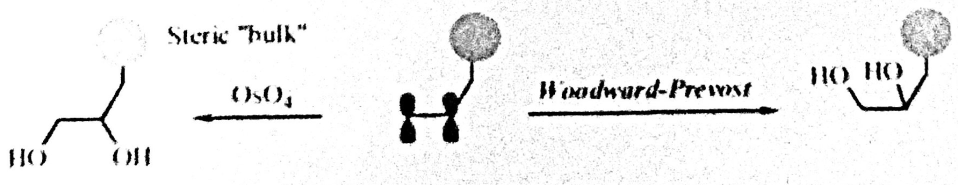
Notes:

The ***Prevost Reaction***:



This ***Woodward-Prevost reaction*** provides *cis* diols at the more hindered face. This is due to the first step, the addition of iodine from the less-hindered face.

Contrast this reaction with OsO_4 or $MnO_4^{\ominus}$



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Tamil Nadu

Hydrogenation Catalysts

Ni

Ni_2B
Nickel Boride

[12007-01-1]

T. J. Caggiano, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3694

Ni Catalysts

[7440-02-0]

C. R. Sarko, M. DiMare, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3701

Raney Nickel

Pd

Pt/BaSO₄

Rosenmund Catalyst

Pd/CaCO₃ / Pb-poisoned

Lindlar Catalyst

Pd/C

[7440-05-3]

A. O. King, I. Shinka, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3867

Pd/Gr (graphite)

[59873-73-3]

E. M. Leahy, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3887

$Pd(OH)_2$

Pearlman's Catalyst

Pt

Pt/Al_2O_3

[7440-06-4]

A. O. King, I. Shinka, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4159

Pt/C

Heyn's Catalyst [7440-06-4]

A. O. King, I. Shinka, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4160

PtO_2

Adam's Catalyst

Rh

Rh/Al_2O_3

[7440-16-6]

S. Siegel, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 6, 4405

$Rh(PPh_3)_3Cl$

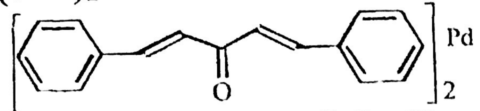
Wilkinson's Catalyst

Ru

Ru Catalysts

S. Siegel, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 6, 4410

Pd(dba)$_2$



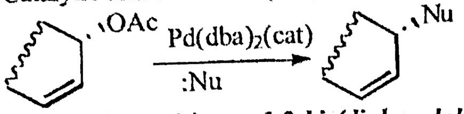
Bis(dibenzylideneacetone)palladium(0)
[32005-36-0]

Commercially available

J. R. Stille, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 482

Notes:

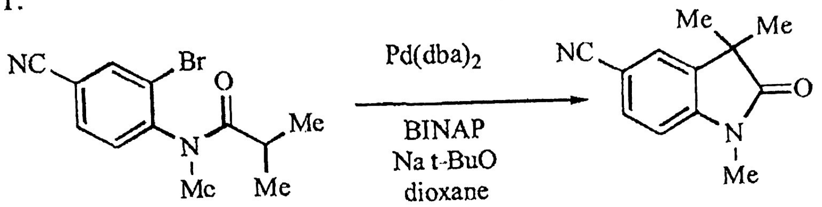
Catalytic amounts of Pd(dba)$_2$ will activate allylic acetates to nucleophilic attack.



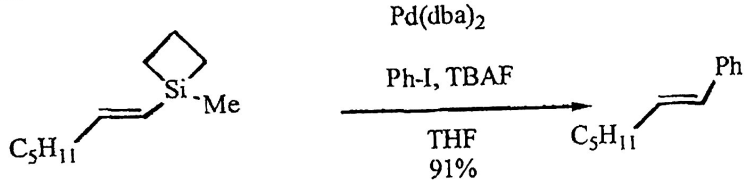
Triphenylphosphine or ***1,2-bis(diphenylphosphino)ethane*** (*dppe*) are often part of the reaction mixture.

Examples:

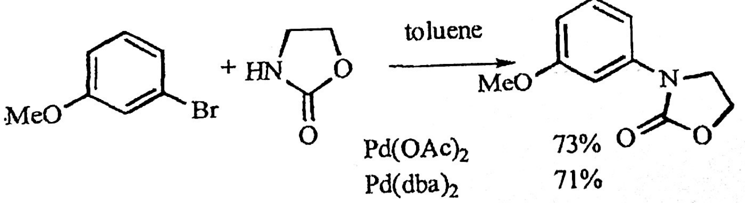
1.[1]



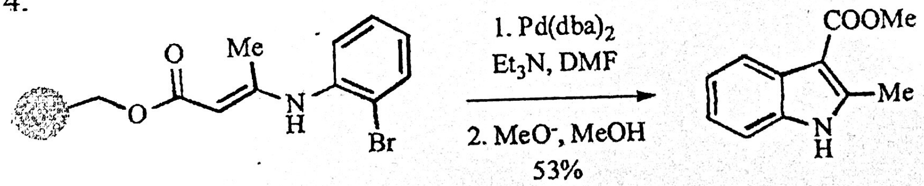
2.[2]



3.[3]



4.[4]



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[1] K. H. Shaughnessy, B. C. Harmann, J. F. Hartwig, *Journal of Organic Chemistry* **1998**, 63, 6546

[2] S. E. Denmark, J. Y. Choi, *Journal of the American Chemical Society* **1999**, 121, 5821

[3] S. Cacchi, G. Fabrizi, A. Goggiamani, G. Zappia, *Organic Letters* **2001**, 3, 2539

[4] K. Yamazaki, Y. Kondo, *Journal of Combinatorial Chemistry* **2002**, 4, 191

Pearlman's Catalyst

$Pd(OH)_2$ / C

Palladium(II) hydroxide on carbon

[7440-05-3]

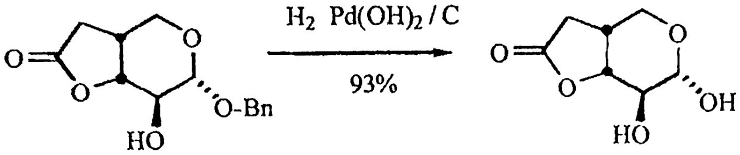
Commercially available

A. O. King, I. Shinkai, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 6, 3888

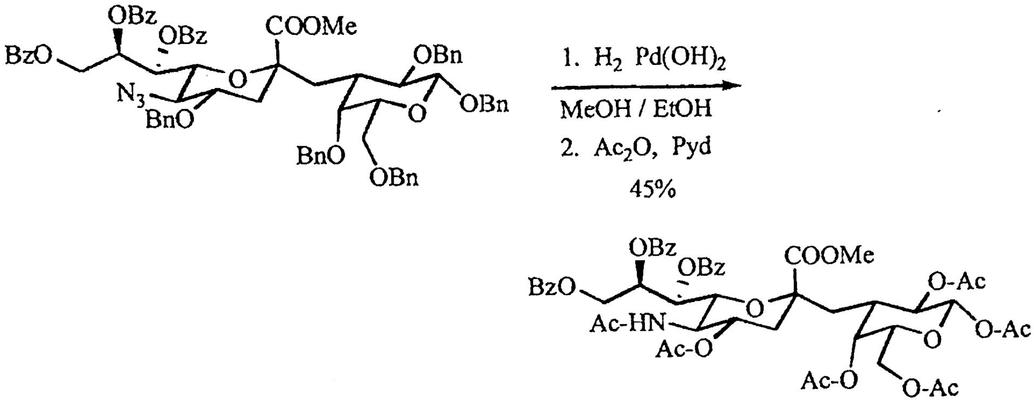
Uses: A catalyst that finds use in the removal of benyzyl groups under hydrogenolysis conditions.

Examples:

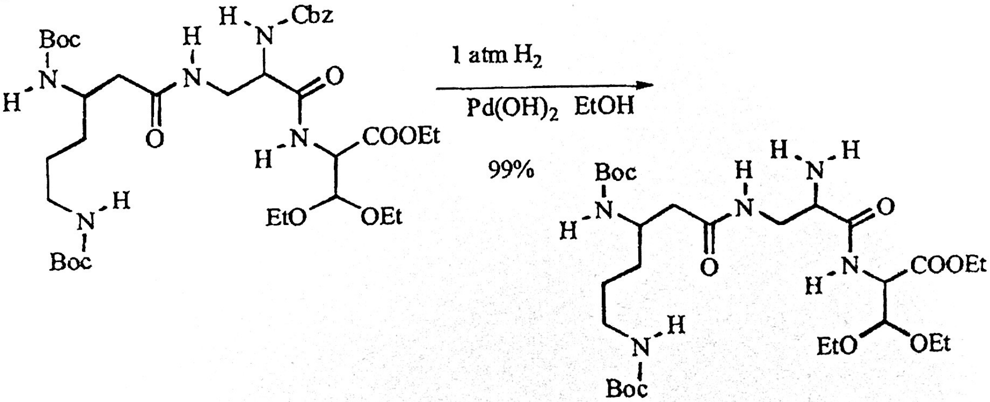
1.[1]



2.[2]



3.[3]



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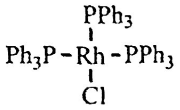
[1] Y. Al-Abed, N. Naz, D. Mootoo, W. Voelter, *Tetrahedron Letters* **1996**, 37, 8641

[2] W. Notz, C. Hartel, B. Waldscheck, R. R. Schmidt, *Journal of Organic Chemistry* **2001**, 66, 4250

[3] D. E. DeMong, R. M. Williams, *Journal of the American Chemical Society* **2003** 125, 8561

Wilkinson's Catalyst



$$Ph_3P-\overset{PPh_3}{\underset{Cl}{Rh}}-PPh_3$$

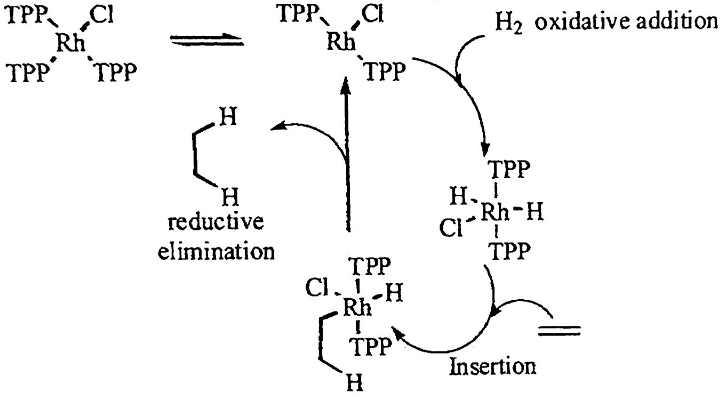
Chlorotris(triphenylphosphine)rhodium (I)
[14694-95-2]

Commercially available

K. Burgess, W. A. van derDonk, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 2, 1253

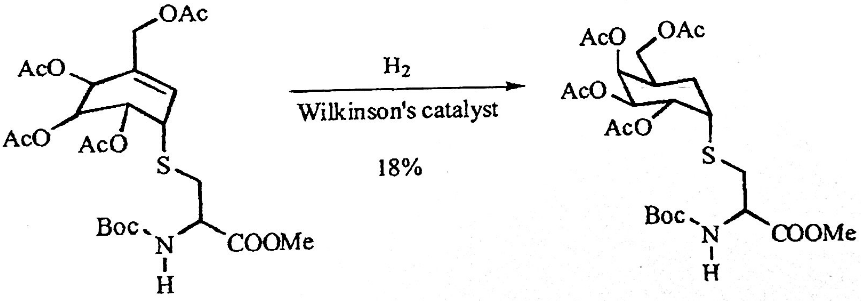
Notes:

Useful for homogeneous reduction of alkenes. As a consequence of the reagent bulk, it is understandable that the reactivity of alkene reduction is dependent on substitution; the less-substituted alkenes react faster. Also, reduction occurs from the less-hindered face in a *cis*-stereochemistry. Many other functional groups are tolerated by conditions.



Examples:

1.[1]



---

[1] L. J. Whalen, R. L. Halcomb, *Organic Letters* 2004, 6, 3221

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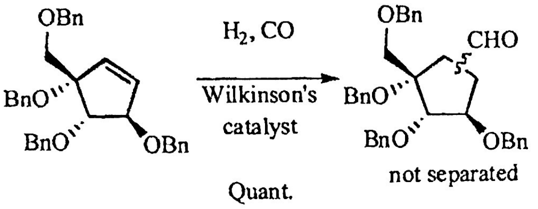
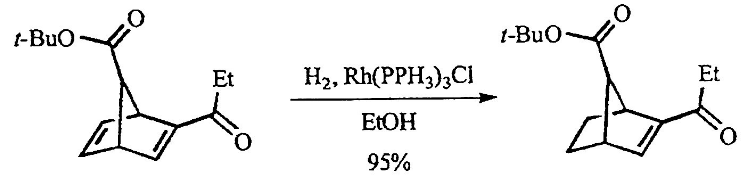
Assistant Professor & Research Advisor
PG & Research Department of Chemistry
Govt. Arts College, Ariyalur - 621 713
Tamil Nadu

Wilkinson's Catalyst

2.[1] Use in hydroformylation:



3.[2]



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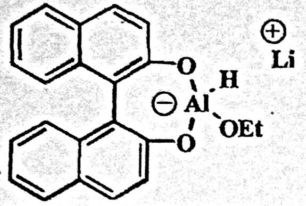
[1] M. Seepersauda, M. Kettunenb, A. S. Abu-Surrahc, T. Repob, W. Voelterd, Y. Al-Abed, *Tetrahedron Letters* **2002**, 43, 1793

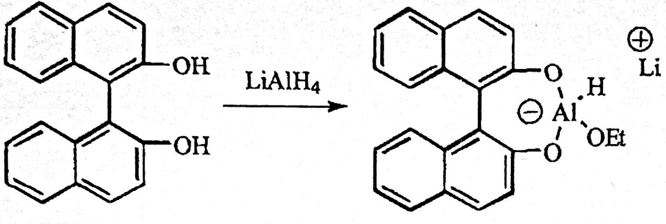
[2] H. M. L. Davies, E. Saikali, N. J. S. Huby, V. J. Gilliatt, J. J. Matasi, T. Sexton, S. R. Childers, *Journal of Medicinal Chemistry* **1994**, 37, 1262

Noyori's Reagent

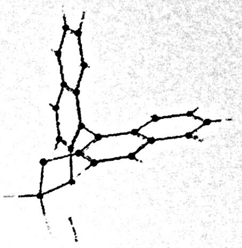


[16853-85-3] ·Lithium aluminum hydride-2,2′-dihydroxy-1,1′-binaphthyl ((*R*)-BINAL)
[18531-94-7] ·Lithium aluminum hydride-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-BINAL)

Preparation:



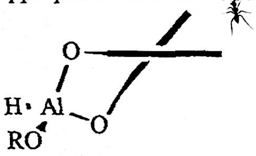
BINOL



Commercially available

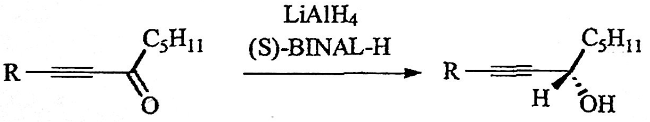
A. S. Gopalan, H. K. Jacobs, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons,
L. A. Paquette, Ed., New York, 1995, 5, 3022

Notes: Used for enantioselective reduction of carbonyl groups. The reducing agent (for the appropriate enantiomer) can be designated in carton style to show the twist in the ring systems as:



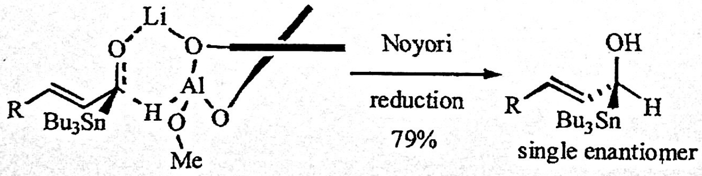
Examples:

1.[1]



R = H	84%
R = C_4H_9	90%

2.[2]



single enantiomer

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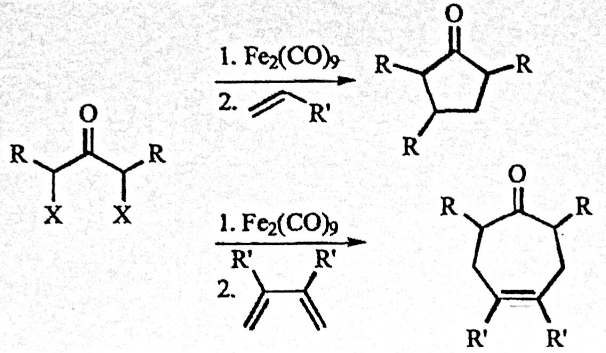
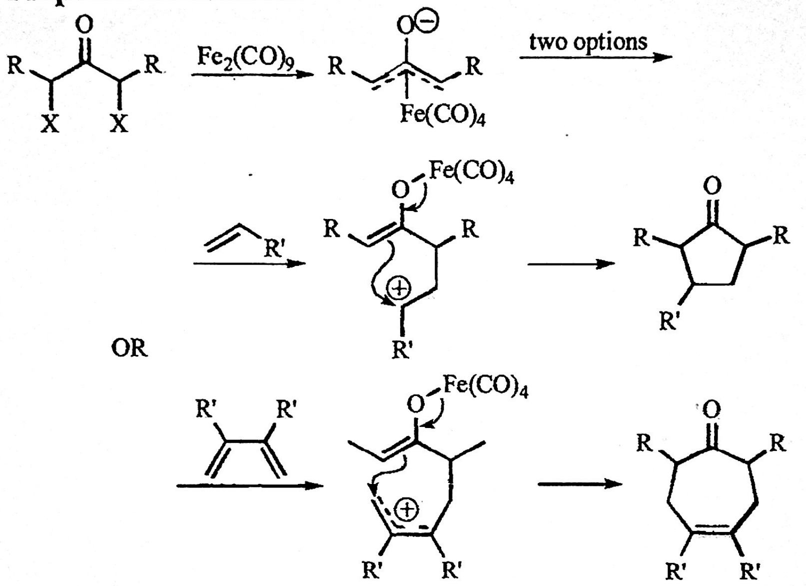
[1] M. Nishizawa, M. Yamada, R. Noyori, *Tetrahedron Letters* **1981**, 22, 247
[2] J. A. Marshall, W. Y. Gung, *Tetrahedron Letters* **1998**, 29, 1657

Noyori Annulation

The Reaction:

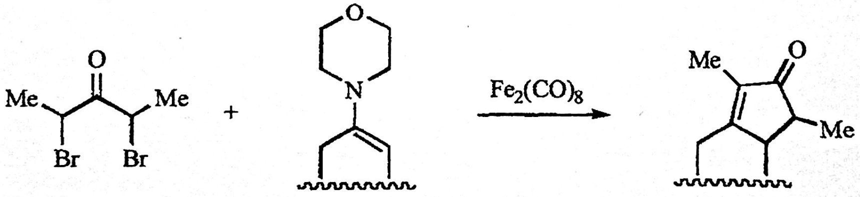


Proposed Mechanism:

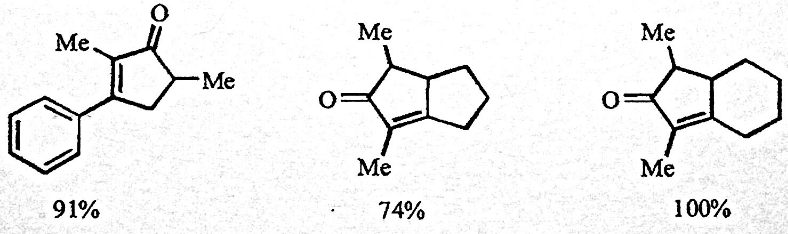


Notes:

In the original work, reaction with enamines:



By this approach:



Y. Hayakawa, K. Yokoyama, R. Noyori, *Journal of the American Chemical Society* **1978,** 100, 1799

Alkalimetal for reduction : Reduction using Li/Na/Ca

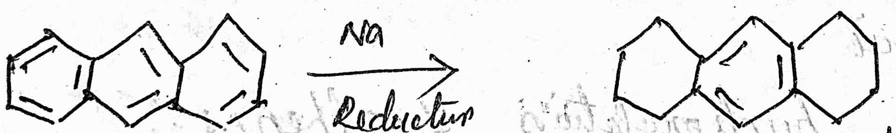
(i) Na-Hg Sodium amalgam

(ii) Lithium is used for the reducing agent

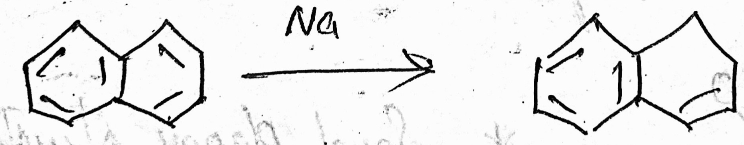
(iii) Sodium is " " " * Acid to aldehyde

Eg :- $CH_3COOH \xrightarrow{Li} CH_3CHO$

$C_2H_5COOCH_3 \xrightarrow{Li} C_2H_5CHO$.



