> Chapter 4 <

Stability and Reactivity: General Concepts, Free Radicals and Other Reactive Intermediates

Stability

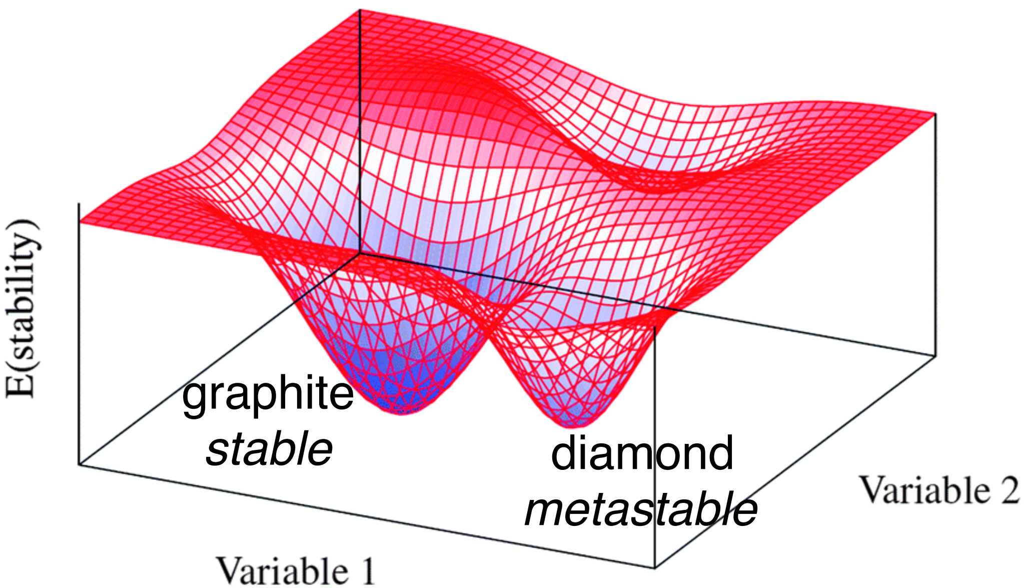
Thermodynamic stability

Reactivity

Kinetic persistence

Metastability Transiency

Lifetime = 1/(rate constant)



In **isolation**: fragmentation, dimerization

In **system**: reactions with other chemicals

! Conditions: temperature, air, moisture, radiation

Hoffmann, Schleyer, Schaefer, *Angew. Chem. Int. Ed.* **2008**, *47*, 7164.

Energy Decomposition Analysis (**EDA**)

intermolecular interaction *reaction* *intramolecular interaction*

Interaction = Electrostatic +
Polarization (Induced electrostatic = orbital relaxation) +
Pauli (Exchange & Repulsion) +
Orbital (Charge Transfer, Delocalisation) +
Dispersion +
Mix

Kitaura-Morokuma
Ziegler-Rauk
Natural Bond Orbital
Localized Molecular Orbital
Pair Interaction
Block Localized Wavefunction
Symmetry-Adapted Perturbation Theory
etc.