Dihydroo anthracen



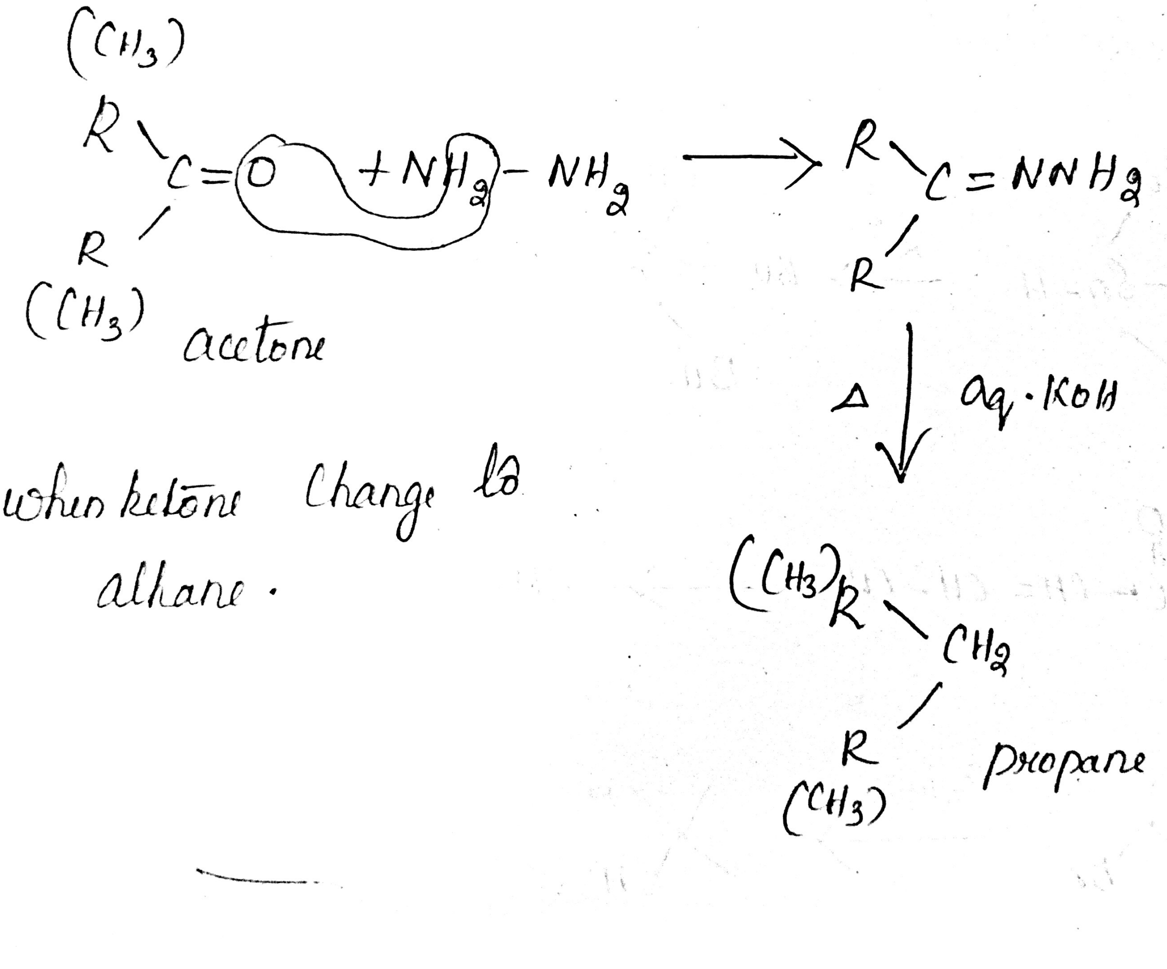
1,2-Dialin

$R-CHO \xrightarrow{Na} R-CH_2OH$

Reduction involving hydrazine :-

Wolf Kishner reduction

(i) hydrazine group used as The reducing agent.



(ii) when ketone Change to alkane.

L-Selectride®

$\mathrm{LiBH}(s\text{-Bu})3$

Lithium Tri-s-butylborohydride

[38721-52-7]

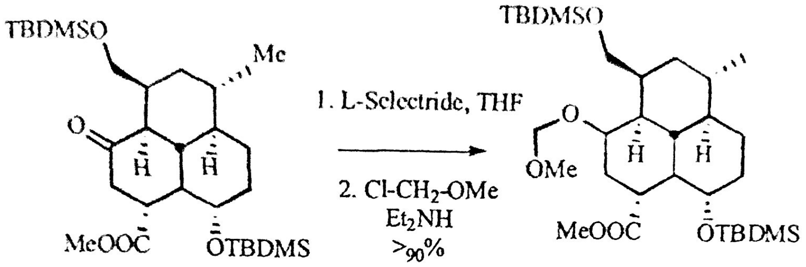
Commercially available

J. L. Hubbard, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 5, 3172

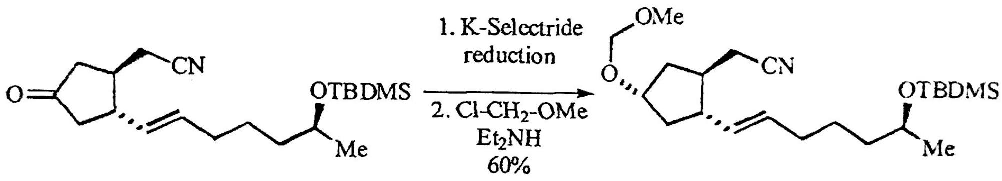
Notes: Selective reducing agent. The potassium and sodium Selectrides are also available. Will convert C-X to C-H, with I>Br>Cl.

Examples:

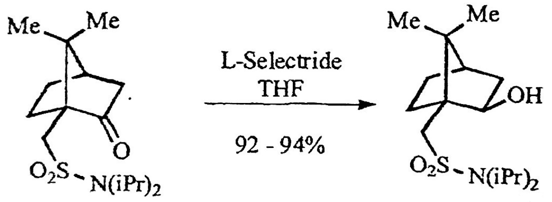
1.[1]



2.[2]



3.[3]



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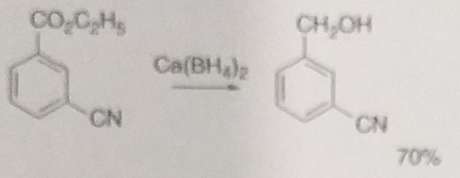
[1] E. Piers, M. A. Romero, *Tetrahedron* 1993, 49, 5791

[2] J. Nokami, M. Ohkura, Y. Dan-Oh, Y. Sakamoto, *Tetrahedron Letters* 1991, 32, 2409

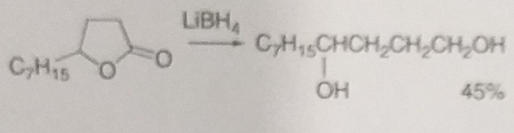
[3] W. Oppolzer, C. Chapuis, G. Bernardinelli, *Tetrahedron Letters* 1984, 25, 5885

K- Selectride

Lewis acid strength and hardness of the lithium cation. Both $LiBH_4$ and $Ca(BH_4)_2$ are more reactive than sodium borohydride. This enhanced reactivity is due to the greater Lewis acid strength of Li^+ and Ca^{2+}, compared with Na^+. Both of these reagents can reduce esters and lactones efficiently.

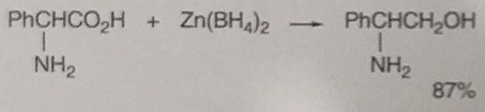


Ref. 64



Ref. 65

Zinc borohydride, which is also a useful reagent,[66] is prepared by reaction of $ZnCl_2$ with $NaBH_4$ in THF. Owing to the stronger Lewis acid character of Zn^{2+}, $Zn(BH_4)_2$ is more reactive than $NaBH_4$ toward esters and amides and reduces them to alcohols and amines, respectively.[67] $Zn(BH_4)_2$ reduces carboxylic acids to primary alcohols.[68] The reagent also smoothly reduces α-aminoacids to β-aminoalcohols.[69]



$$\underset{NH_2}{PhCHCO_2H} + Zn(BH_4)_2 \rightarrow \underset{NH_2}{PhCHCH_2OH} \quad 87\%$$

Sodium borohydride is sometimes used in conjunction with $CeCl_3$ (*Luche's reagent*).[70] The active reductants under these conditions are thought to be alkoxyborohydrides. Sodium cyanoborohydride is a useful derivative of sodium borohydride.[71] The electron-attracting cyano substituent reduces reactivity and only iminium groups are rapidly reduced by this reagent.

Alkylborohydrides are also used as reducing agents. These compounds have greater steric demands than the borohydride ion and therefore are more stereoselective in situations in which steric factors come into play.[72] These compounds are prepared by reaction of trialkylboranes with lithium, sodium, or potassium hydride.[73] Several of the compounds are available commercially under the trade name Selectrides®.[74]

[64] H. C. Brown, S. Narasimhan, and Y. M. Choi, *J. Org. Chem.*

[65] K. Soai and S. Ookawa, *J. Org. Chem.*, **51**, 4000 (1986).

[66] S. Narasimhan and R. Balakumar, *Aldrichimica Acta*, **31**, 19 (1998).

[67] S. Narasimhan, S. Madhavan, R. Balakumar, and S. Swamalakshmi, *Synth. Commun.*, **27**, 391 (1997).

[68] S. Narasimhan, S. Madhavan, and K. G. Prasad, *J. Org. Chem.*, **60**, 5314 (1995); B. C. Ranue and A. R. Das, *J. Chem. Soc., Perkin Trans. 1*, 1561 (1992).

[69] S. Narasimhan, S. Madhavan, and K. G. Prasad, *Synth. Commun.*, **26**, 703 (1996).

[70] A. C. Gemal and J.-L. Luche, *J. Am. Chem. Soc.*, **103**, 5454 (1981).

[71] C. F. Lane, *Synthesis*, 135 (1975).

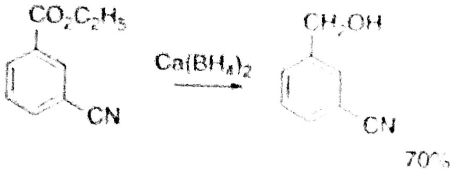
[72] H. C. Brown and S. Krishnamurthy, *J. Am. Chem. Soc.*, **94**, 7159 (1972); S. Krishnamurthy and H. C. Brown, *J. Am. Chem. Soc.*, **98**, 3383 (1976).

[73] H. C. Brown, S. Krishnamurthy, and J. L. Hubbard, *J. Am. Chem. Soc.*, **100**, 3343 (1978).

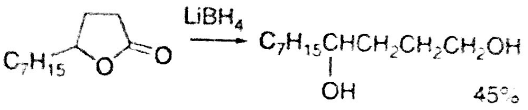
[74] Selectride is a trade name of the Aldrich Chemical Company.

K-Selectride

Lewis acid strength and hardness of the lithium cation. Both $LiBH_4$ and $Ca(BH_4)_2$ are more reactive than sodium borohydride. This enhanced reactivity is due to the greater Lewis acid strength of Li^+ and Ca^{2+}, compared with Na^+. Both of these reagents can reduce esters and lactones efficiently.

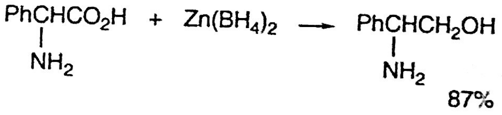


Ref. 64



Ref. 65

Zinc borohydride, which is also a useful reagent,[66] is prepared by reaction of $ZnCl_2$ with $NaBH_4$ in THF. Owing to the stronger Lewis acid character of Zn^{2+}, $Zn(BH_4)_2$ is more reactive than $NaBH_4$ toward esters and amides and reduces them to alcohols and amines, respectively.[67] $Zn(BH_4)_2$ reduces carboxylic acids to primary alcohols.[68] The reagent also smoothly reduces α-aminoacids to β-aminoalcohols.[69]



$$\underset{NH_2}{PhCHCO_2H} + Zn(BH_4)_2 \longrightarrow \underset{NH_2}{PhCHCH_2OH} \quad 87\%$$

Sodium borohydride is sometimes used in conjunction with $CeCl_3$ (*Luche's reagent*).[70] The active reductants under these conditions are thought to be alkoxyborohydrides. Sodium cyanoborohydride is a useful derivative of sodium borohydride.[71] The electron-attracting cyano substituent reduces reactivity and only iminium groups are rapidly reduced by this reagent.

Alkylborohydrides are also used as reducing agents. These compounds have greater steric demands than the borohydride ion and therefore are more stereoselective in situations in which steric factors come into play.[72] These compounds are prepared by reaction of trialkylboranes with lithium, sodium, or potassium hydride.[73] Several of the compounds are available commercially under the trade name Selectrides®.[74]

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[64] H. C. Brown, S. Narasimhan, and Y. M. Choi, *J. Org. Chem.*

[65] K. Soai and S. Ookawa, *J. Org. Chem.*, **51**, 4000 (1986).

[66] S. Narasimhan and R. Balakumar, *Aldrichimica Acta*, **31**, 19 (1998).

[67] S. Narasimhan, S. Madhavan, R. Balakumar, and S. Swamalakshmi, *Synth. Commun.*, **27**, 391 (1997).

[68] S. Narasimhan, S. Madhavan, and K. G. Prasad, *J. Org. Chem.*, **60**, 5314 (1995); B. C. Ranue and A. R. Das, *J. Chem. Soc., Perkin Trans. 1*, 1561 (1992).

[69] S. Narasimhan, S. Madhavan, and K. G. Prasad, *Synth. Commun.*, **26**, 703 (1996).

[70] A. C. Gemal and J.-L. Luche, *J. Am. Chem. Soc.*, **103**, 5454 (1981).

[71] C. F. Lane, *Synthesis*, 135 (1975).

[72] H. C. Brown and S. Krishnamurthy, *J. Am. Chem. Soc.*, **94**, 7159 (1972); S. Krishnamurthy and H. C. Brown, *J. Am. Chem. Soc.*, **98**, 3383 (1976).

[73] H. C. Brown, S. Krishnamurthy, and J. L. Hubbard, *J. Am. Chem. Soc.*, **100**, 3343 (1978).

[74] Selectride is a trade name of the Aldrich Chemical Company.

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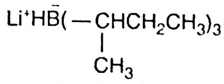
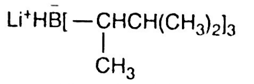
K-selectride

(14)



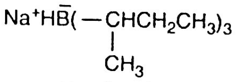
$Li^+H\bar{B}(-CH(CH_3)CH_2CH_3)_3$

L-selectride



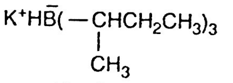
$Li^+H\bar{B}[-CH(CH_3)CH(CH_3)_2]_3$

LS-selectride



$Na^+H\bar{B}(-CH(CH_3)CH_2CH_3)_3$

N-selectride



$K^+H\bar{B}(-CH(CH_3)CH_2CH_3)_3$

K-selectride

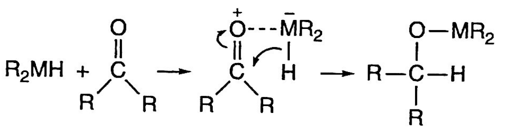
Derivatives of aluminum hydrides in which one or more of the hydrides is replaced by an alkoxide ion can be prepared by addition of the calculated amount of the appropriate alcohol.

$$LiAlH_4 + 2\,ROH \longrightarrow LiAlH_2(OR)_2 + 2\,H_2$$

$$LiAlH_4 + 3\,ROH \longrightarrow LiAlH(OR)_3 + 3\,H_2$$

These reagents generally show increased solubility in organic solvents, particularly at low temperatures, and are useful in certain selective reductions.[75] Lithium tri-*t*-butoxyaluminum hydride and sodium *bis*-(2-methoxyethoxy)aluminum hydride (Red-Al)[76] are examples of these types of reagents that have synthetic use. Their reactivity toward carbonyl groups is summarized in Table 5.3.

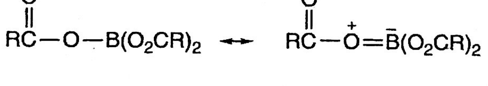
Closely related to, but distinct from, the anionic boron and aluminum hydrides are the neutral boron (borane, BH_3) and aluminum (alane, AlH_3) hydrides. These molecules also contain hydrogen that can be transferred as hydride. Borane and alane differ from the anionic hydrides in being electrophilic species by virtue of the vacant *p* orbital and are Lewis acids. Reduction by these molecules occurs by an intramolecular hydride transfer in a Lewis acid-base complex of the reactant and reductant.



Alkyl derivatives of boron and alane can function as reducing reagents in a similar fashion. Two reagents of this type, disiamylborane and diisobutylaluminum hydride (DiBAlH) are included in Table 5.3. The latter is an especially useful reagent.

Diborane also has a useful pattern of selectivity. It reduces carboxylic acids to primary alcohols under mild conditions that leave esters unchanged.[77] Nitro and cyano groups are relatively unreactive toward diborane. The rapid reaction between carboxylic acids and diborane is the result of formation of a triacyloxyborane intermediate by protonolysis of the B–H bonds. The resulting compound is essentially a mixed anhydride of the carboxylic acid and boric acid in which the carbonyl groups have enhanced reactivity toward borane or acetoxyborane.

$$3\,RCO_2H + BH_3 \longrightarrow (RCO_2)_3B + 3\,H_2$$



$$RC(=O)-O-B(O_2CR)_2 \longleftrightarrow RC(=O)-\overset{+}{O}=\bar{B}(O_2CR)_2$$

Diborane also reduces amides to amines (see Section 5.3.1.2).

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[75] J. Malek and M. Cerny, *Synthesis*, 217 (1972); J. Malek, *Org. React.*, **34**, 1 (1985).

[76] Red-Al is a trademark of the Aldrich Chemical Company.

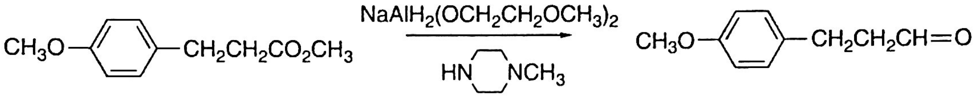
[77] N. M. Yoon, C. S. Pak, H. C. Brown, S. Krishnamurthy, and T. P. Stocky, *J. Org. Chem.*, **38**, 2786 (1973).

(15)

K-Selectride

In synthesis, the principal factors that affect the choice of a reducing agent are selectivity among functional groups (chemoselectivity) and stereoselectivity. Chemoselectivity can involve two issues. One may wish to effect a *partial reduction* of a particular functional group or it may be necessary to *reduce one group in preference to another.*[78] In the sections that follow, we consider some synthetically useful partial and selective reductions.

5.3.1.1. Partial Reduction of Carboxylic Acid Derivatives. One of the more difficult partial reductions is the conversion of a carboxylic acid derivative to an aldehyde without overreduction to the alcohol. Aldehydes are inherently more reactive than acids or esters, so the challenge is to stop the reduction at the aldehyde stage. Several approaches have been used to achieve this objective. One is to replace some of the hydrogens in the hydride with more bulky groups, thus modifying reactivity by steric factors. Lithium tri-*t*-butoxyaluminum hydride is an example of this approach.[79] Sodium tri-*t*-butoxyaluminum hydride can be used to reduce acid chlorides to aldehydes without overreduction to the alcohol.[80] The excellent solubility of sodium *bis*-(2-methoxyethoxy)aluminum hydride (Red-Al) makes it a useful reagent for selective reductions. The reagent is soluble in toluene even at −70° C, and selectivity is enhanced by the low temperature. It is possible to reduce esters to aldehydes and lactones to lactols with this reagent.



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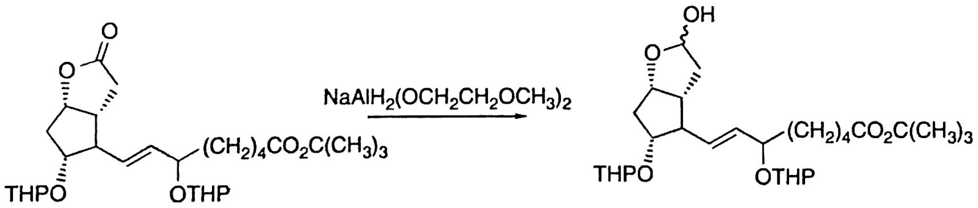

Ref. 82

The most widely used reagent for partial reduction of esters and lactones at the present time is diisobutylaluminum hydride (DiBAlH).[83] By use of a controlled amount of the reagent at low temperature, partial reduction can be reliably achieved. The selectivity results from the relative stability of the hemiacetal intermediate that is formed. The aldehyde is not liberated until the hydrolytic workup and is therefore not

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[78] For more complete discussion of functional group selectivity of hydride reducing agents, see E. R. H. Walter, *Chem. Soc. Rev.*, **5**, 23 (1976).

[79] H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **80**, 5377 (1958).

[80] J. S. Cha and H. C. Brown, *J. Org. Chem.*, **58**, 4732 (1993).

[81] R. Kanazawa and T. Tokoroyama, *Synthesis*, 526 (1976).

[82] H. Disselnkoetter, F. Lieb, H. Oediger, and D. Wendisch, *Liebigs Ann. Chem.*, 150 (1982).

[83] F. Winterfeldt, *Synthesis*, 617 (1975); N. M. Yoon and Y. G. Gyoung, *J. Org. Chem.*, **50**, 2443 (1985).

Luche Reagent[1]

$NaBH_4 + CeCl_3$

[1191-15-7]

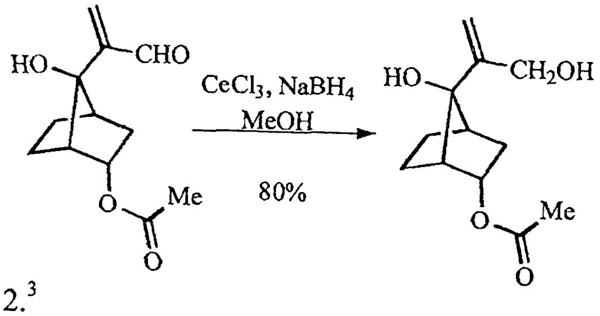
Preparation: Equal amounts of $NaBH_4$ and $CeCl_3$ (7 H_2O) in methanol

L. A. Paquette, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 2, 1031

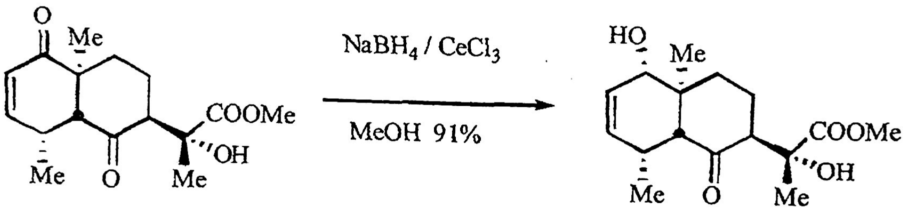
Notes: Specifically reduces enones to allylic alcohols via 1,2-addition. Sometimes stereochemistry is different from $NaBH_4$ alone.

Examples:

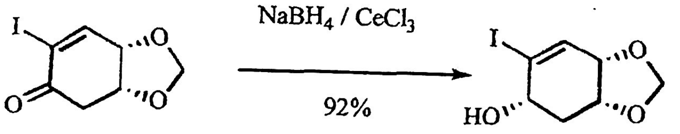
1.[2]



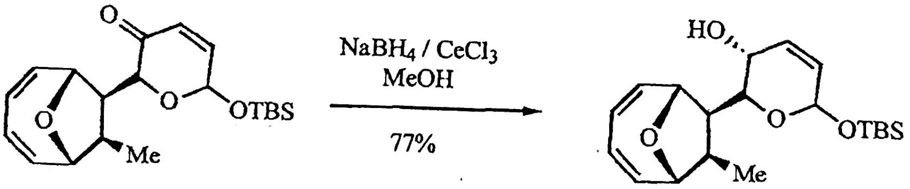
2.[3]



3.[4]



4.[5]



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[1] J.-L. Luche, A. L. Gemal, *Journal of the Chemical Society, Chemical Communications* **1978**, 976

[2] D. L. J. Clive, S. Sun, V. Gagliardini, M. K. Sano, *Tetrahedron Letters* **2000**, 41, 6259

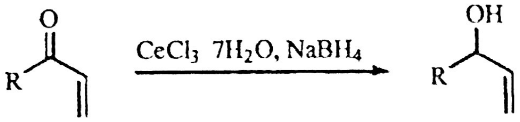
[3] F. J. Moreno-Dorado, F. M. Guerra, F. J. Aladro, J. M. Bustamanta, Z. D. Jorge, G. M. Massanet, *Tetrahedron* **1999**, 55, 6997

[4] C.-K. Sha, A.-W. Hong, C.-M. Huang, *Organic Letters* **2001**, 3, 2177

[5] K. Takao, G. Watanabe, Y. Yasui, K. Tadano, *Organic Letters* **2002**, 4, 2941

Luche Reduction

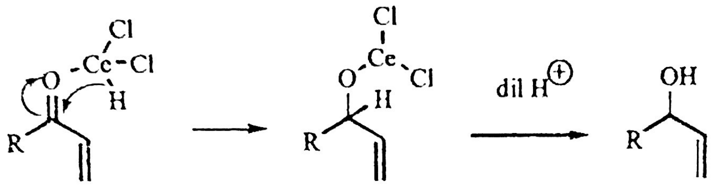
The Reaction:



Proposed Mechanism:

A. L. Gemal, J. -L. Luche, *Journal of the American Chemical Society* **1981**, 103, 5454

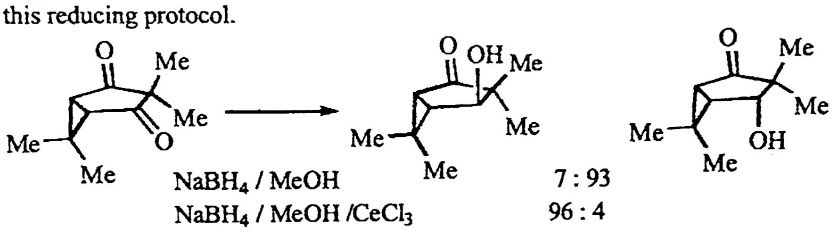
$CeCl_3 + NaBH_4 \longrightarrow HCeCl_2$



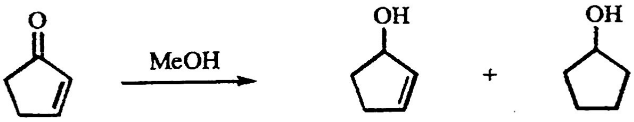
The cerium reagent coordinates to the carbonyl, making only a 1,2 addition possible.

Notes:

The major use of the ***Luche conditions*** is found in applications where conjugate addition needs to be suppressed. However, there are a number of reports where stereoselectivity has been modified with this reducing protocol.



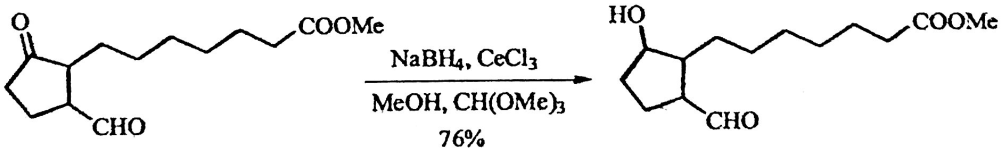
Reported in: L. A. Paquette, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1031



$NaBH_4$	0	100
$NaBH_4$ / $CeCl_3$	97	3

J. L. Luche, *Journal of the American Chemical Society* **1978**, 100, 2226

Examples:



A. L. Gemal, J. L. Luche, *Journal of Organic Chemistry* **1979**, 44, 4187

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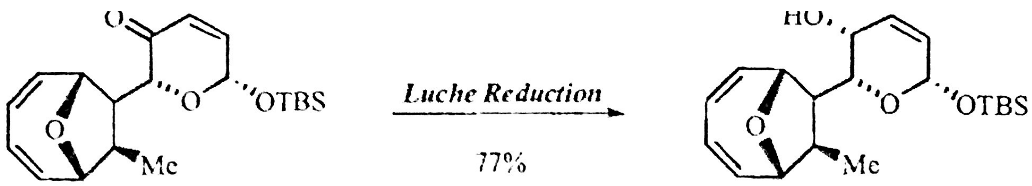
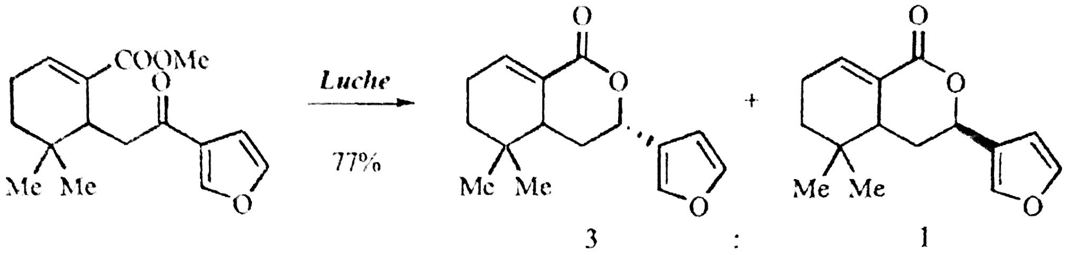
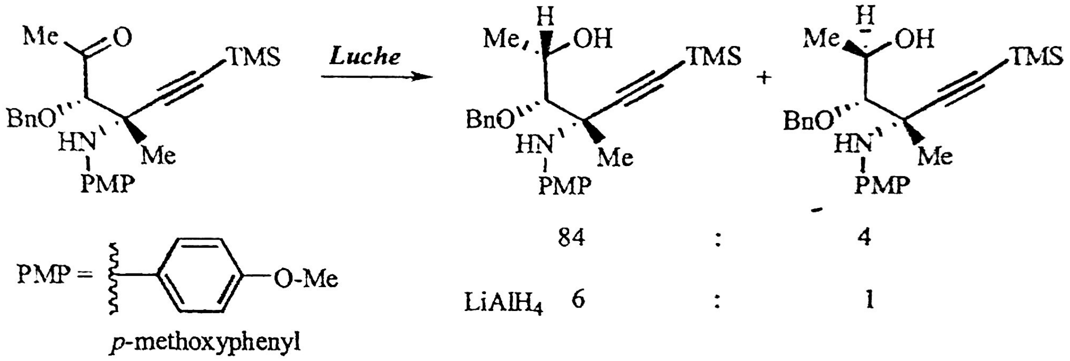


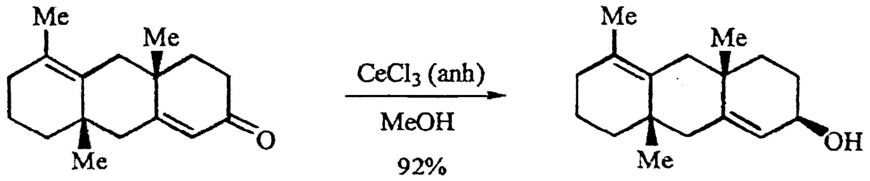
K. Takao, G. Watanabe, H. Yasui, K. Tadano, *Organic Letters* **2002**, 4, 2941



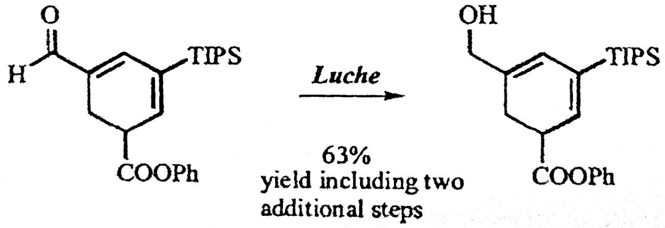
K. Agapiou, M. J. Krische, *Organic Letters* **2003**, 5, 1737



W. W. Cutchins, F. E. McDonald, *Organic Letters* **2002**, 4, 749



L. A. Paquette, D. T. Belmont, Y. -L. Hsu, *Journal of Organic Chemistry* **1985**, 50, 4667



D. L. Comins, A. L. Williams, *Organic Letters* **2001**, 3, 3217

SODIUM BOROHYDRIDE, $NaBH_4$

Sodium borohydride is a reducing agent. It reduces by transfer of hydride ions to substrates as in the case of lithium aluminium hydride.

Preparation

It is prepared by heating sodium hydride with trimethoxyborane to 250°C.

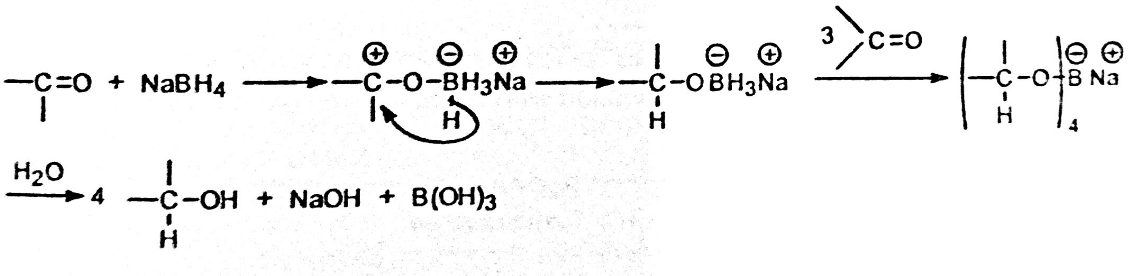
$$4NaH + B(OCH_3)_3 \xrightarrow{250^\circ C} NaBH_4 + 3CH_3ONa$$

The reagent is insoluble in ether but soluble in water or alcohol. Hence, it can be used in hydrolytic solvents, e.g., water or alcohol. The reaction is carried out in ethanol or isopropanol.

It is a milder reducing agent than $LiAlH_4$. Reduction with $NaBH_4$ is more selective. It reduces carbonyl groups of aldehydes, ketones and acid chlorides in the presence of many reducible groups such as nitro, ester, carboxyl, epoxide, nitrile, double bond, etc., which remain unaffected. Double bonds either isolated or conjugated are not affected. The reagent is slowly hydrolysed with water. Hence, reductions which are resonably rapid can be carried out in water without considerable hydrolysis of the reagent. Thus, water soluble sugars can be reduced in aqueous medium.

Mechanism

The mechanism of reduction is similar to that of $LiAlH_4$. The reaction proceeds by complexing the oxygen atom of the carbonyl group with boron and simultaneous transfer of the hydride ion to the carbonyl carbon. All the four hydrogens of the reagent are transferred to the four molecules of the substrate. Subsequent hydrolysis gives alcohol.



$$-\underset{|}{C}=O + NaBH_4 \longrightarrow -\underset{|}{\overset{\oplus}{C}}-O-\overset{\ominus}{B}H_3\overset{\oplus}{Na} \longrightarrow -\underset{H}{\overset{|}{C}}-O\overset{\ominus}{B}H_3\overset{\oplus}{Na} \xrightarrow{3\,>C=O} \left(-\underset{H}{\overset{|}{C}}-O\right)_4\overset{\ominus}{B}\overset{\oplus}{Na}$$

$$\xrightarrow{H_2O} 4\ -\underset{H}{\overset{|}{C}}-OH + NaOH + B(OH)_3$$

$$NaOH + B(OH)_3 \longrightarrow NaH_2BO_3 + H_2O$$

Applications

Some of its important applications are:

1. Reduction of carbonyl compounds and acid chlorides to alcohol

$$CH_3COCH_2CH_2COOC_2H_5 \xrightarrow{NaBH_4} CH_3\cdot CH(OH)\cdot CH_2\cdot CH_2\cdot COOC_2H_5$$

Ethyl-γ-ketopentanoate → Ethyl-4-hydroxypentanoate

$$C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot COOH \xrightarrow{NaBH_4} C_6H_5\cdot CH(OH)\cdot CH_2\cdot CH_2\cdot COOH$$

β-Benzoyl propanoic acid → γ-Hydroxy -4-phenylbutanoic acid

$$CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3 \xrightarrow{NaBH_4} CH_3\cdot CH(OH)\cdot CH_2\cdot CH_2\cdot CH(OH)\cdot CH_3$$

Hexan-2, 5-dione → Hexan-2, 5-diol

$$CH_2OH\cdot(CHOH)_4\cdot CHO \xrightarrow{NaBH_4} CH_2OH\cdot(CHOH)_4\cdot CH_2OH$$

Glucose → Sorbitol

$$C_6H_5\cdot CH{=}CH{-}CHO \xrightarrow{NaBH_4} C_6H_5\cdot CH{=}CH\cdot CH_2OH$$

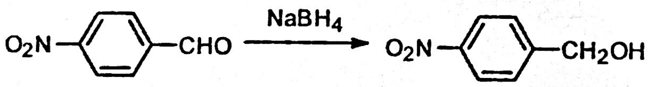
Cinnamaldehyde → Cinnamyl alcohol

$$NC\cdot CH_2\cdot CH_2\cdot CHO \xrightarrow{NaBH_4} NC\cdot CH_2\cdot CH_2\cdot CH_2OH$$

3-Cyanopropionaldehyde → 4-Hydroxybutyronitrile

$$R\cdot CO\cdot Cl \xrightarrow{NaBH_4} R\cdot CH_2OH$$

Acid chloride → Alcohol



p-Nitrobenzaldehyde → *p*-Nitrobenzyl alcohol

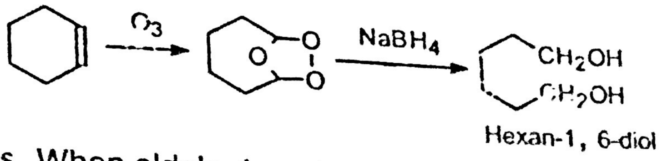
In the above compounds it will be seen that only the carbonyl group is reduced and the other functional groups remain unaffected. This high selectivity of $NaBH_4$ makes it the preferred reagent for the reduction of carbonyl groups in sensitive polyfunctional molecules.

2. Reduction of carbonyl group to methylene group *p*-Toluenesulphonyl hydrazine condenses with carbonyl compounds to give tosylhydrazones which on reduction with $NaBH_4$ give hydrocarbons.

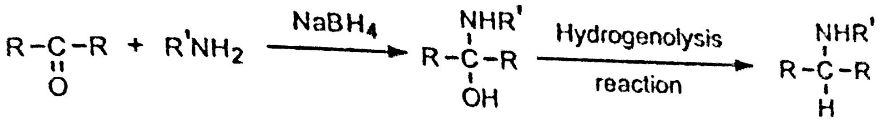
$$R_2C{=}O + H_2N{-}NHTs \longrightarrow \underset{\text{Tosylhydrazone}}{R_2C{=}N{-}NHTs} \xrightarrow{NaBH_4} R_2CH_2$$

The method is useful in the synthesis, e.g., ketosteriods.

3. Reduction of ozonides Sodium borohydride reduces ozonides to two molecules of alcohol and ozonides of cycloolefins to diols.

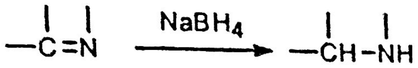


4. **Reductive alkylation of amines** When aldehyde or ketone is treated with amines (1° or 2°) in the presence of $NaBH_4$ reductive alkylation occurs.



$$R-\underset{\underset{O}{\parallel}}{C}-R + R'NH_2 \xrightarrow{NaBH_4} R-\overset{NHR'}{\underset{OH}{C}}-R \xrightarrow[\text{reaction}]{\text{Hydrogenolysis}} R-\overset{NHR'}{\underset{H}{C}}-R$$

5. **Reduction of carbon–nitrogen double bond** Although sodium borohydride does not reduce nitriles, it reduces carbon–nitrogen double bond.

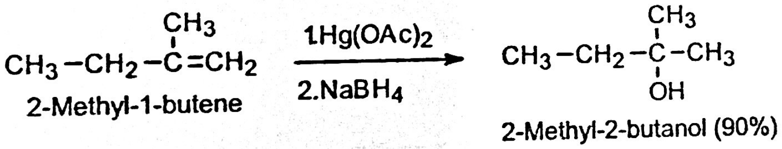


$$-\overset{|}{C}=\overset{|}{N} \xrightarrow{NaBH_4} -\overset{|}{C}H-\overset{|}{N}H$$

6. **Reduction of ester groups** Ordinarily ester groups are unaffected by $NaBH_4$ but in the presence of LiCl or $AlCl_3$ in diglyme (diethylene glycol dimethyl ether) they are reduced to alcohols.

$$RCOOR' \xrightarrow[\text{LiCl in diglyme}]{NaBH_4} RCH_2OH + R'OH$$

7. **Hydration of olefins** Olefins are hydrated under mild condition without rearrangement in high yield on treatment with mercuric acetate followed by $NaBH_4$ 'in situ'.



$$\underset{\text{2-Methyl-1-butene}}{CH_3-CH_2-\overset{CH_3}{\overset{|}{C}}=CH_2} \xrightarrow[2.NaBH_4]{1.Hg(OAc)_2} \underset{\text{2-Methyl-2-butanol (90\%)}}{CH_3-CH_2-\overset{CH_3}{\underset{OH}{C}}-CH_3}$$

8. **Preparation of diborane** Diborane which is used for the hydroboration of alkenes is prepared by reacting boron trifluoride with sodium borohydride.

$$\underset{\text{Boron trifluoride}}{4BF_3} + 3NaBH_4 \longrightarrow \underset{\text{Diborane}}{2B_2H_6} + \underset{\text{Sodium borofluoride}}{2NaBF_4}$$

Hydroboration is done 'in situ' either in THF or in diglyme.

$$4BF_3 + 3NaBH_4 + 12R-CH=CH_2 \xrightarrow[\text{Diglyme}]{\text{THF}} 4(RCH_2CH_2)_3B + 3NaBF_4$$

9. **Reduction of diazonium borofluoride** Diazonium borofluoride can be reduced with $NaBH_4$ in dimethylformamide or alcohol.

$$C_6H_5N_2Cl \xrightarrow{HBF_4} C_6H_5\overset{\oplus}{N_2}\overset{\ominus}{BF_4} \xrightarrow[CH_3OH]{NaBH_4} C_6H_6$$

10. **Reduction of azides** Azides containing sulphur are not reduced to amines by the usual methods. However, sodium borohydride reduces azides to amines.

Soduim Cyano Borohydride ($NaBH_3CN$)

(i) It is more selective the $NaBH_4$

(ii) weaker than $NaBH_4$ & LAH

(iii) Neutral Solution

(iv) Removal of I, Br and tosyloxy group

(v) $>C=O$ is not affected.

* Sensitive to more basic Condition.

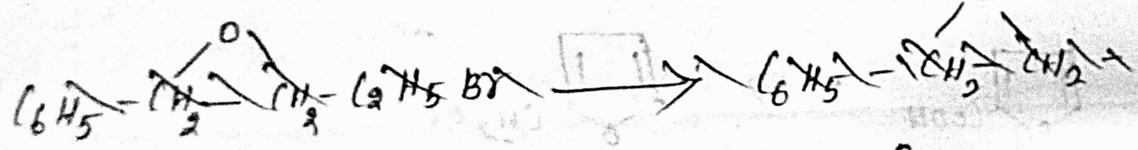
Eg :-

(i) $CH_3-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-I$

$$\downarrow NaBH_3CN$$

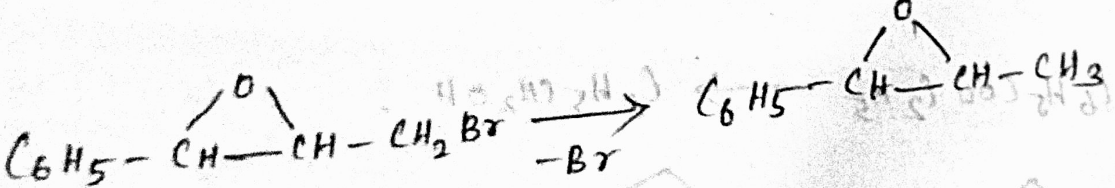
$CH_3-CH_2-CH_2-CH_2-CH_2-CH_2(CH_2)_2-CH_3$

(ii)



$C_6H_5-CH_2-CH_2-C_2H_5Br \longrightarrow C_6H_5-CH_2-CH_2$

(ii)



$C_6H_5-CH-CH-CH_2Br \xrightarrow[-Br]{} C_6H_5-CH-CH-CH_3$

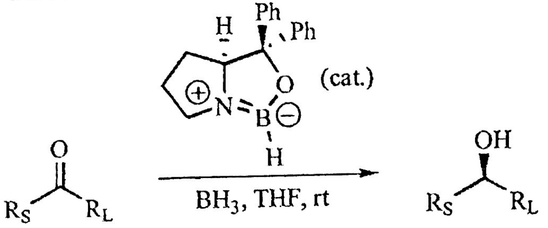
(iii) $CH_3(CH_2)_2CHO \xrightarrow{\text{Tosylhydrin}} CH_3(CH_2)_2CH_3$

Butanaldehyde

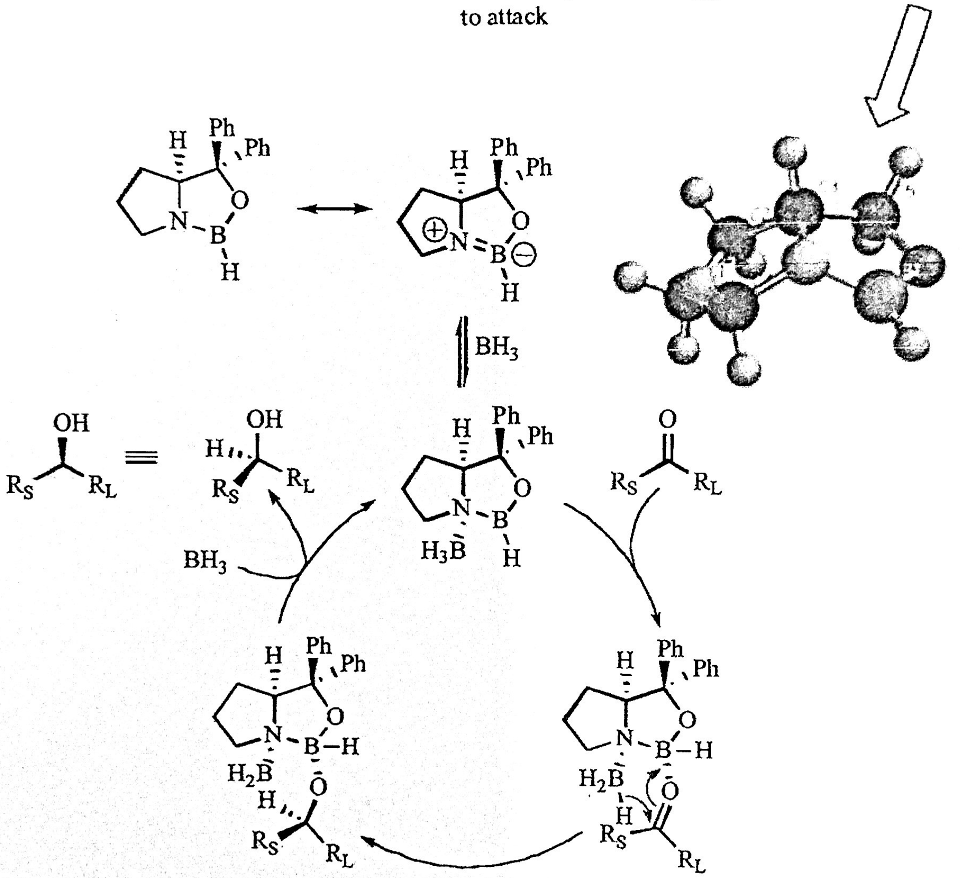
Butane.