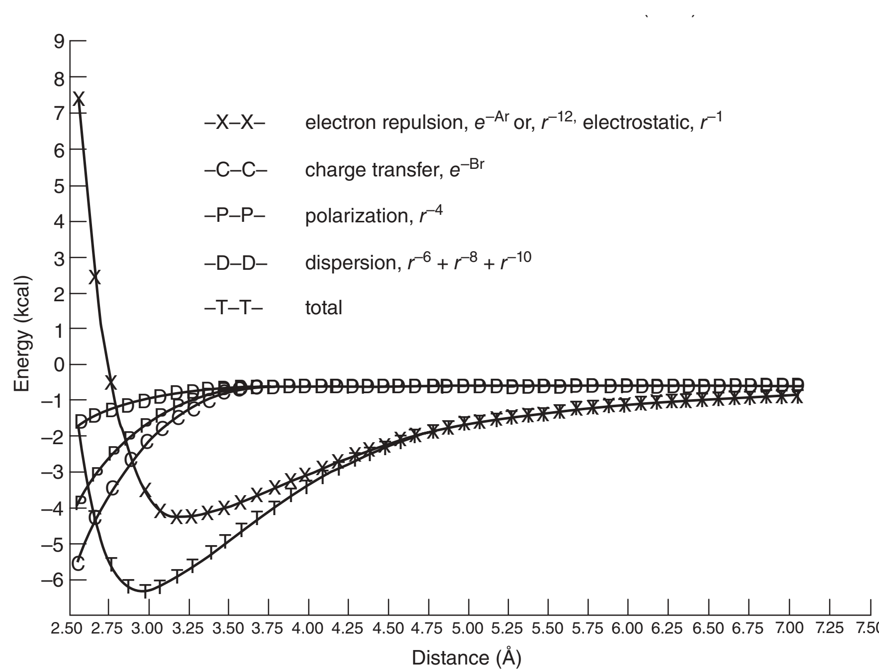


Figure 9.1. Morokuma decomposition of an ab initio molecular orbital calculation for the water dimer.[3b] (From Jeffrey and Saenger.[4] Copyright 1991 by Springer. Reprinted by permission of Springer.)

What makes a molecule stable or reactive?

Effect – it's the reason behind an observation that is not in accord with reasonable expectation of the time

Polar / Electrostatic

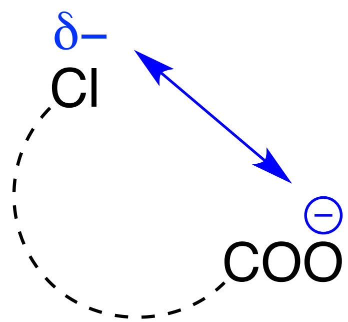
Resonance / Conjugation

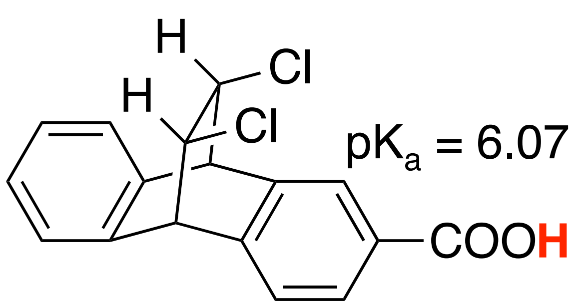
Steric

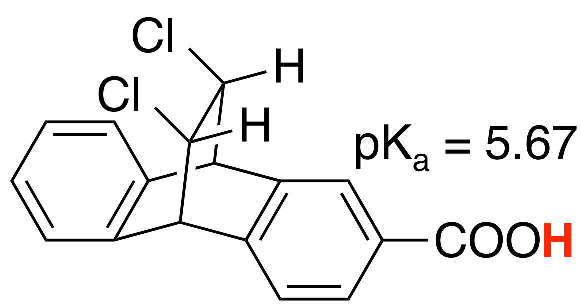
All three are always present and combined!

Electrostatic (Polar) effects

Field	*Inductive*
due to Coulombic forces	due to electronegativity
stereospecific	conformationally independent





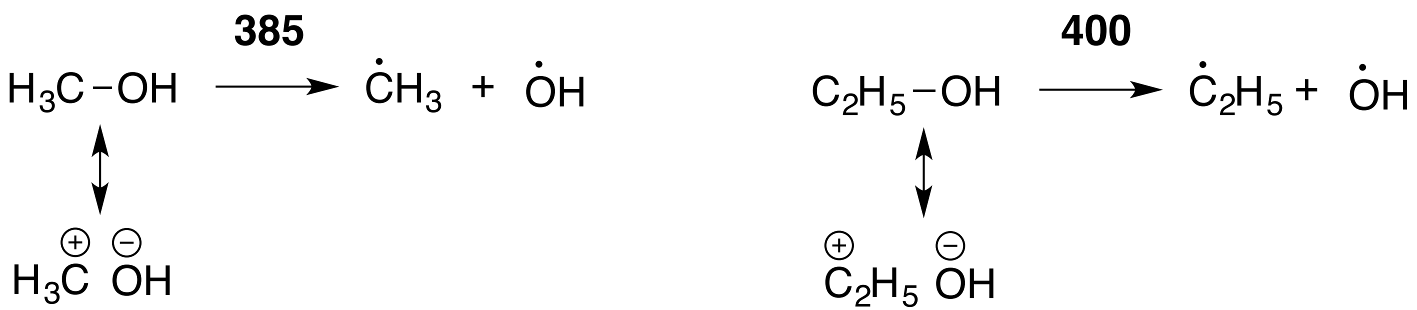


Electronegativity

tendency to attract electron density

Pauling: R-X bond strength increases with increasing differences in the electronegativity of the R and X in the bond

Bond strength = stabilities of both the R–X and the R• + •X!