Corey-Bakshi-Shibata (CBS Reduction)

The Reaction:



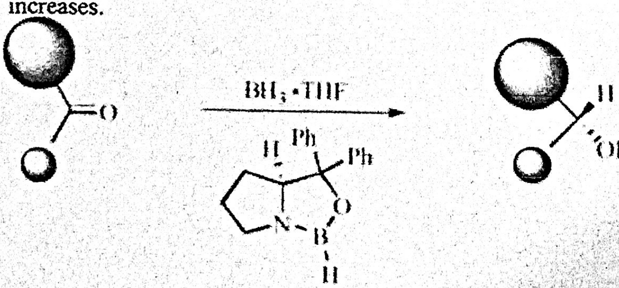
Proposed Mechanism:

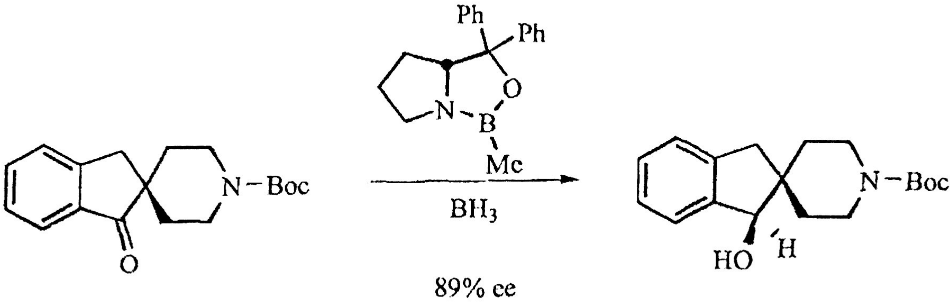

The face syn to the ring proton is more available to attack

Notes:

For a discussion of the reaction, see D. J. Mathre, I. Shinkai, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., NewYork, 1995, 7, 4767

Enatioselectivity for the reduction improves as the size differential of the groups on the carbonyl increases.





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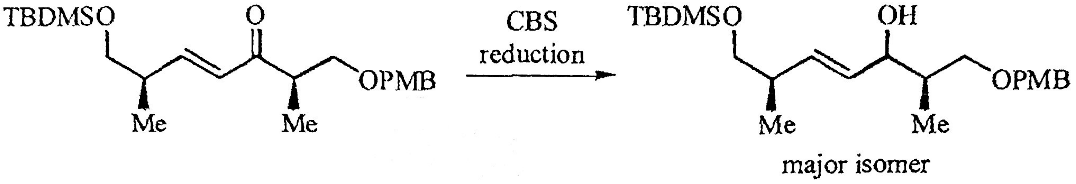

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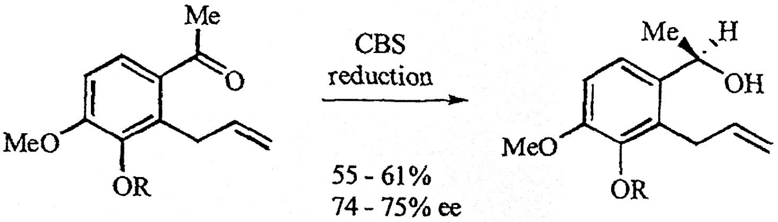

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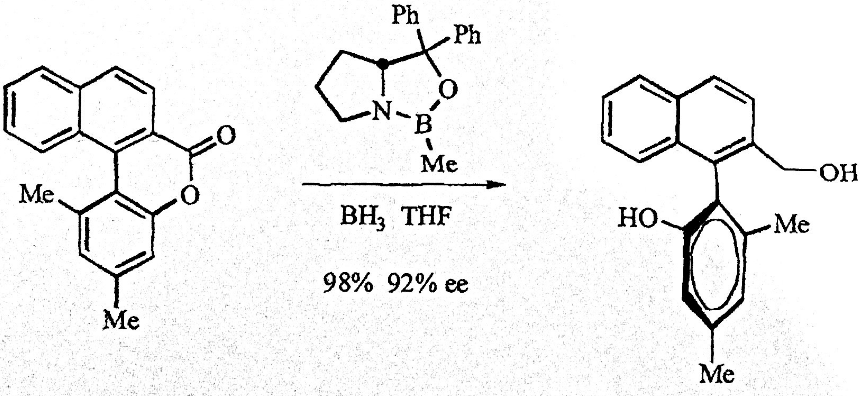


G. Bringmann, M. Breuning, P. Henschel, J. Hinrichs, *Organic Syntheses*, 79, 72

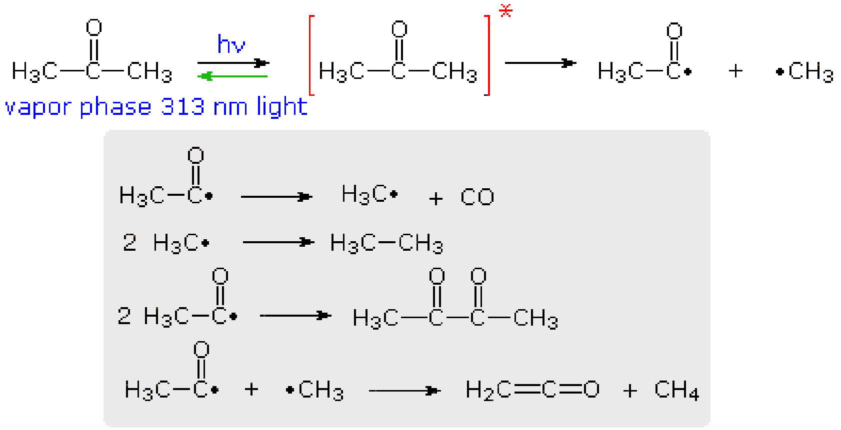
P16CH11: Organic Chemistry-I

Unit-IV: Organic Photochemistry

Photochemistry

The study of chemical reactions, isomerizations and physical behaviour that may occur under the influence of light is called photochemistry. Two fundamental principles are the foundation for understanding photochemical transformations:

Quantum yield is defined as the number of moles of a stated reactant disappearing, or the number of moles of a stated product produced, per einstein of monochromatic light absorbed.", where an einstein is one mole of photons. For example, irradiation of acetone with 313 nm light (3130 Å) gives a complex mixture of products, as shown in the following diagram. The quantum yield of these products is less than 0.2, indicating there are radiative (fluorescence & phosphorescence) and non-radiative return pathways. The primary photochemical reaction is the homolytic cleavage of a carbon-carbon bond shown in the top equation.



Fundamental Concepts of Photochemistry

First law of photochemistry: Grotthuss-Draper law, states that light must be absorbed by a compound in order for a photochemical reaction to take place.

Second law of photochemistry: Stark-Einstein law, states that for each photon of light absorbed by a chemical system, only one molecule is activated for subsequent reaction. This "photoequivalence law" was derived by Albert Einstein during his development of the quantum (photon) theory of light.

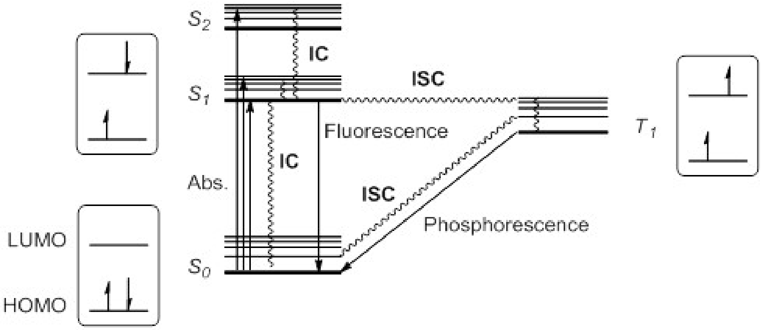
The light is absorbed by chlorine molecule, the low energy of this transition being indicated by the yellowish colour of the gas. The photon induces homolysis of the Cl-Cl bond, and the resulting chlorine radical converts toluene to the benzyl radical:

$Cl_2 + h\nu \rightarrow 2Cl\cdot$
$C_6H_5CH_3 + Cl\cdot \rightarrow C_6H_5CH_2\cdot + HCl$
$C_6H_5CH_2\cdot + Cl\cdot \rightarrow C_6H_5CH_2Cl$

Mercaptans can be produced by photochemical addition of hydrogen sulfide (H_2S) to alpha olefins.

When a molecule or atom in the ground state (S_0) absorbs light, one electron is excited to a higher orbital level. The excitation to a higher singlet state can be from HOMO to LUMO or to a higher orbital, so that singlet excitation states S_1, S_2, S_3… at different energies are possible.

Kasha's rule stipulates that higher singlet states would quickly relax by radiationless decay or internal conversion (IC) to S_1. Thus, S_1 is usually, but not always, the only relevant singlet excited state. This excited state S_1 can further relax to S_0 by IC, but also by an allowed radiative transition from S_1 to S_0 that emits a photon; this process is called fluorescence.



Jablonski diagram radiative is straight arrows and non-radiative is curly lines.

Alternatively, it is possible for the excited state S_1 to undergo spin inversion and to generate a triplet excited state T_1 having two unpaired electrons with the same spin. This violation of the spin selection rule is possible by intersystem crossing (ISC) of the vibrational and electronic levels of S_1 and T_1. According to Hund's rule of maximum multiplicity, this T_1 state would be somewhat more stable than S_1.

This triplet state can relax to the ground state S_0 by radiationless IC or by a radiation pathway called phosphorescence. This process implies a change of electronic spin, which is forbidden by spin selection rules, making phosphorescence (T_1 to S_0) much slower than fluorescence (S_1 to S_0). Thus, triplet states generally have longer lifetimes than singlet states. These transitions are usually summarized in a state energy diagram or Jablonski diagram, the paradigm of molecular photochemistry. These excited species, either S_1 or T_1, have a half empty low-energy orbital, and are consequently more oxidizing than the ground state. But at the same time, they have an electron in a high energy orbital, and are thus more reducing. In general, excited species are prone to participate in electron transfer processes.

Electronic Transitions

Absorption of light in the ultraviolet and visible regions produces changes in the electronic energies of molecules associated with excitation of an electron from a stable to an unstable orbital. Because the energy required to excite the valence-shell electrons of molecules is comparable to the strengths of chemical bonds, absorption may lead to chemical reactions. The lower energy state is known as bonding orbital. The higher state orbital is described by antibonding orbital. The antibonding orbital are associated with the σ and π bond that are σ* and π*. The n orbital does not form bond, which is called nonbonding. For most organic molecules, there are consequently four types of electronic Excitation.,

- σ - σ* : Alkanes, which have no n or p electrons, can be excited only in this way.
- n - σ* : Alcohols, amines, ethers, and so on, can also be excited in this manner.
- π - π*: This pathway is open to alkenes as well as to aldehydes, carboxylic esters, and so on.
- n - π*: Aldehydes, ketones, carboxylic esters, and so on, can undergo this promotion as well as the other three.

The four excitation types above are listed in what is normally the order of decreasing energy. Thus light of the highest energy (in the far uv) is necessary for σ - σ* excitation, while n - π* excitations are caused by ordinary uv light. However, the order may sometimes be altered in some solvents. In 1,3-butadiene (and other compounds with two conjugated double bonds) there are two π and two π* orbitals. The energy difference between the higher π and the lower π* orbital is less than the difference between the π and π* orbitals of ethylene. Therefore 1,3-butadiene requires less energy than ethylene, and thus light of a higher wavelength, to promote an electron. This is a general phenomenon, and it may be stated that, in general, the more conjugation in a molecule, the more the absorption is displaced toward higher wavelengths.

Photochemical Kinetics

Quantum yield is the major characteristics of a photochemical reaction. The quantum yield, also called the quantum efficiency, is defined as the number of events occurring per photon absorbed. These events might be related to physical processes responsible for energy dissipation (such processes are discussed in Basic Photophysics), but they also might be related to molecules of a chemical product formed upon photo irradiation. Generally, the (total) quantum yield of a photoreaction, ϕ is.,

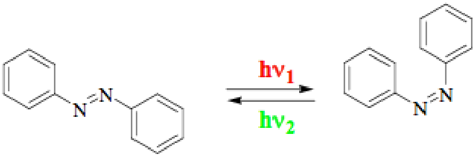
$$\phi = \frac{\text{number of molecules undergoing the reaction of interest}}{\text{number of photons absorbed by the photoreactive substance}}$$

Eq. would define the quantum yield of product formation, ϕp, if the number of product molecules would be determined. If the two numbers are measured per time and volume unit then the quantum yield is expressed in terms of rates.

$$\phi = \frac{\text{rate of the reaction of interest}}{\text{rate of light absorption by the photoreactive substance}}$$

The latter quantity is also referred to as the differential quantum yield. Notice that these two definitions of the quantum yield agree only if the yield is constant during the course of the reaction. An actinometer is a physical device or chemical system, which is used to determine the number of photons in a light beam. Physical devices convert the energy of absorbed photons into another energy form, which may be easily quantified. The devices that operate by converting photon energy into heat represent 'primary' standards of actinometry. Other physical devices and chemical systems must be calibrated. Chemical actinometers are photoreactive mixtures with well-established photochemistry and known quantum yields.

Two representative systems for liquid-phase actinometry are potassium ferrioxalate system and azobenzene system. In both cases, the photoconversion is monitored spectrophotometrically. It is interesting that the most frequently used ferrioxalate system has relatively complex chemistry. Its description in the textbooks hardly goes beyond the statement that Fe (III) is reduced and oxalate is simultaneously oxidized upon photoirradiation. In contrast, the photochemistry of azobenzene is extremely simple. The isomerization reaction proceeds cleanly in both directions and the solution may be regenerated and reused many times.



Energy Transfer

A triplet sensitizer absorbs the radiation undergo vibrational relaxation and intersystem crossing to its triplet state and then taking part in an energy transfer process with alkene. It is more efficient if triplet sensitizer has just a little higher in triplet state energy than one of the alkene isomer and lowers than other isomer. In such situation the alkene isomer with lower triplet energy is sensitized more efficiently than the isomer with higher triplet energy and the result is a photostationary state rich in the latter isomer. For example,

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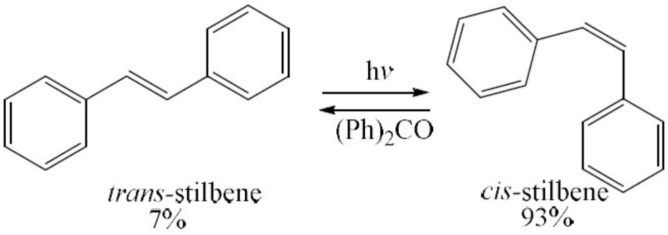


There is a ketone such as benzophenone is raised by an n - π* transition from the singlet ground state (S0) to an excited state (S1) by absorption of light. Intersystem crossing then occurs rapidly to give the triplet state (T1) of the sensitizer. The next step is excitation of the alkene by energy transfer from the triplet state of the sensitizer. Remember, the net electron spin is conserved during energy transfer, which means that the alkene will be excited to the triplet state. The triplet state of the alkene is most stable when the p orbitals, which make up the normal π-system of the double bond, are not parallel to one another. Therefore, if the energy transfer process leads initially to a planar triplet, this is converted rapidly to the more stable nonplanar form. The excitation of either the cis or the trans isomer of the alkene appears to lead to a common triplet state.

In some cases the excited species may simply transfer its excess energy to a second species. This process is called intermolecular energy transfer. Photosynthesis relies on intermolecular energy transfer to redistribute the light energy gathered by chlorophyll to a reaction center where the carbohydrates that nourish the plant are produced. Physical quenching is a special case of intermolecular energy transfer in which the chemical behavior of the species to which the energy is transferred does not change. An example of a physical quencher is the walls of a container in which a reaction is confined. If the energy transfer occurs within the same molecule, for example, and if the excess electron energy is transferred into internal motion of the molecule, such as vibration, it is called intramolecular energy transfer.

Photo-oxidation

With Photo oxidation, sometimes also called advanced oxidation (AOP) or uv catalyzed wet oxidation, you may destroy organic components inside the air or the water under the help of strong oxidizing agents, like Hydrogen peroxide or Ozone. It is possible to have a complete oxidation down to carbon dioxide, water and if existing other chemicals. The effectiveness of the process depends on the oxidation potential of the used oxidizing agent. In the following table you'll find the oxidation potentials of some important oxidizing agents.

Oxidizing agent	Symbol	Potential (V)
Fluor	F2	3,06
Hydroxyl radical	*OH	2,80
Atomic oxygen	*O	2,42
Ozone	O3	2,08
Hydrogen peroxide	H_2O_2	1,78
Hypochlorous acid	HClO	1,49
Chlorine	Cl_2	1,36
Chlor dioxide	ClO_2	1,27
Oxygene	O_2	1,23

Advantages

- Irreversible remove of organic pollution
- Process free from residues
- No use of chemistry no increase of salinity
- Treatment of difficult degradable pollutions
- Easy process control, high operational safety
- Also usable for batch reactions

- Easy combination with biological processes
- Effective use of oxidation agent caused in the use of special vacuum-uv-lamps.

You can see in the table, which the free hydroxyl radical has the high oxidzing potential and will be the best for use in oxidation processes. UV radiation in a wave length range between 190 nm and 280 nm causes the breakdown of the hydrogen peroxide to hydroxyl radicals. For this reaction the hydrogen peroxide molecule must absorb a photon.

$$H_2O_2 + h\nu \rightarrow 2 \cdot OH \qquad (1)$$

Also in the case of using Ozone it is possible to generate hydroxyl radicals. However in this case we have a two step reaction and two photons are needed to produce one radical.

$$O_3 + h\nu \rightarrow O_2 + \cdot O \qquad (2)$$

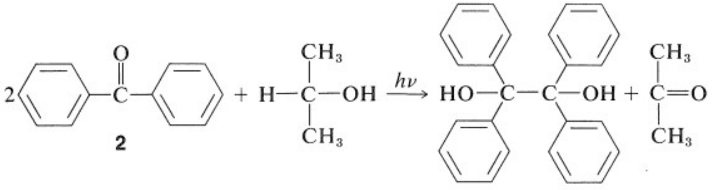
$$O \cdot + h\nu + H_2O \rightarrow 2 \cdot OH \qquad (3)$$

Parallel to the production of hydroxyl radical’s direct reactions of the organic compounds may be activated by the photons. Further may be occur recombination reactions. Photochemical indicated oxidizing processes are under the influence of different factors. These factors may be interference among each other. The substantially factors of influence are:

- Type and concentration of used oxidizing agent
- Concentration of pollution which is to be oxidise
- Wavelength and intensity of the uv radiation
- Concentration of active oxidizing radicals (e.g. Hydroxyl radicals)

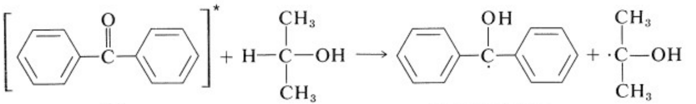
Photoreduction

Diaryl ketones do not undergo photodissociation in the same way as alkyl ketones, probably because cleavage to phenyl and other aryl radicals is unfavorable. Nevertheless, aromatic ketones are photochemically reactive in the presence of compounds that can donate a hydrogen atom, with the result that the carbonyl group is reduced. Indeed, one of the classic photochemical reactions of organic chemistry is the formation of 1,2-tetraphenyl-1,2-ethanediol by the action of light on a solution of diphenylmethanone in isopropyl alcohol. The yield is quantitative.



benzopinacol, 3

The light is absorbed by 22 and the resulting activated ketone, 2∗2∗, removes hydrogen from isopropyl alcohol:

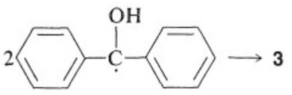


2*

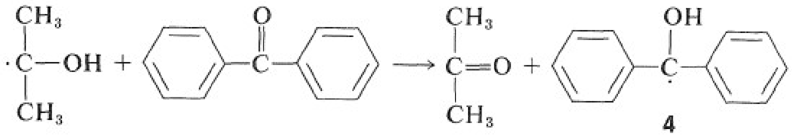
diphenylhydroxy-methyl radical, 4

(28-7)

Benzopinacol results from dimerization of the radicals,



Since the quantum yields of 2-propanone and benzopinacol both are nearly unity when the light intensity is not high, it is clear that two of the radicals, 44, must be formed for each molecule of 22 that becomes activated by light. This is possible if the 2-hydroxy-2-propyl radical formed by Equation 28-7 reacts with 22 to give a second diphenylhydroxymethyl radical:



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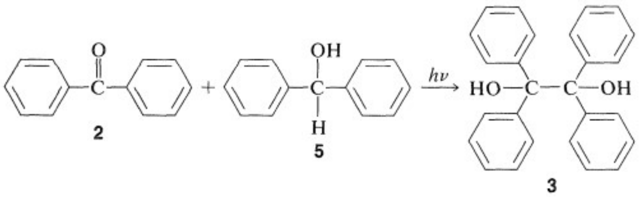
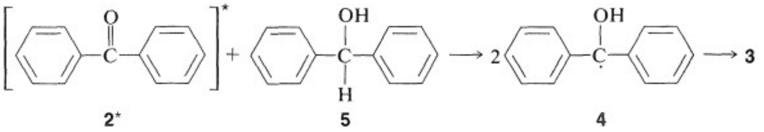
This reaction is energetically favorable because of the greater possibility for delocalization of the odd electron in than in the 2-hydroxy-2-propyl radical. Photochemical formation of 33 also can be achieved from diphenylmethanone and diphenylmethanol.



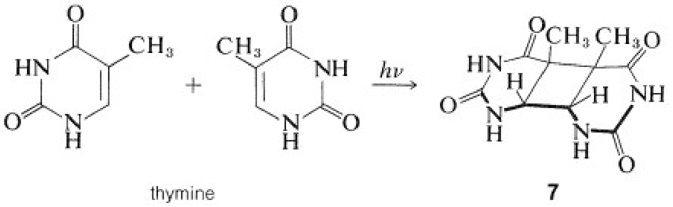
The mechanism is similar to that for isopropyl alcohol as the reducing agent:



Photosensidized Reactions

Photosensitized reactions of oxygen are largely damaging to living organisms. Indeed, singlet oxygen reacts destructively with amino acids, proteins, and nucleic acids. Chlorophyll is an excellent sensitizing dye for singlet oxygen; yet green plants evidently are not harmed because of it. A reason may be that singlet oxygen is quenched very efficiently by other plant pigments, especially the carotenoid pigments such as ββ-carotene.

That direct irradiation with ultraviolet light is damaging to single-cell organisms is well known. It also is known that the nucleic acids, DNA and RNA, are the important targets of photochemical damage, and this knowledge has stimulated much research in the field of photobiology in the hope of unravelling the chemistry involved. An interesting and significant outcome is the finding that the pyrimidine bases of nucleic acids are photoreactive and undergo [2 + 2] cycloadditions on irradiation with ultraviolet light. Thymine, for example, gives a dimer of structure.



Comparable experiments with the nucleic acids have confirmed that cycloaddition of their pyrimidine bases also occurs with ultraviolet light and effectively cross-links the chains, a process obviously quite inimical to the functioning of the DNA. On the positive side, there are photochemical reactions that are essential for human health. One of these is the formation of vitamin D (the antirachitic vitamin) by irradiation of ergosterol. This photochemical reaction is an electrocyclic ring opening of the cyclohexadiene ring of ergosterol of the type described in Section 28-2D. The product, previtamin D_2, subsequently rearranges thermally to vitamin D_2:

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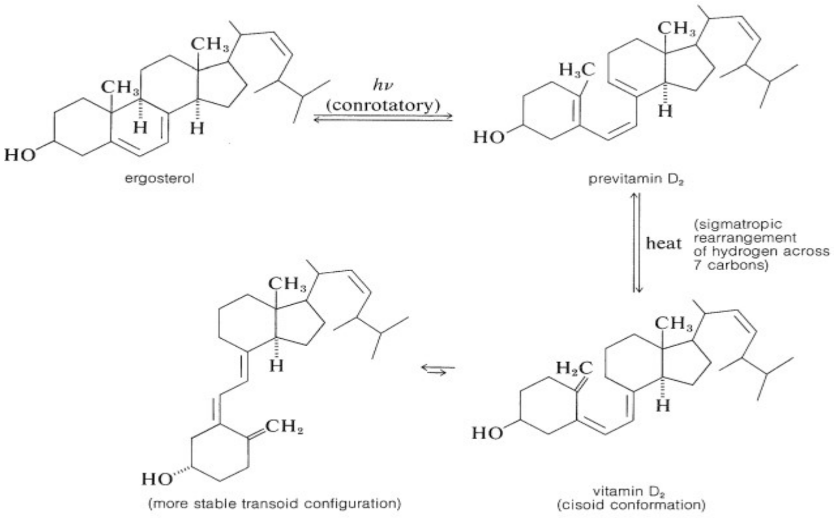


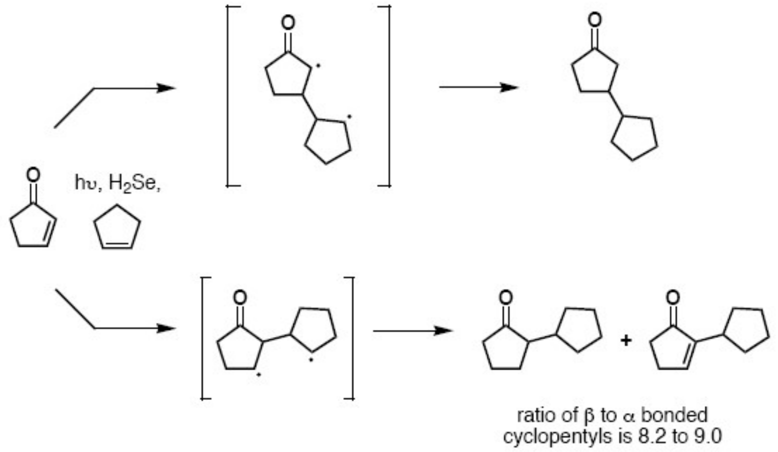
Photochemistry of Ketone and Enone

Enone photochemistry is theoretically interesting for its synthetic utility: efficient cyclobutane synthesis, regiochemical control, predictable stereochemistry at the ring fusion(s), and great method for accessing medium sized rings via fragmentation. When an enone is irradiated with UV radiation excitation will occur.

$$E = hu = (hl) / c$$

An enone in the first excited state (singlet) can return to the singlet ground state (fluorescence) and undergo internal conversion to the ground state via "trickle down" energy loss. And also it undergoes intersystem crossing to give the lower energy triplet and proceed to the next step of product formation.

The excited enone (triplet state) can proceed to the next set of events like exciplex formation with the alkene, The exciplex has a lifetime of 10 to 100's of ns. In this time it can initiate carbon-carbon bond formation at either a or b carbon of the enone and revert to starting materials. All intermediates up to the 1, 4 diradical are suceptible to this process. If the diradical survives long enough, it may revert to a singlet state via ISC to give an excited singlet state which can then form the second bond and give the product.



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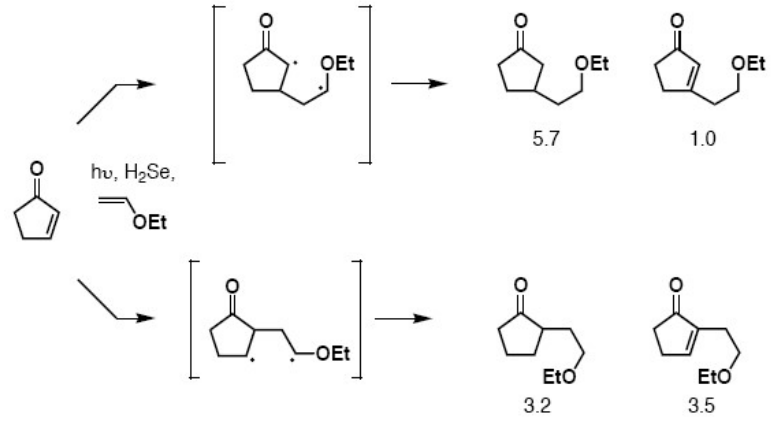
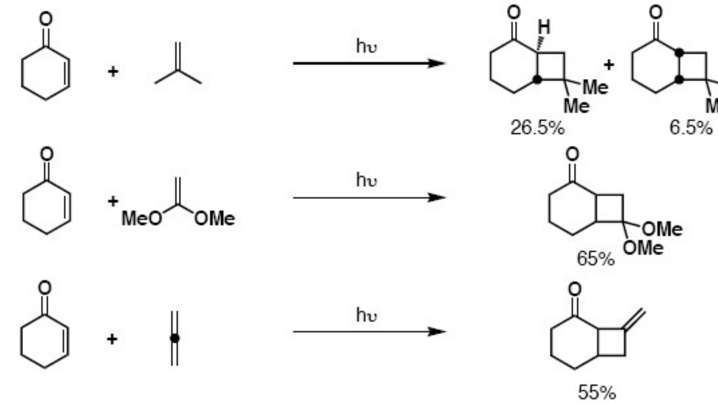


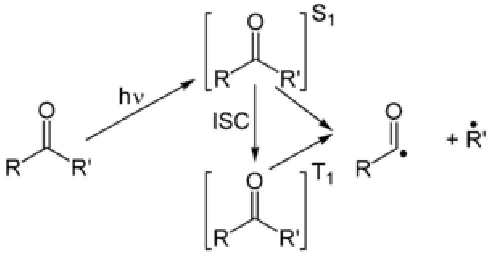


Norrish reactions

The Norrish reaction in organic chemistry describes the photochemical reactions with ketones and aldehydes. This type of reaction is subdivided in Norrish type I reactions and Norrish type II reactions.

Type-I

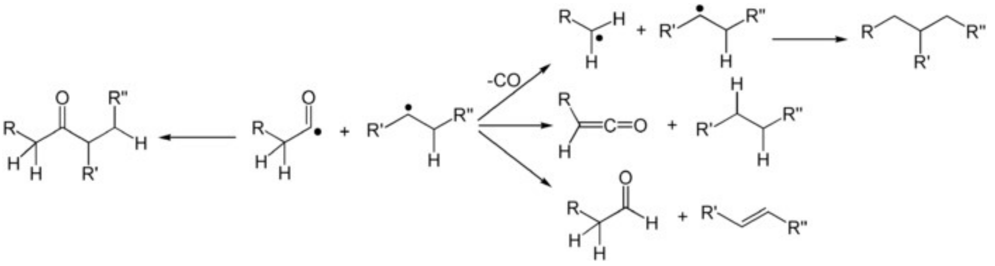
The Norrish type I reaction is the photochemical cleavage or homolysis of aldehydes and ketones into two free radical intermediates. The carbonyl group accepts a photon and is excited to a photochemical singlet state. Through intersystem crossing the triplet state can be obtained. On cleavage of the α-carbon bond from either state, two radical fragments are obtained. The size and nature of these fragments depends upon the stability of the generated radicals; for instance, the cleavage of 2-butanone largely yields ethyl radicals in favour of less stable methyl radicals.



Several secondary reaction modes are open to these fragments depending on the exact molecular structure.

- The fragments can simply recombine to the original carbonyl compound, with racemisation at the α-carbon.

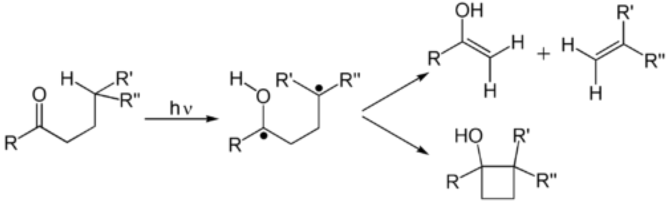
- The acyl radical can lose a molecule of carbon monoxide, forming a new carbon radical at the other α-carbon, followed by formation of a new carbon–carbon bond between the radicals. The ultimate effect is simple extraction of the carbonyl unit from the carbon chain.
- The abstraction of a α-proton from the carbonyl fragment may form a ketene and an alkane.
- The abstraction of a β-proton from the alkyl fragment may form an aldehyde and an alkene.



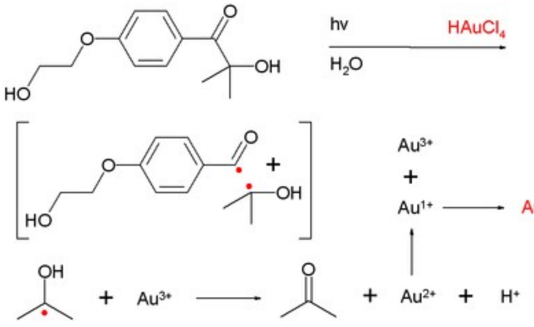
The synthetic utility of this reaction type is limited.

Type II

A Norrish type II reaction is the photochemical intramolecular abstraction of a γ-hydrogen by the excited carbonyl compound to produce a 1, 4-biradical as a primary photoproduct.



Secondary reactions that occur are fragmentation to form an enol and an alkene, or intramolecular recombination of the two radicals to a substituted cyclobutane. The photolysis of an Acyloin derivative in water in presence of hydrogen tetrachloroaurate ($HAuCl_4$) generated nanogold particles with 10 nm diameter. The species believed to responsible for reducing Au^{3+} to Au^0 the Norrish generated ketyl radical.



An example of a synthetically useful Norrish type II reaction can be found early in the total synthesis of the biologically active cardenolide ouabagenin. The optimized conditions minimize side reactions, such as the competing Norrish type I pathway, and furnish the desired intermediate in good yield on a multi-gram scale.

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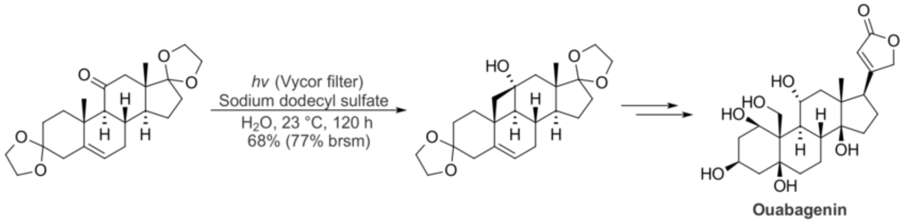


Paternò–Büchi reaction

The Paternò–Büchi reaction, named after Emanuele Paternò and George Büchi who established its basic utility and form, is a photochemical reaction that forms four-membered oxetane rings from a carbonyl and an alkene. With substrates benzaldehyde and 2-methyl-2-butene the reaction product is a mixture of structural isomers:

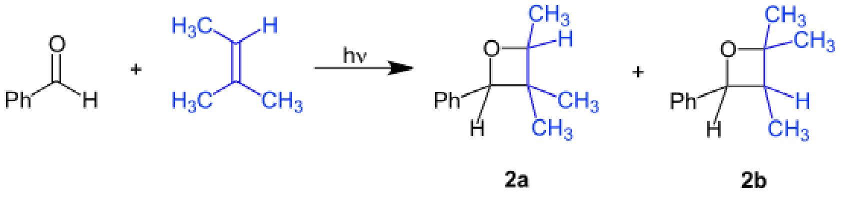
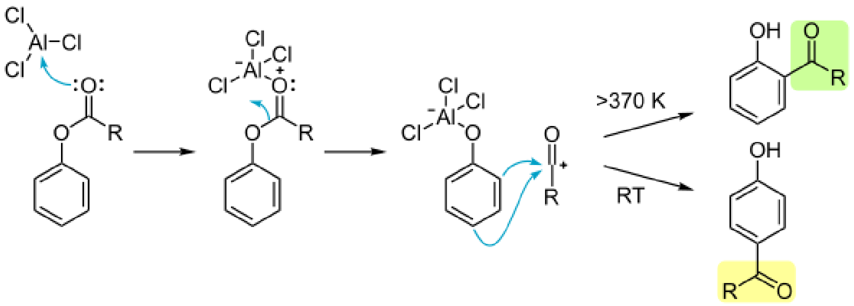


Photo-Fries rearrangement

A rearrangement reaction of a phenolic ester to hydroxyaryl ketone by catalysis of Lewis acids. It involves migration of an acyl group of phenol ester to the aryl ring. The reaction is ortho and para selective and one of the two products can be favoured by changing reaction conditions, such as temperature and solvent. Fries rearrangement has not been determined. Evidence for inter and intramolecular mechanisms have been obtained by crossover experiments with mixed reactants. The reaction progress is not dependent on solvent or substrate. A widely accepted mechanism involves a carbocation intermediate.



In the first reaction step a Lewis acid for instance aluminium chloride AlCl$_3$ co-ordinates to the carbonyl oxygen atom of the acyl group. This oxygen atom is more electron rich than the phenolic oxygen atom and is the preferred Lewis base. This interaction polarizes the bond between the acyl residue and the phenolic oxygen atom and the aluminium chloride group rearranges to the phenolic oxygen atom. This generates a free acylium carbocation which reacts in a classical electrophilic aromatic substitution with the aromatic ring. The abstracted proton is released as hydrochloric acid where the chlorine is derived from aluminium chloride. The orientation of the substitution reaction is temperature dependent. A low reaction temperature favors para substitution and with high temperatures the ortho product prevails, this can be rationalised as exhibiting classic Thermodynamic versus kinetic reaction control as the ortho product can form a more stable bidentate complex with the Aluminium.[5] Formation of the ortho product is also favoured in non-polar solvents; as the solvent polarity increases, the ratio of the para product also increases.

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Fries rearrangement may occur naturally, for example when a plastic bottle made of polycarbonate (PC) is exposed to the sun, particularly to UV light at a wavelength of about 310 nm, if the plastic has been heated to 40° Celsius or above (as might occur in a car with windows closed on a hot summer day). In this case, photolysis of the ester groups would lead to leaching of phthalate from the plastic.

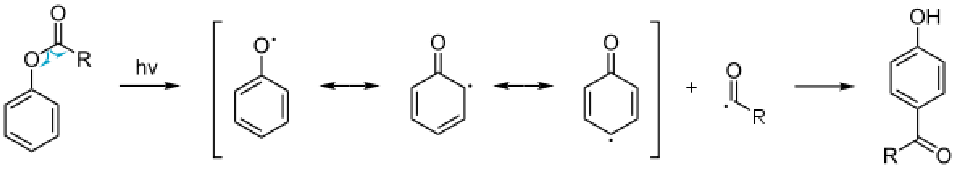
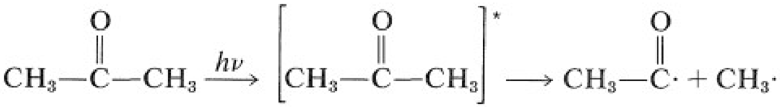


Photo dissociation Reactions

We have mentioned how chlorine molecules dissociate to chlorine atoms on absorption of near-ultraviolet light and thereby cause radical-chain chlorination of saturated hydrocarbons. Photochemical chlorination is an example of a photochemical reaction that can have a high quantum yield - that is, many molecules of chlorination product can be generated per quantum of light absorbed. The quantum yield of a reaction is said to be unity when 1mol of reactant is converted to product(s) per einstein of light absorbed. The symbol for quantum yield is usually Φ.

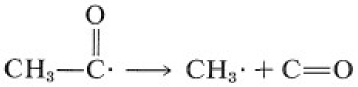
2-Propanone (acetone) vapor undergoes a photodissociation reaction with 313-nmnm light with Φ somewhat less than unity. Absorption of light by 2-propanone results in the formation of an excited state that has sufficient energy to undergo cleavage of a C−C−C bond (the weakest bond in the molecule) and form a methyl radical and an ethanoyl radical. This is a primary photochemical reaction:



$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3 \xrightarrow{h\nu} \left[CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3\right]^* \longrightarrow CH_3-\overset{\overset{\displaystyle O}{\|}}{C}\cdot + CH_3\cdot$$

The subsequent steps are dark reactions.

At temperatures much above room temperature, the ethanoyl radical breaks down to give another methyl radical and carbon monoxide:

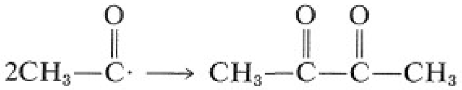


$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}\cdot \longrightarrow CH_3\cdot + C{=}O$$

If this reaction goes to completion, the principal reaction products are ethane and carbon monoxide:

2CH3·→CH3−CH3 2CH3·→CH3−CH3

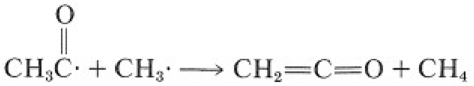
If the ethanoyl radical does not decompose completely, then some 2,3-butanedione also is formed. This reaction is quite important at room temperature or below:



$$2CH_3-\overset{\overset{\displaystyle O}{\|}}{C}\cdot \longrightarrow CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$$

2,3-butanedione (biacetyl)

Lesser amounts of methane and ketene also are formed as the result of disproportionation reactions involving hydrogen-atom transfers of the types we have encountered previously in radical reactions (see Section 10-8C):



$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}\cdot + CH_3\cdot \longrightarrow CH_2{=}C{=}O + CH_4$$

The product-forming reactions, Equations 28-2 through 28-5, all depend on the primary photochemical event, Equation 28-1, which breaks the C−CC−C bond to the carbonyl group. This cleavage has been termed a Norrish type I process.

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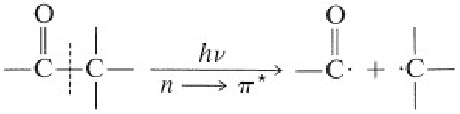
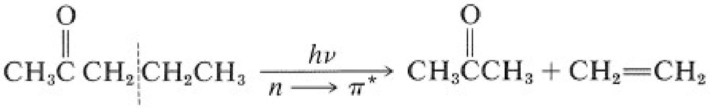


$$-\overset{O}{\overset{\|}{C}}-\overset{|}{\underset{|}{C}}- \xrightarrow[n \longrightarrow \pi^*]{h\nu} -\overset{O}{\overset{\|}{C}}\cdot + \cdot\overset{|}{\underset{|}{C}}-$$

Another photochemical reaction is important for ketones that have atleast one γ hydrogen on a chain connected to the carbonyl group, as in

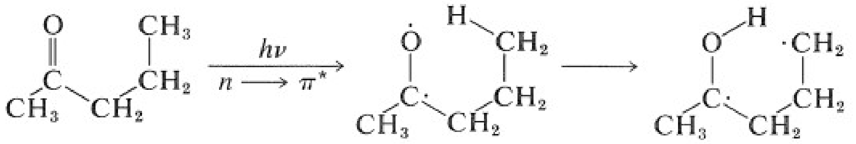
$$-\overset{O}{\overset{\|}{C}}-C_\alpha-C_\beta-C_\gamma-H$$

In this (Norrish type II process), cleavage occurs at the Cα−CβCα−Cβ bond to give, as the major product, a ketone of shorter chain length and an alkene. Thus for 2-pentanone:



$$CH_3\overset{O}{\overset{\|}{C}}\,CH_2CH_2CH_3 \xrightarrow[n \longrightarrow \pi^*]{h\nu} CH_3\overset{O}{\overset{\|}{C}}CH_3 + CH_2{=}CH_2$$

This reaction occurs in an interesting way. Whatever the nature of then n→π∗n→π∗ excited state, S1 or T1, the primary photochemical reaction is the abstraction of a hydrogen atom from the γγ carbon by the carbonyl oxygen to give the diradical:



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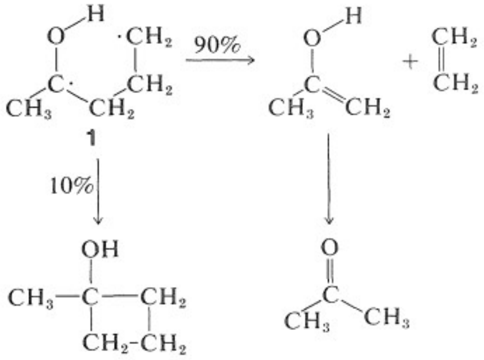
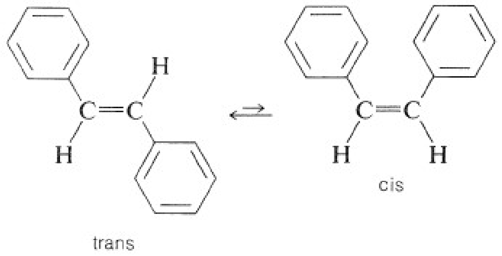
The subsequent dark reactions readily are understood as typical of diradicals. Cleavage of 1 at Cα−CβCα−Cβ gives ethene and an enol, which rearranges to the ketone. Alternatively, 1 can cyclize to a cyclobutanol:



Photochemical Isomerization of Cis and Trans Alkenes

An important problem in many syntheses is to produce the desired isomer of a cis-trans pair of alkenes. The problem would not arise if it were possible to isomerize the undesired isomer to the desired isomer. In many cases such isomerizations can be carried out photochemically. A typical example is afforded by cis- and trans-1,2-diphenylethene (stilbene):



Here the trans form is easily available by a variety of reactions and is more stable than the cis isomer because it is less sterically hindered. However, it is possible to produce a mixture containing mostly cis isomer by irradiating a solution of the trans isomer in the presence of a suitable photosensitizer. This process in no way contravenes the laws of thermodynamics because the input of radiant energy permits the equilibrium point to be shifted from what it would be normally.