Izgorodina, Coote, Radom, *J. Phys. Chem.* A **2005**, *109*, 7558.

Electronegativity

tendency to attract electron density

Pauling: R-X bond strength increases with increasing differences in the electronegativity of the R and X in the bond

$$R{-}X \xrightarrow{\textit{BDE}} R^{\bullet} + X^{\bullet}$$

R = alkyl

X = NH_2, OH, F

X is <u>more electronegative</u> than R

Protonation

$$R{-}\overset{\oplus}{X}H \longrightarrow R^{\bullet} + {}^{\bullet}\overset{\oplus}{X}H$$

Higher *BDE*

X becomes even <u>more electronegative</u> than R

Deprotonation

$$R{-}\overset{\ominus}{X}(\text{-H}) \longrightarrow R^{\bullet} + {}^{\bullet}\overset{\ominus}{X}(\text{-H})$$

Lower *BDE*

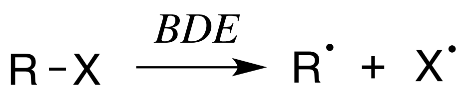
Electronegativities of R and X become <u>closer</u>

Boyd, Boyd, Bessonette, Kerdraon, Aucoin, *J. Am. Chem. Soc.* **1995**, *117*, 8816.

Electronegativity

tendency to attract electron density

Pauling: R-X bond strength increases with increasing differences in the electronegativity of the R and X in the bond



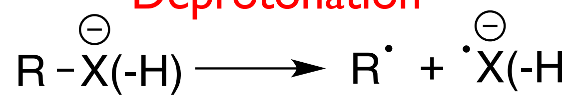
R = alkyl

X = NH_2, OH, F

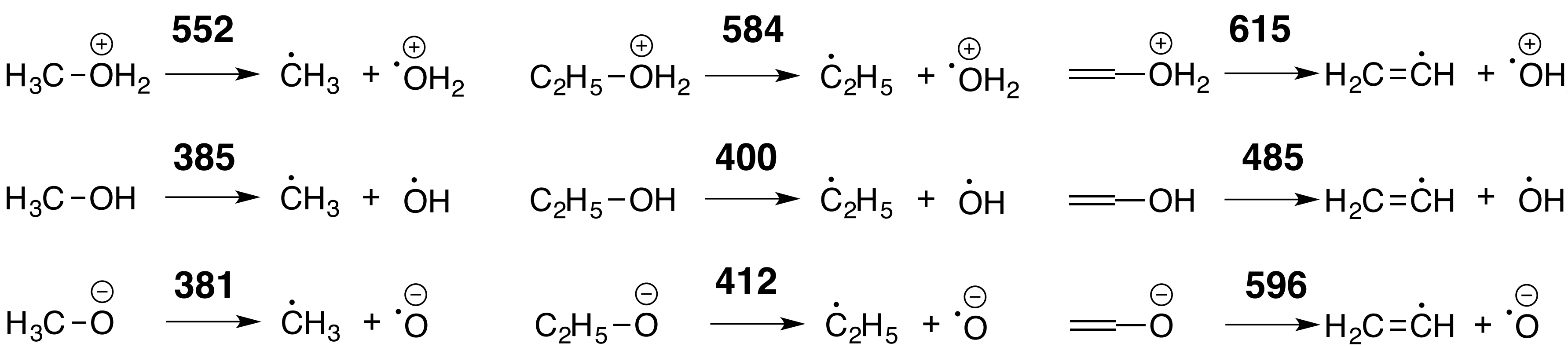
Protonation

Higher *BDE*

Deprotonation



Lower *BDE*

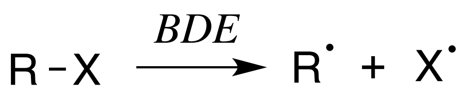


Boyd, Boyd, Bessonette, Kerdraon, Aucoin, *J. Am. Chem. Soc.* **1995**, *117*, 8816.