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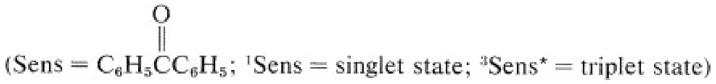
Isomerization appears to occur by the following sequence: The sensitizer, usually a ketone such as benzophenone or 1-(2-naphthyl)ethanone, is raised by an n→π∗n→π∗ transition from the singlet ground state (S0)(S0) to an excited state (S1)(S1) by absorption of light. Intersystem crossing then occurs rapidly to give the triplet state (T1)(T1) of the sensitizer:

$$^{1}\text{Sens} \xrightarrow[n \longrightarrow \pi^*]{h\nu} {}^{1}\text{Sens}^* \xrightarrow{\text{intersystem crossing}} {}^{3}\text{Sens}^*$$



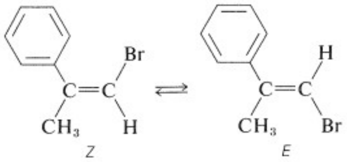
$$(\text{Sens} = C_6H_5\overset{\overset{\text{O}}{\|}}{C}C_6H_5;\ {}^{1}\text{Sens} = \text{singlet state};\ {}^{3}\text{Sens}^* = \text{triplet state})$$

The next step is excitation of the alkene by energy transfer from the triplet state of the sensitizer. Remember, the net electron spin is conserved during energy transfer, which means that the alkene will be excited to the triplet state:

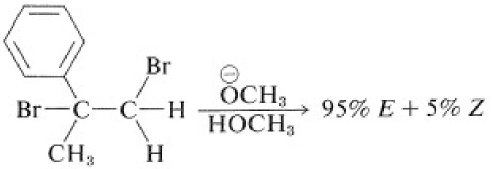
3Sens∗(↑↑)+1Alkene(↑↓)→1Sens(↑↓)+3Alkene∗(↑↑)(28.2.1)(28.2.1)3Sens∗(↑↑)+1Alkene (↑↓)→1Sens(↑↓)+3Alkene∗(↑↑)

The triplet state of the alkene is most stable when the pp orbitals, which make up the normal ππ system of the double bond, are not parallel to one another. Therefore, if the energy-transfer process leads initially to a planar triplet, this is converted rapidly to the more stable nonplanar form. The excitation of either the cis or the trans isomer of the alkene appears to lead to a common triplet state.

Another example of how photochemical isomerization can be used is provided by the equilibration of the EE and ZZ form of 1-bromo-2-phenyl-1-propene:



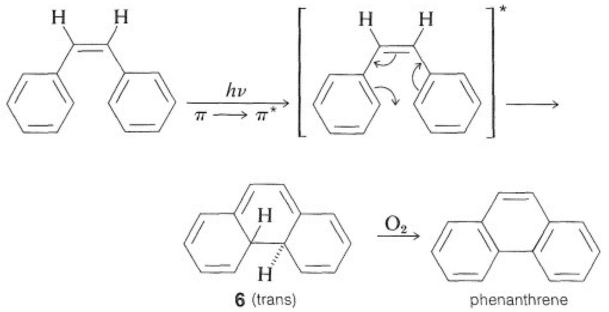
The EE isomer is formed to the extent of 95%95% in the dehydrohalogenation of 1,2-dibromo-2-phenylpropane:



Photoisomerization of the elimination product with 1-(2-naphthyl)ethanone as sensitizer produce a mixture containing 85%85% of the ZZ isomer.

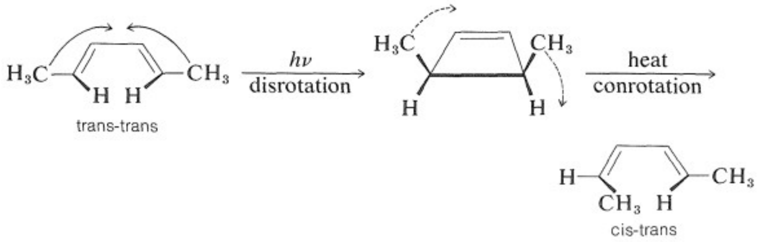
Photochemical Cyclization Reactions

One may well ask why the isomerization of alkenes discussed in the preceding section requires a sensitizer. Why cannot the same result be achieved by direct irradiation? One reason is that a π→π∗π→π∗ singlet excited state (S1)(S1) produced by direct irradiation of an alkene or arene crosses over to the triplet state (T1)(T1) inefficiently (compared to n→π∗n→π∗ excitation of ketones). Also, the S1S1 state leads to other reactions beside isomerization which, in the case of 1,2-diphenylethene and other conjugated hydrocarbons, produce cyclic products. For example, cis-1,2-diphenylethene irradiated in the presence of oxygen gives phenanthrene by the sequence of Equation 28-8. The primary photoreaction is cyclization to a dihydrophenanthrene intermediate, 66, which, in the presence of oxygen, is converted to phenanthrene:

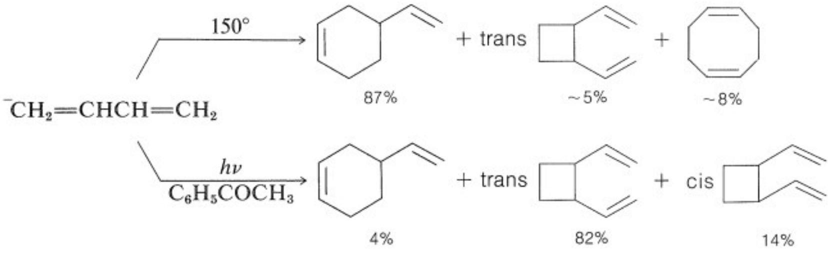


(28-8)

The cyclization step of Equation 28-8 is a photochemical counterpart of the electrocyclic reactions discussed in Section 21-10D. Many similar photochemical reactions of conjugated dienes and trienes are known, and they are of great interest because, like their thermal relatives, they often are stereospecific but tend to exhibit stereochemistry opposite to what is observed for formally similar thermal reactions. For example,



These reactions are 4n4n-electron concerted processes controlled by the symmetry of the reacting orbitals. The thermal reaction is most favorable with a Mobius transition state (achieved by conrotation), whereas the photochemical reaction is most favorable with a Huckel transition state (achieved by disrotation). Conjugated dienes also undergo photochemical cycloaddition reactions. Related thermal cycloadditions of alkadienes have been discussed in Sections 13-3A, 21-10A, and 21-10D, but the thermal and photochemical reactions frequently give different cyclic products. Butadiene provides an excellent example of the differences:



In the thermal reaction the [4 + 2] or Diels-Alder adduct is the major product, whereas in the photochemical reaction [2 + 2] cycloadditions dominate. Because the photochemical additions are sensitized by a ketone, C6H5COCH3C6H5COCH3, these cycloadditions occur through the triplet state of 1,3-butadiene and, as a result, it is not surprising that these cycloadditions are stepwise, nonstereospecific, and involve diradical intermediates.

Excitation:

$$^{1}\text{Sens} \xrightarrow[n \longrightarrow \pi^*]{h\nu} {}^{1}\text{Sens}^* \xrightarrow{\text{intersystem crossing}} {}^{3}\text{Sens}^*$$

$$^{3}\text{Sens}^* + CH_2{=}CH{-}CH{=}CH_2 \xrightarrow[\text{transfer}]{\text{energy}} {}^{1}\text{Sens} + \overset{\uparrow}{C}H_2{-}\overset{\uparrow}{C}H{-}CH{=}CH_2{}^*$$

(one of several VB structures)

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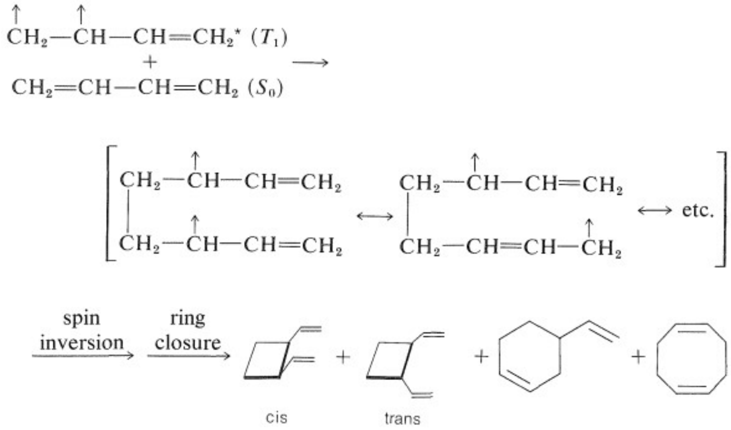
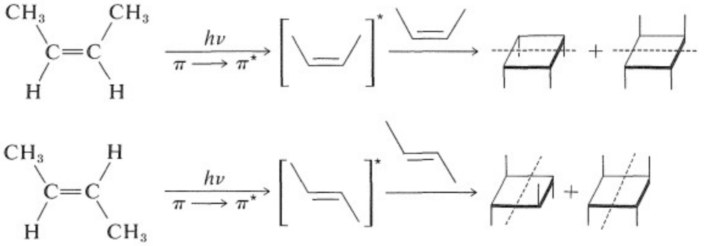
Cycloaddition

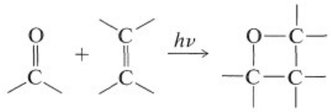
Direct irradiation of 1, 3-butadiene with 254254-nmnm light produces cyclobutene and small amounts of bicycle [1.1.0] butane along with dimers.



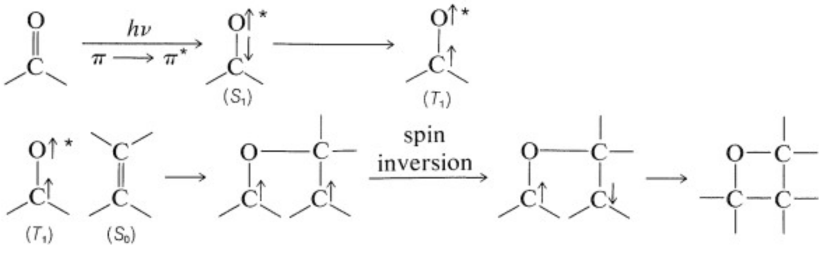
In contrast to conjugated dienes, simple alkenes such as 2-butene do not react easily by photosensitized cycloaddition. But they will form [2 + 2] cycloadducts on direct irradiation. These additions occur by way of a singlet excited state and are stereospecific:



A related reaction, which has no precedent in thermal chemistry, is the cycloaddition of an alkene and an aldehyde or ketone to form an oxacyclobutane:



In this kind of addition the ground-state alkene (S0) (S0) reacts with an excited state (usually T1T1) of the carbonyl compound by way of a diradical intermediate:



Cycloaddition [6+4] is a type of cycloaddition between a six-atom pi system and a four-atom pi system, leading to a ten-membered ring. Because this is a higher-order cycloaddition, issues of periselectivity arise in addition to the usual concerns about regio- and stereoselectivity. Six-atom pi systems that have been employed in the reaction include tropone and tropone derivatives, fulvenes, and cycloheptatriene cobalt complexes.

Introduction

Cycloaddition [6+4] is a thermally allowed, higher-order cycloaddition process leading to ten-membered rings. Although most linear, acyclic trienes do not give products selectively, cyclic trienes give high yields of products in many cases. Both cycloheptatrienes and fulvenes can be employed in this

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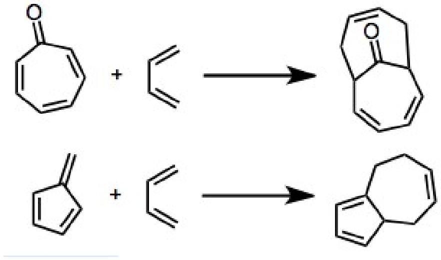
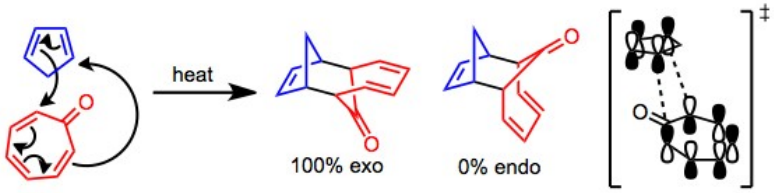
reaction, and electron-deficient tropones in particular work well. The pericyclic and transition-metal-mediated versions of the reaction are stereocomplementary: the former gives exo products, and the latter endo products, with essentially complete selectivity in nearly all cases. The possibility of building complex carbocyclic frameworks efficiently has made this reaction particularly attractive synthetically.



The metal-free version of the [6+4] cycloaddition takes place through a concerted, pericyclic process. The frontier molecular orbitals involved in reactions of tropone illustrate that a repulsive secondary orbital interaction likely destabilizes the endo transition state, leading to complete selectivity for exo products.



Fulvenes react similarly, although selective [6+4] reactions require the use of an electron-rich diene. Fulvene's frontier orbitals illustrate that it will only act as a 6π component in LUMO-controlled reactions. The next-highest occupied molecular orbital (NHOMO, not shown) also has the proper symmetry and orbital coefficients to participate in [6+4] cycloaddition; the NHOMO can be activated for reaction by substituting the exo methylene with electron-donating groups.

Photocycloaddition reactions of aromatic hydrocarbons constitute an important branch of organic chemistry. The dimerizations of anthracene, acenaphthylene, and indene may be cited as examples. A number of interesting cross-additions leading to cyclic structures are also known. These include the additions of maleic anhydride and derivatives to benzene, indene, phenanthrene, and anthracene, and the reactions of benzene with alkenes, acrylonitrile, dienes, and acetylenes. Cross additions of the bicyclic hydrocarbon naphthalene which have been reported are few in number. Naphthalene reportedly does not react with maleic anhydride on irradiation but does form a photo-adduct with diphenylacetylene.

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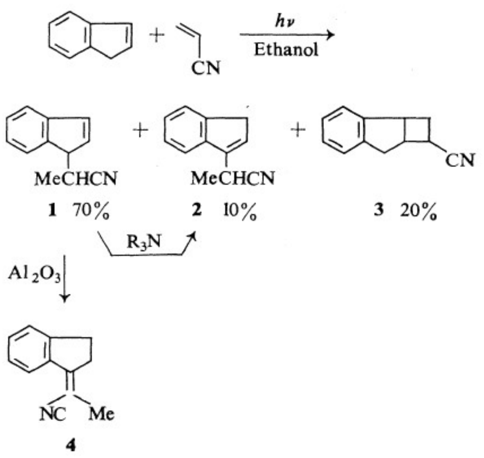
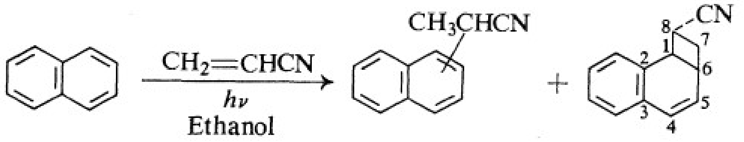
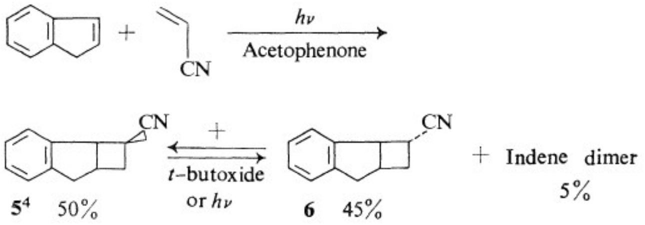
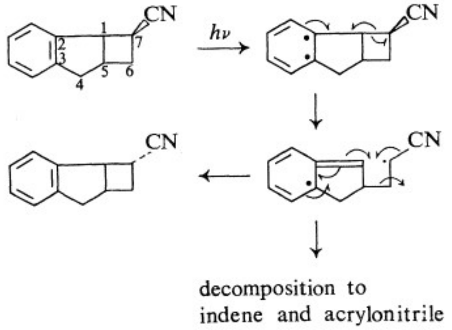


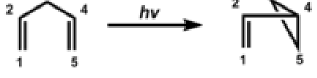






Di-pi-methane rearrangement

The di-pi-methane rearrangement is a photochemical reaction of a molecular entity that contains two π-systems separated by a saturated carbon atom (1,4-diene or allyl-substituted aromatic ring), to form an ene- (or aryl-) substituted cyclopropane. The rearrangement reaction formally amounts to a 1,2 shift of one ene group (in the diene) or the aryl group (in the allyl-aromatic analog) and bond formation between the lateral carbons of the non-migrating moiety.



The structural requirement was having two pi groups attached to an sp^3-hybridized carbon, and then a variety of further examples are obtained. One is the photolysis of the Mariano Compound, 3, 3-methyl-1, 1, 5, 5-tetraphenyl-1, 4-pentadiene. Another is the reaction of the Pratt diene

The mechanism of the Mariano diene rearranging

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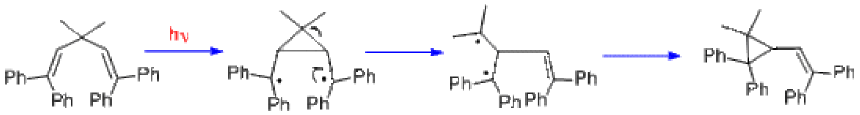
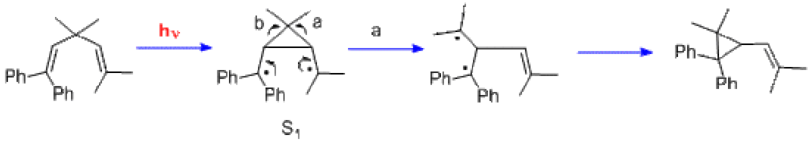


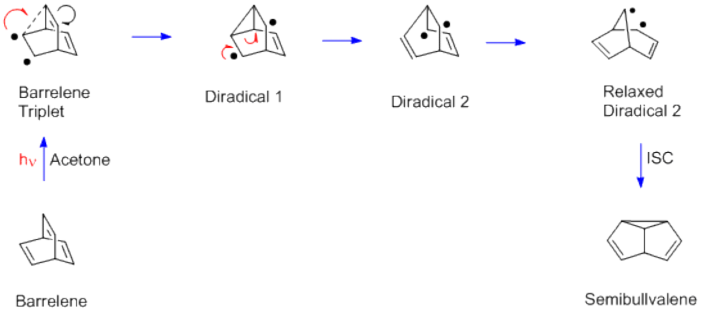
In contrast, in the case of the Pratt diene rearranging, there are two possible regiochemistries - a and b. Process a is preferred since it leaves benzhydryl odd-electron stabilization intact.

Mechanism of the Pratt diene rearranging



The barrelene rearrangement is now presented. It is a bit more complex than the Mariano and Pratt examples since there are two sp3-hybridized (i.e. methane) carbons. Each such bridgehead carbon has three (ethylenic) pi bonds while two are needed for the di-pi-methane rearrangement. Another difference is that the barrelene reaction requires the triplet excited state while the Mariano and Pratt acyclic dienes used the excited singlet. Thus acetone is used in the barrelene reaction; acetone captures the light and then delivers triplet excitation to the barrelene reactant. In the final step of the rearrangement there is a spin-flip, termed intersystem-crossing (ISC) to provide paired electrons and a new sigma bond.

Mechanism of the Barrelene to Semibullvalene transformation

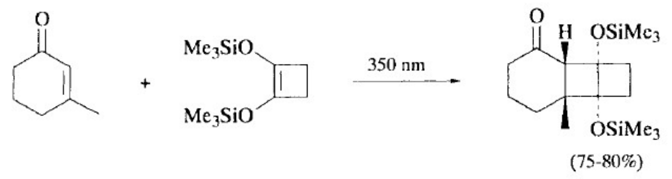


The dependence of the success of the Di-pi-Methane rearrangement on singlet versus triplet multiplicity arises primarily from the Free-Rotor Effect The triplet acyclic 1,4-dienes are free to undergo cis-trans interconversion of the diene double bonds (i.e. free-rotation) thus inhibiting the Di-pi-Methane process. The cis-trans isomerization proceeds by weakening of a pi-bond and then twisting. The singlet excited states don't rotate and then are free to undergo the Di-pi-Methane mechanism. For cyclic dienes, as in the barrelene example, the ring structure prevents cis-trans isomerization and the Di-pi-Methane can then occur.

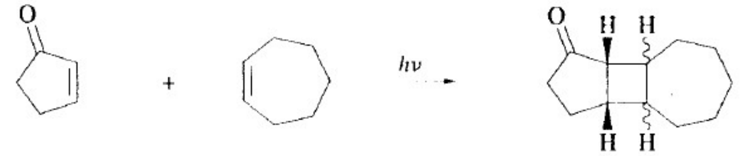
Photochemistry of beta, gamma-unsaturated ketones

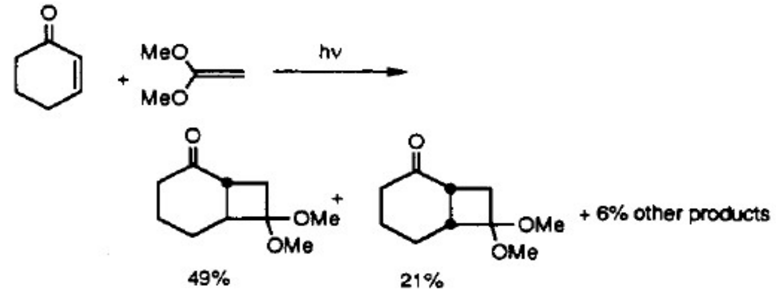
Beta, gamma-unsaturated ketones can undergo Norrish photoreactions from the excited singlet state. For example, in the case below R′RX′ would be an allyl radical if we had started with a beta, gamma-unsaturated ketone.

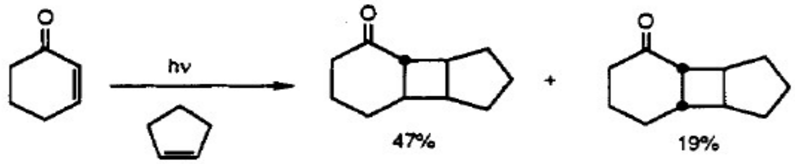
Photocycloaddition is NOT concerted and proceeds through an intermediate 1,4- iradical → Rotation about single bonds in the diradical can result in scrambling of alkene eometry IF:- 1) Alkene is acyclic. 2) Double bond is contained in a ring larger than six. When cyclic alkenes which have ring sizes of five members or less are used as the alkene partner, the alkene geometry is preserved since cis-trans isomerisation is inhibited.



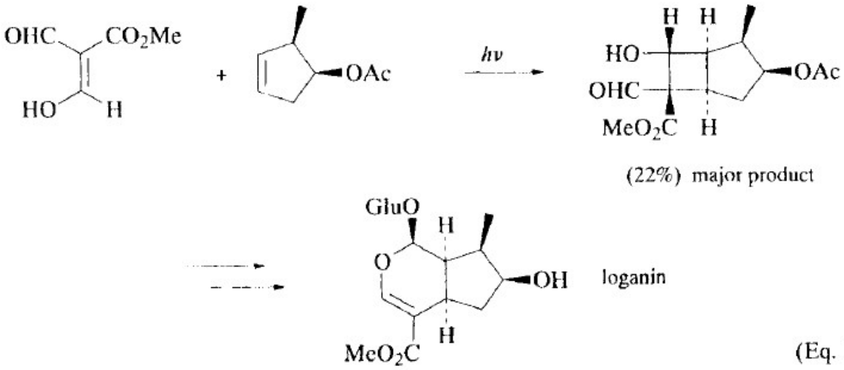
Use of larger rings can result in loss of alkene stereochemistry.







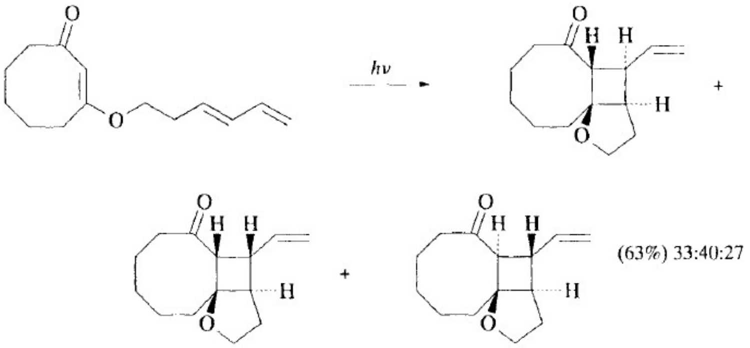
Excited state enone will normally undergo addition to the sterically most accessible face of the ground state alkene.



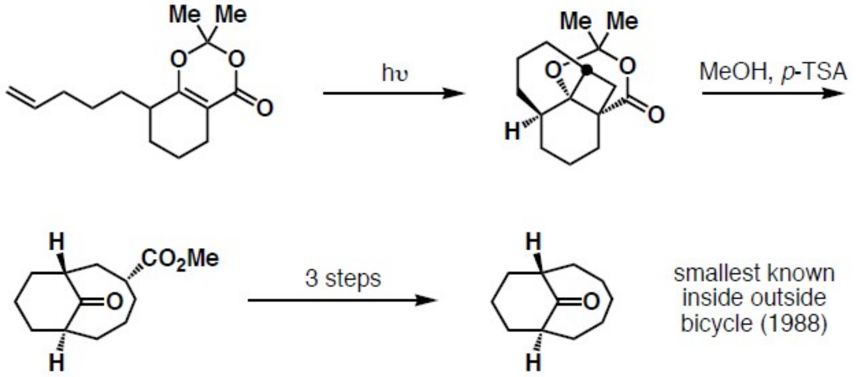
(Eq. 37)

Intramolecular photocycloaddition

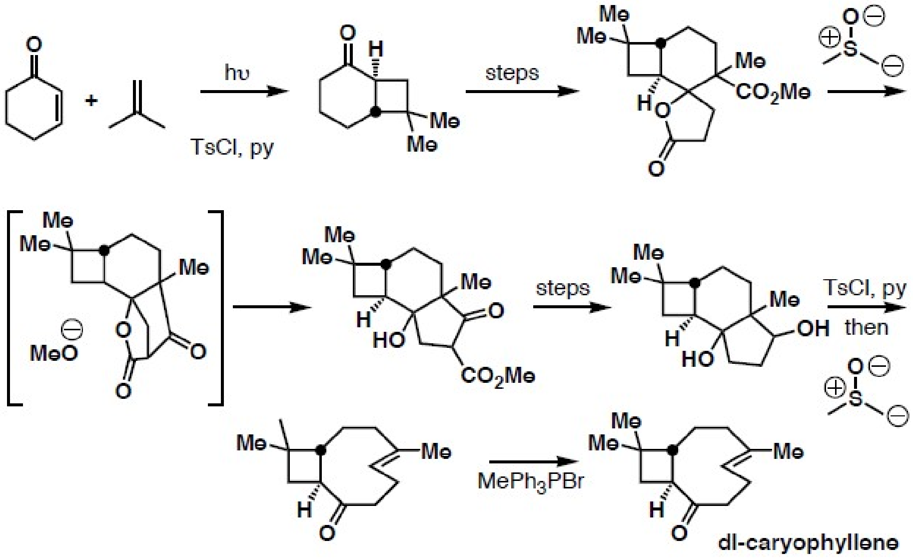
Intramolecular photocycloadditions are generally highly stereoselective. Additionally, stereogenic centres in the starting enone-alkene can be utilized to dictate the stereogenecity of newly formed stereocentres in the photoadduct. Stereochemistry of ring fusion between cyclobutane and other rings in the photoadducts is almost always cis. Exceptions result when the enone ring contains seven or more atoms or when the enone-alkene tether can easily accommodate the transcyclobutane.



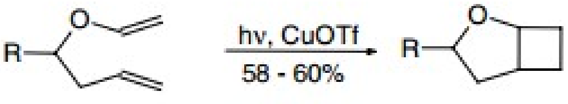
A noteworthy exception where the dioxolene which produces exclusively the trans 6-4 junction in cycloadduct.



The photoaddition of 2-cyclohexanone to isobutylene where the unstable trans isomer is produced in larger amount than to the cis form (which has already been discussed in regioselectivity factors).



[2+2] Photocycloaddition of Diallyl Ethers and Homoallyl Vinyl Ethers



R = H, CH:CH$_2$

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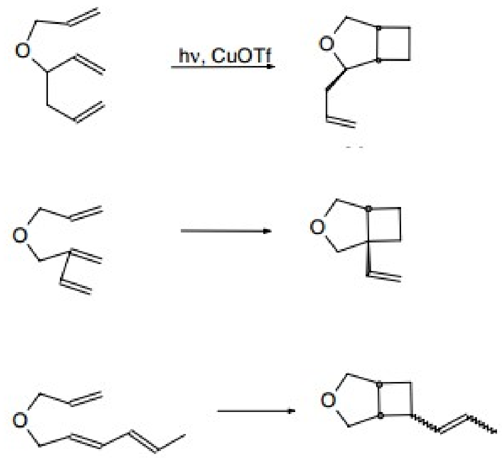
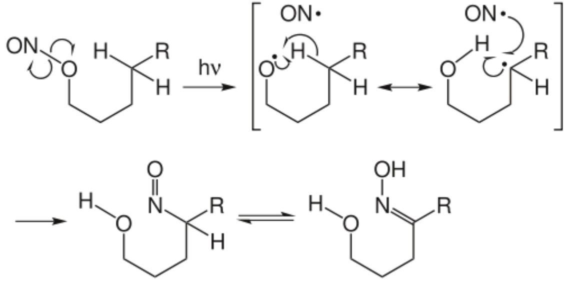
Copper(I)-catalysed intramolecular [2+2] photocycloaddition is selective for 1,6-dienes only.



Barton reaction

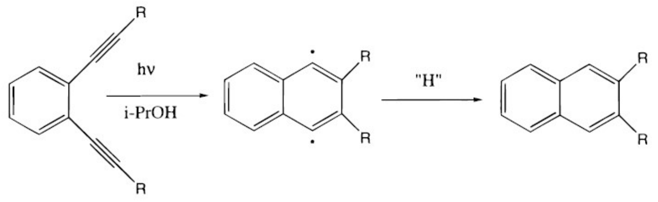
The Barton reaction, also known as the Barton Nitrite Ester Reaction, is a photochemical reaction that involves the photolysis of an alkyl nitrite to form a δ-nitroso alcohol. The Barton Reaction involves a homolytic RO–NO cleavage, followed by δ-hydrogen abstraction, free radical recombination, and tautomerization to form an oxime. Selectivity for the δ-hydrogen is a result of the conformation of the 6-membered radical intermediate. Often, the site of hydrogen atom abstraction can be easily predicted. This allows the regio- and stereo-selective introduction of functionality into complicated molecules with high yield.

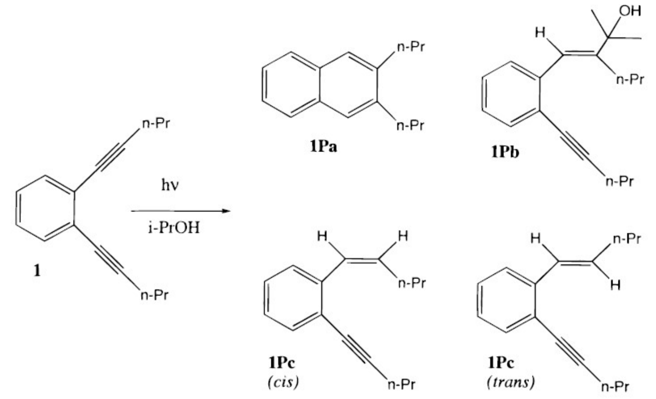
The Barton reaction commences with a photochemically induced cleavage of the nitrite O-N bond, typically using a high pressure mercury lamp. This produces an alkyoxyl radical which immediately abstracts a hydrogen atom from the δ-carbon. In the absence of other radical sources or other proximal reactive groups, the alkyl radical recombines with the nitrosyl radical. The resultant nitroso compounds undergoes tautomerization to the isolated oxime product.

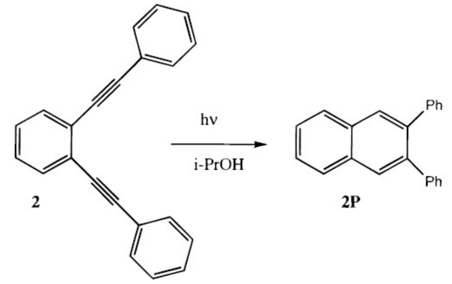


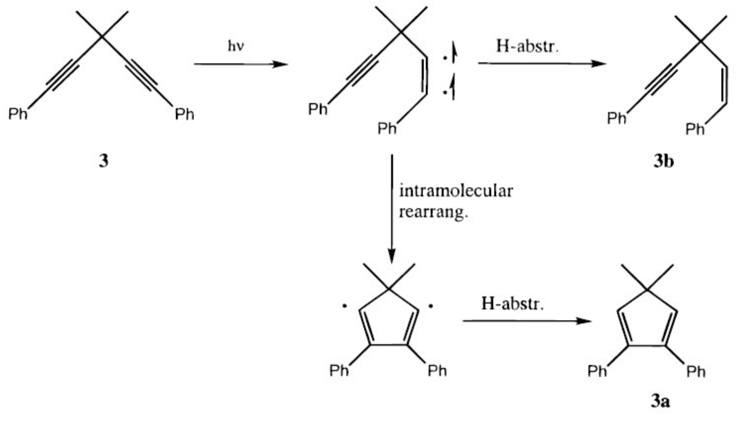
Photochemical Rearrangement of Enediynes

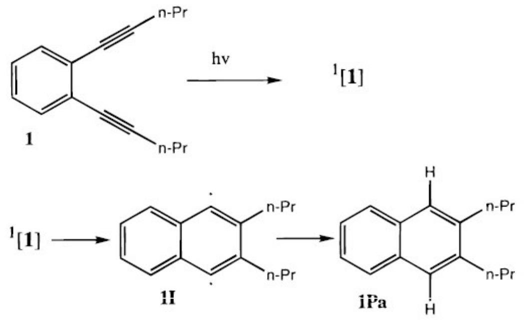
The chemistry of enediynes has been an area of avid scientific interest during the past two decades, as a result of its application in the design of a class of potent antitumor antibiotics. For example, the drugs calicheamicin, dynemicin, and esperamicin, each of which possesses an enediyne unit, have been extensively studied, and have been shown to produce a highly reactive aromatic 1,4-biradical intermediate, which is responsible for the biological activity. Such intermediates were first characterized by Bergman, who trapped the resulting p-benzyne biradical upon thermolysis of an acyclic enediyne. Since then the thermal rearrangement, commonly referred to as the Bergman rearrangement, has been thoroughly explored both experimentally and theoretically, and both the thermodynamic and kinetic properties of the thermal cyclization are becoming better understood.











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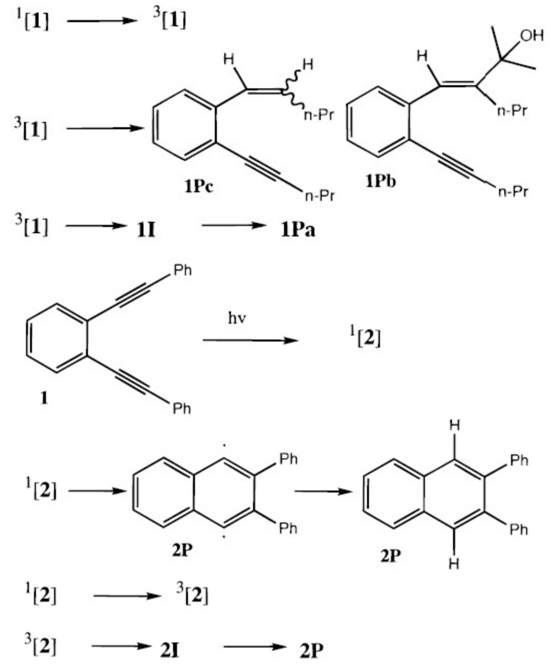


Photosensitization: The foreign substance absorbs the radiation and transfers the absorbed energy to the reactants is called a photosensitizer. This process is called photosensitized reaction (or) photosensitization. Examples, i) Atomic photosensitizers: mercury, cadmium, zinc and ii) Molecular photosensitizers: benzophenone, sulphur dioxide.

Quenching: When the excited foreign substance collides with another substance it gets converted into some other product due to the transfer of its energy to the colliding substance. This process is known as quenching.

Types of transitions: The activated molecules returns to the ground state by emitting its energy through the following general types of transitions.

1. Non-radiative transitions do not involve the emission of any radiations, so theses are also known as non-radiative or radiationless transitions. Non-radiative transitions involve the following two transitions.

(i) **Internal conversion (IC)**: These transitions involve the return of the activated molecule
from the higher excited states to the first excited states, ie.

$S_3 \rightarrow S_1$; $S_2 \rightarrow S_1$ (or) $T_3 \rightarrow T_1$; $T_2 \rightarrow T_1$

The energy of the activated molecule is given out in the form of heat through molecular collisions. This process is called internal conversion (IC) and occurs in less than about 10^{-11} second.

(ii) **Inter system crossing (ISC)**: The molecule may also lose energy by another process called inter system crossing (ISC). These transitions involve the return of the activated molecules from the states of different spins ie. Different multiplicity ie., $S_2 \rightarrow T_2$; $S_1 \rightarrow T_1$. These transitions are forbidden, occurs relatively at slow rates.

2. Radiative transitions involve the return of activated molecules from the singlet excited state S_1 and triplet state T_1 to the ground state S_0. These transitions are accompanied by the emission of radiations. Thus, radiative transitions involve the following two radiations.

(i) **Fluorescence**: The emission of radiation due to the transition from singlet excited state S_1 to ground state S_0 is called fluorescence ($S_1 \rightarrow S_0$). This transition is allowed transition and occurs in about 10^{-8} second.

(ii) **Phosphorescence**: The emission of radiation due to the transition from the triplet excited state T_1 to the ground state S_0 is called phosphorescence ($T_1 \rightarrow S_0$). This transition is slow and forbidden transition.

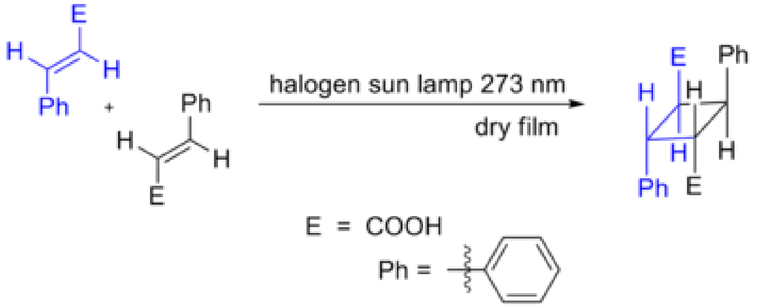
3. Quenching of fluorescence: The fluorescence may be quenched, when the excited molecule collides with a normal molecule before it fluoresces. During quenching, the energy of the excited molecule gets transferred to the molecule with which it collides. Quenching occurs in two ways.

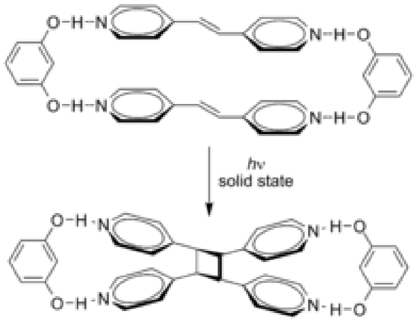
(i) **Internal quenching**: Quenching may also occur, when the molecule changes from the singlet excited state to the triplet excited state. This phenomenon is called internal quenching.

(ii) **External quenching**: Quenching may also occur from the addition of an external substance, which absorbs energy from the excited molecule. This phenomenon is called external quenching.

Photochemical cycloadditions and their stereochemistry

Cycloadditions in which 4n π electrons participate can also occur via photochemical activation. Here, one component has an electron promoted from the HOMO (π bonding) to the LUMO (π* antibonding). Orbital symmetry is then such that the reaction can proceed in a suprafacial-suprafacial manner. An example is the DeMayo reaction. Another example is shown below, the photochemical dimerization of cinnamic acid.[3] The two trans alkenes react head-to-tail, and the isolated isomers are called truxillic acids.





Cycloaddition of trans-1,2-bis(4-pyridyl)ethene

Supramolecular effects can influence these cycloadditions. The cycloaddition of trans-1,2-bis(4-pyridyl)ethene is directed by resorcinol in the solid-state in 100% yield.[4]

Some cycloadditions instead of π bonds operate through strained cyclopropane rings, as these have significant π character. For example, an analog for the Diels-Alder reaction is the quadricyclane-DMAD reaction:

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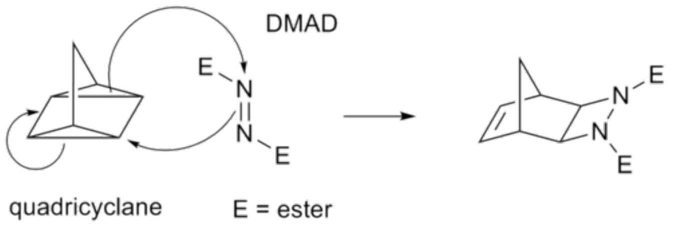
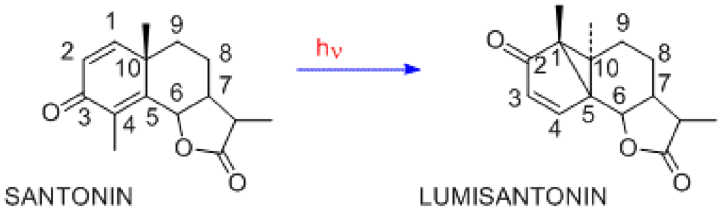


In the (i+j+...) cycloaddition notation i and j refer to the number of atoms involved in the cycloaddition. In this notation, a Diels-Alder reaction is a (4+2)cycloaddition and a 1,3-dipolar addition such as the first step in ozonolysis is a (3+2)cycloaddition. The IUPAC preferred notation however, with [i+j+...] takes electrons into account and not atoms. In this notation, the DA reaction and the dipolar reaction both become a [4+2]cycloaddition. The reaction between norbornadiene and an activated alkyne is a [2+2+2]cycloaddition.

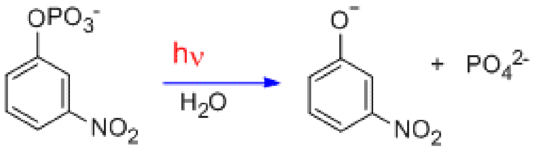
Photolytic Rearrangements

One of the earliest photochemical studies dealt with the natural product santonin. In the 19th century it had been observed by Ciamician that in Italian sunlight santonin gave several photoproducts.[3][4] The structure of santonin was first correctly described by Clemo and Hayworth in 1929.[5] The initial photoproduct obtained from santonin is lumisantonin.[6] As depicted in Eqn. 1, the photoreaction involves a rearrangement. Using steroid numbering, we note that the C-3 carbonyl group has moved to C-2, the C-4 methyl has moved to C-1, and the C-10 carbon has been inverted.

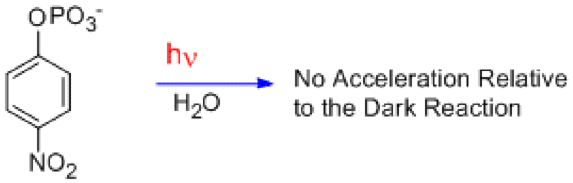


(1)

A comparatively bizarre example was uncovered by Egbert Havinga in 1956.[7] The curious result was activation on photolysis by a meta nitro group in contrast to the usual activation by ortho and para groups.



(2)

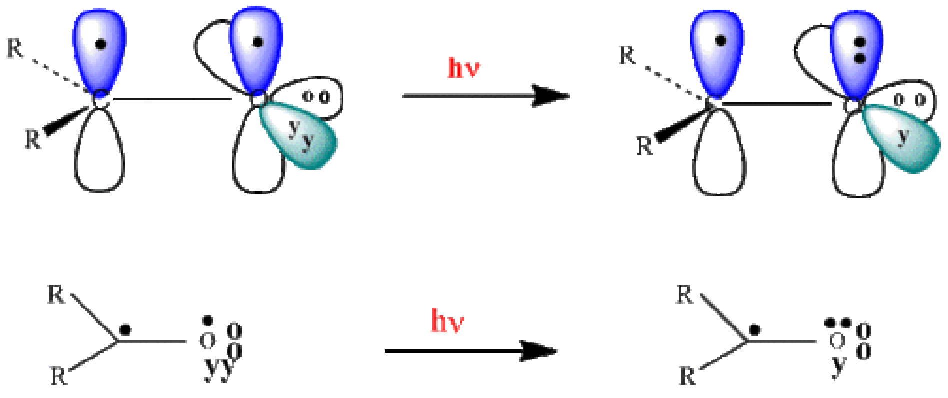


(3)

Over the decades, many interesting but puzzling organic photochemical reactions were discovered that did not proceed by ordinary organic ground state processes. Rather, they arose from the excited states of electrons in the compounds. The real problem was that, at the time, organic chemists were not versed in quantum mechanics and physical chemists were not versed in organic chemistry. Real mechanistic treatments were not possible.