Electronegativity

tendency to attract electron density

Pauling: R-X bond strength increases with increasing differences in the electronegativity of the R and X in the bond



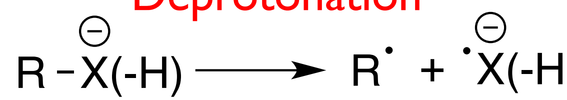
R = alkyl

X = NH_2, OH, F

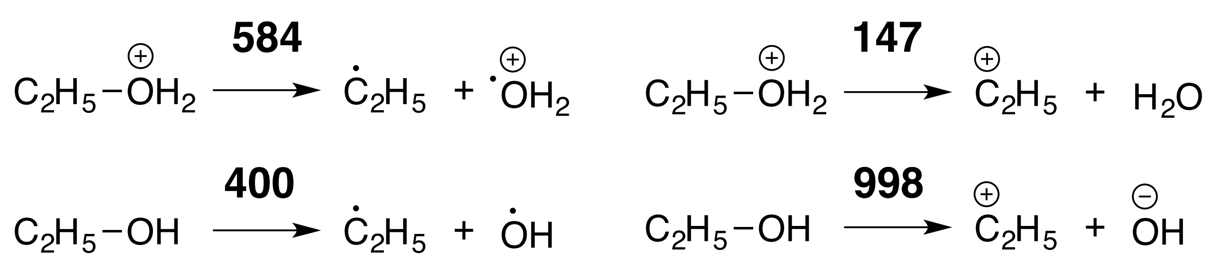
Protonation

Higher *BDE*

Deprotonation



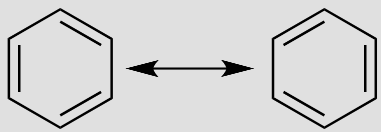
Lower *BDE*

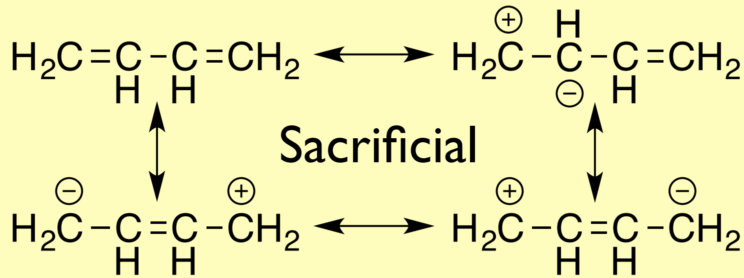


Boyd, Boyd, Bessonette, Kerdraon, Aucoin, *J. Am. Chem. Soc.* **1995**, *117*, 8816.

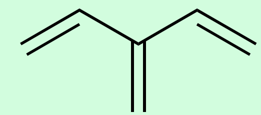
Resonance / Conjugation

Isovalent

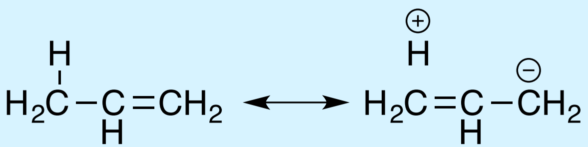




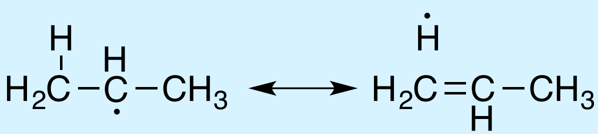
Cross-Conjugation

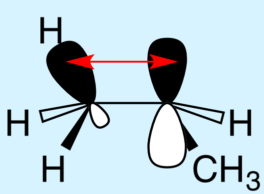


Hyperconjugation

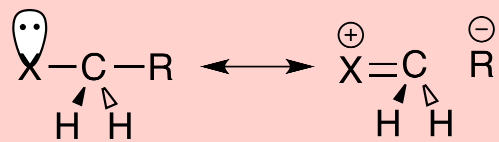


overlap of C–H σ and C=C π orbitals (stereospecific)