Starting in 1961 it was found that one could understand organic photochemical reactions in the context of the relevant excited states.[8][9][10] One example is the n-pi* excitation of mono-carbonyl compounds, the simplest being that of formaldehyde. The structure was first described by

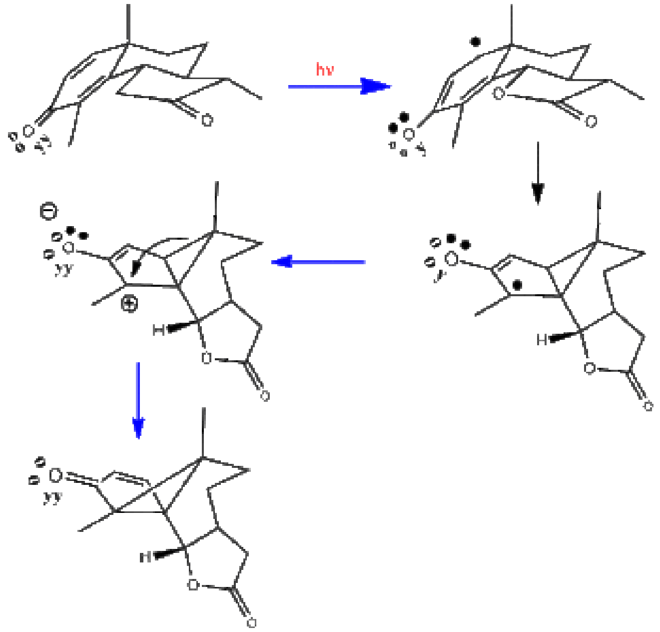
Mulliken.[11] The three-dimensional representation (top drawing) is simplified in the second line using a two-dimensional representation, which facilitates arrow pushing.[9][10]



Solid dots represent pi-system electrons; 0 dots represent sp-hybrids; y's are p_y electrons

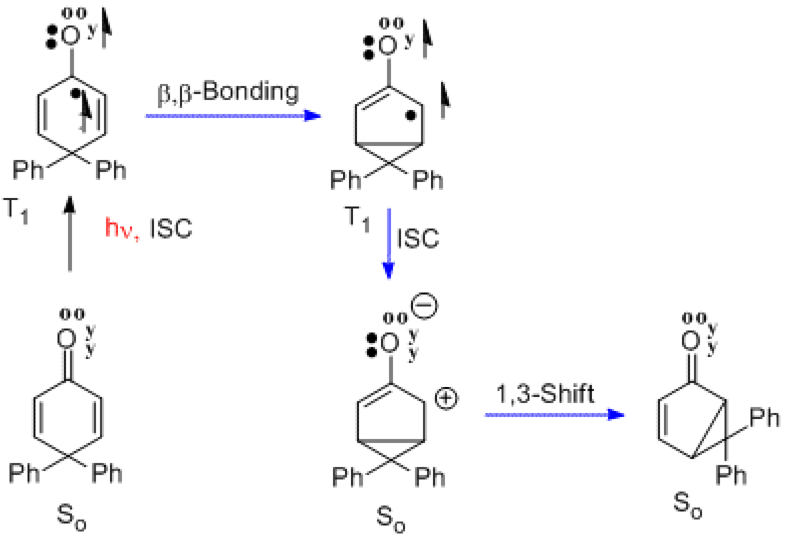
In this early research simple Hückel computations were used to get excited state electron densities and bond-orders.[9][10] The stereochemistry in Scheme 1 is shown three-dimensionally. The Hückel computations revealed that the beta-carbons (i.e. C2 and C5) of the cyclohexadienone ring had a large bond-order. As seen in the scheme a beta-beta bond is formed. Subsequent to this, radiationless decay leads to a zwitterion ground state. The final rearrangement leads to lumisantonin as can be discerned by comparing the three-dimensional drawing with the earlier two-dimensional representation.

Scheme 1. The santonin to lumisantonin rearrangement in three-dimensions



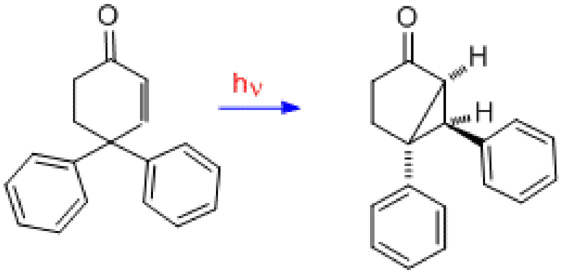
4,4-Diphenylcyclohexadienone rearrangement

Quite parallel to the santonin to lumisantonin example is the rearrangement of 4,4-diphenylcyclohexadienone[10] Here the n-pi* triplet excited state undergoes the same beta-beta bonding. This is followed by intersystem crossing (i.e. ISC) to form the singlet ground state which is seen to be a zwitterion. The final step is the rearrangement to the bicyclic photoproduct. The reaction is termed the type A cyclohexadienone rearrangement.

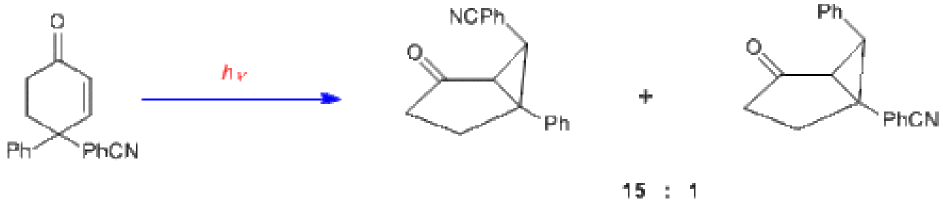


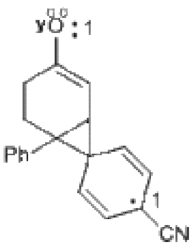
The contrasting case of 4,4-diphenylcyclohexenone, one double bond missing

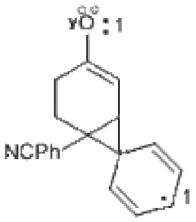
To provide further evidence on the mechanism of the dienone in which there is bonding between the two double bonds, the case of 4,4-diphenylcyclohexenone is presented here. It is seen that the rearrangement is quite different; thus two double bonds are required for a type A rearrangement. With one double bond one of the phenyl groups, originally at C-4, has migrated to C-3 (i.e. the beta carbon).[12]



It is of considerable interest that when one of the aryl groups has a para-cyano or para-methoxy group, that substituted aryl group migrates in preference.[13] Inspection of the alternative phenonium-type species, in which an aryl group has begun to migrate to the beta-carbon, reveals the greater electron delocalization with a substituent para on the migrating aryl group and thus a more stabilized pathway.

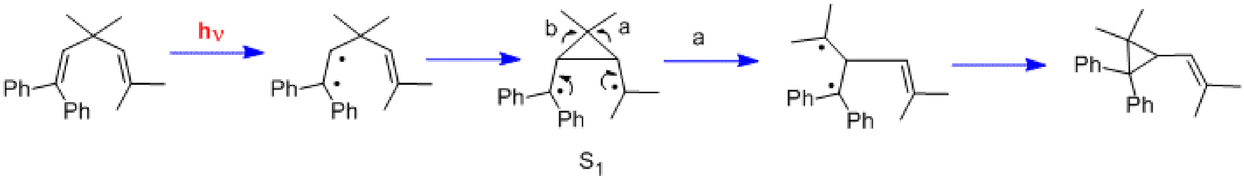






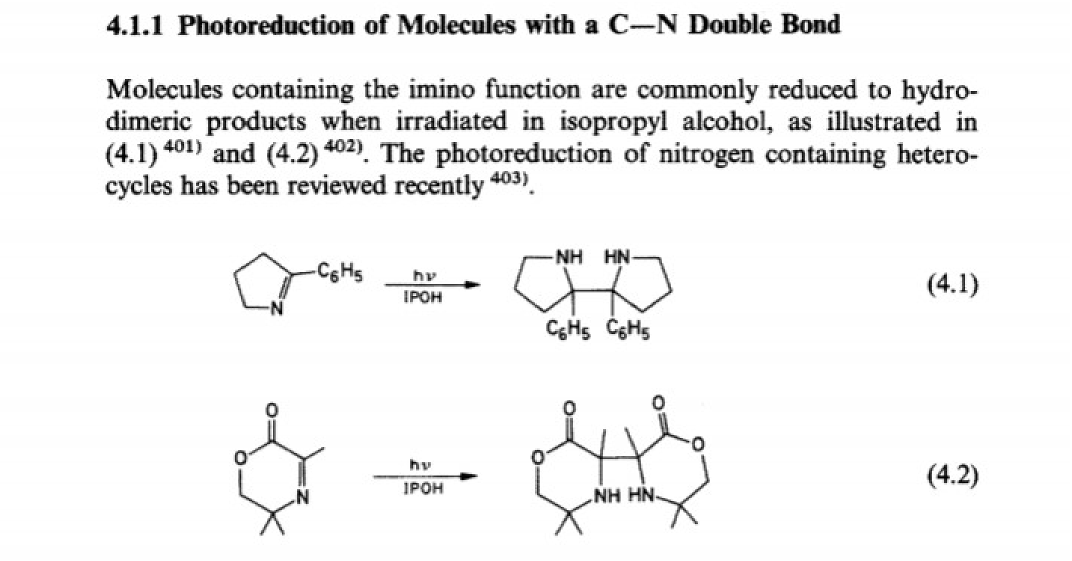
π-π* reactivity

Still another type of photochemical reaction is the di-pi-methane rearrangement.[14] Two further early examples were the rearrangement of 1,1,5,5-tetraphenyl-3,3-dimethyl-1,4-pentadiene (the "Mariano" molecule)[15] and the rearrangement of barrelene to semibullvalene.[16] We note that, in contrast to the cyclohexadienone reactions which used n-π* excited states, the di-π-methane rearrangements utilize π-π* excited states.



Parallel studies on multiplicity; the role of triplets

Parallel to the structural studies of the Zimmerman group as described above, the Caltech group with George Hammond pursued the role of multiplicity on reactivity. The importance of triplet excited species was emphasized. The triplets tend to be longer lived than singlets and of lower energy than the singlet of the same configuration. Hammond had summarized the energies of triplets of the more common molecules. He noted that triplets may arise from (A) conversion of the initially formed singlets or by (B) interaction with a higher energy triplet (sensitization). Another contribution of Hammond was the determination of triplet reaction rates. Finally, with low-energy triplets present it was shown possible to quench a triplet reaction.[17] The groundwork had been laid by very earlier studies in Russia by Terenin and Ermolaev, who demonstrated intermolecular triplet transfer at low temperatures and described the kinetics.

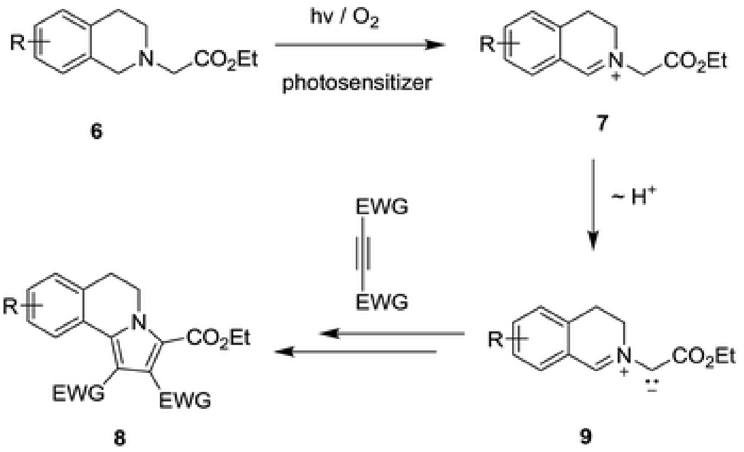


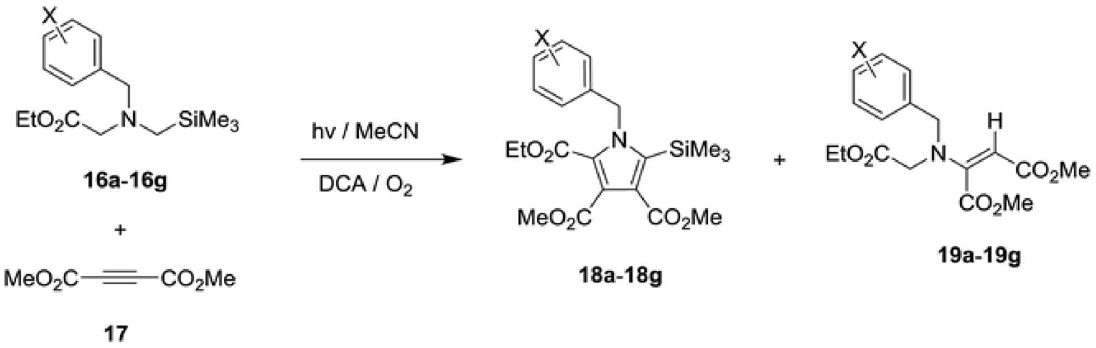
4.1.1 Photoreduction of Molecules with a C—N Double Bond

Molecules containing the imino function are commonly reduced to hydrodimeric products when irradiated in isopropyl alcohol, as illustrated in (4.1)[401)] and (4.2)[402)]. The photoreduction of nitrogen containing heterocycles has been reviewed recently[403)].

(4.1)

(4.2)

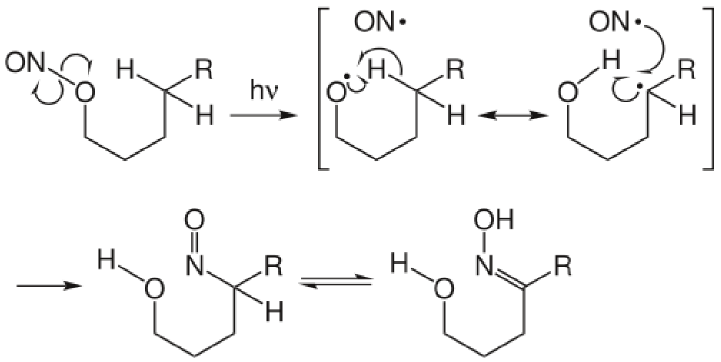




Barton reaction

The Barton reaction, also known as the Barton nitrite ester reaction, is a photochemical reaction that involves the photolysis of an alkyl nitrite to form a δ-nitroso alcohol.

The Barton reaction commences with a photochemically induced cleavage of the nitrite O-N bond, typically using a high pressure mercury lamp.[8] This produces an alkyoxyl radical which immediately abstracts a hydrogen atom from the δ-carbon. In the absence of other radical sources or other proximal reactive groups, the alkyl radical recombines with the nitrosyl radical. The resultant nitroso compounds undergoes tautomerization to the isolated oxime product.



The carbon centered radical can be intercepted by other radical sources such as iodine or acrylonitrile. The first instance results in the δ-hydrogen being replaced with iodine, then subsequent cyclization to a tetrahydrofuran by an SN2 reaction.[9] The second example results in a chain elongation product with the oxime formed 2 carbon units further from the oxygen than normal.[10]

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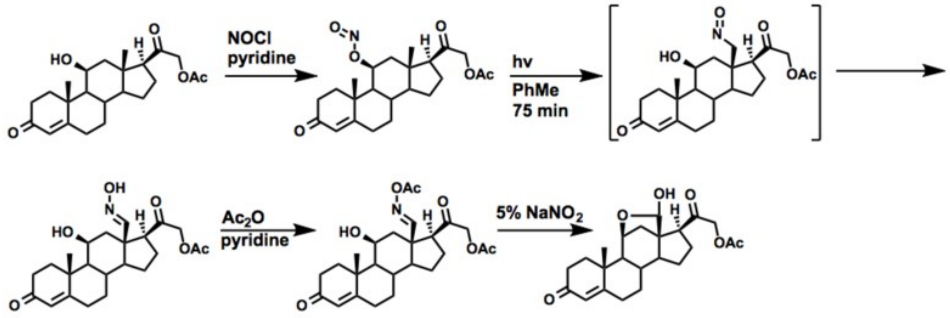
Applications in complex molecule synthesis

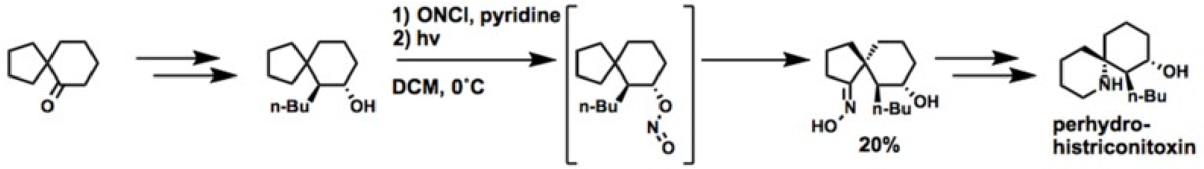
Aldosterone acetate

In a publication immediately proceeding Barton's initial disclosure of the methodology in the Journal of the American Chemical Society, a synthesis of aldosterone acetate is demonstrated.[23] Allowing corticosterone acetate to react with nitrosyl chloride in dry pyridine yields the nitrite. Subsequently, irradiation under inert atmosphere followed by treatment with aqueous sodium nitrite selectively gives the desired oxime. The oxime is then acetylated and hydrolyzed to yield the natural product hemiacetal.



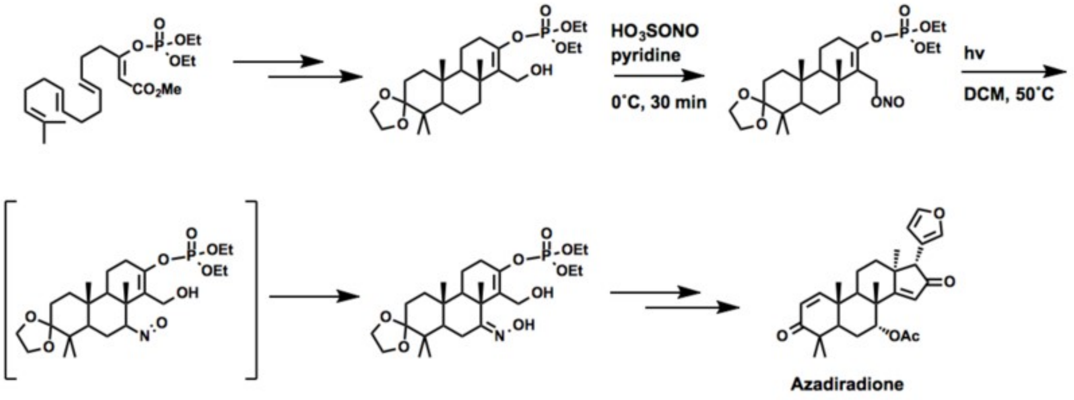
Perhydrohistrionicotoxin

After a short synthesis to obtain the desired spiro-[5.4] system, Nobel Laureaute E.J. Corey and co-workers employed a Barton reaction to selectively introduce an oxime in a 1,3-diaxial position to the nitrite ester. The oxime is converted to a lactam via a Beckmann rearrangement and then reduced to the natural product.[24]



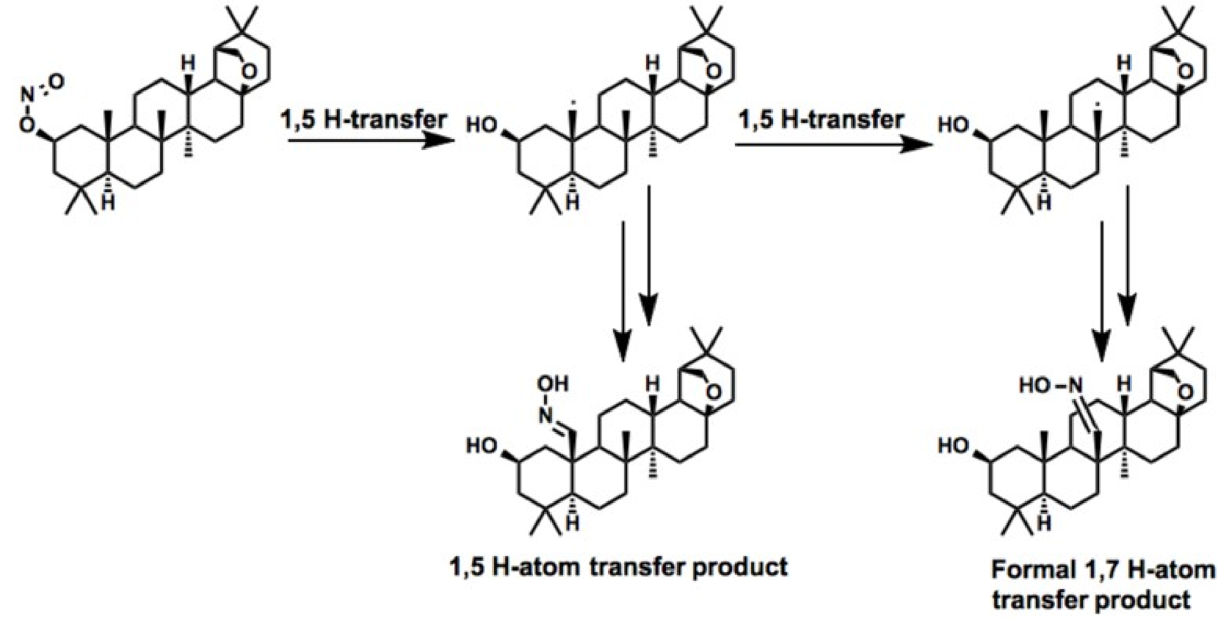
Azadiradione

Corey again employed the Barton reaction in the synthesis of Azadiradione, a member of the limonoid family of natural products. In this case, nitrosylsulfuric acid is used in place of nitrosyl chloride.[25]



Allobetulin derivatives

In the process of preparing a series of derivatives of the triterpenoid allobetulin, Dehan and coworkers observed a remarkable transformation resulting from two consecutive 1,5-hydrogen atom transfers. While the product of the single 1,5-hydrogen atom transfer was also observed, the former transformation represent a formal 1,7-hydrogen atom transfer across an enormous distance.[26]



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