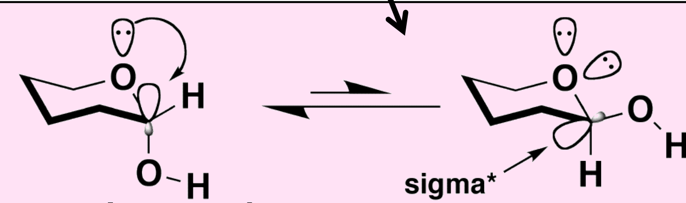


Negative Hypercojugation

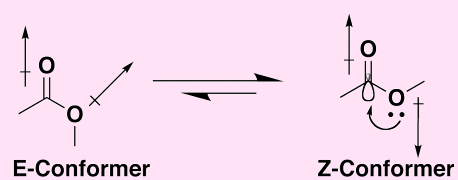


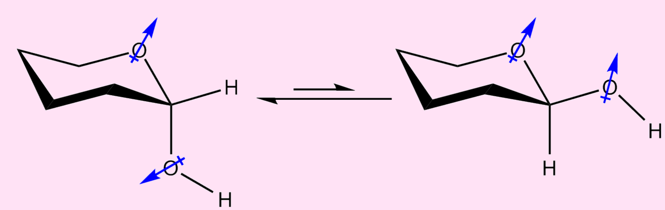
overlap of X lone pair and C–R σ* orbitals stereospecific

Anomeric effect

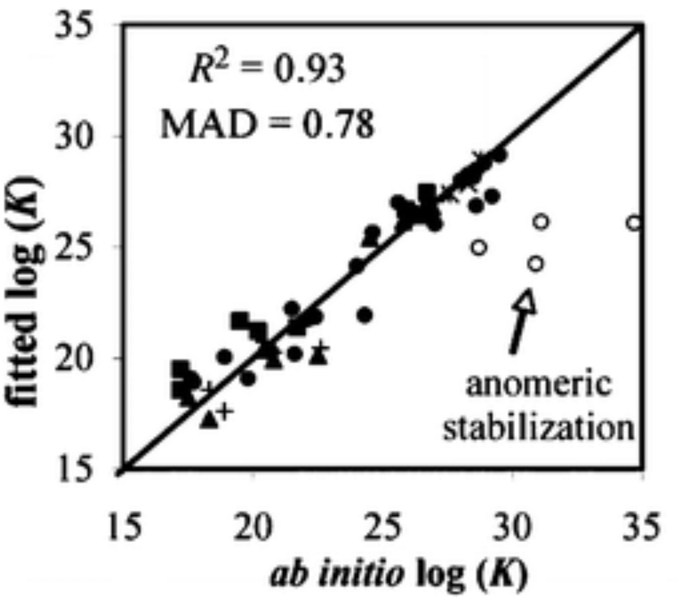


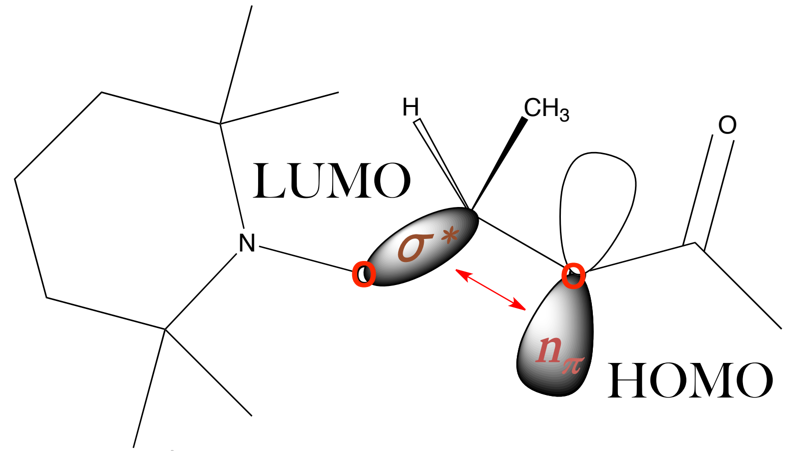
α-glucoside

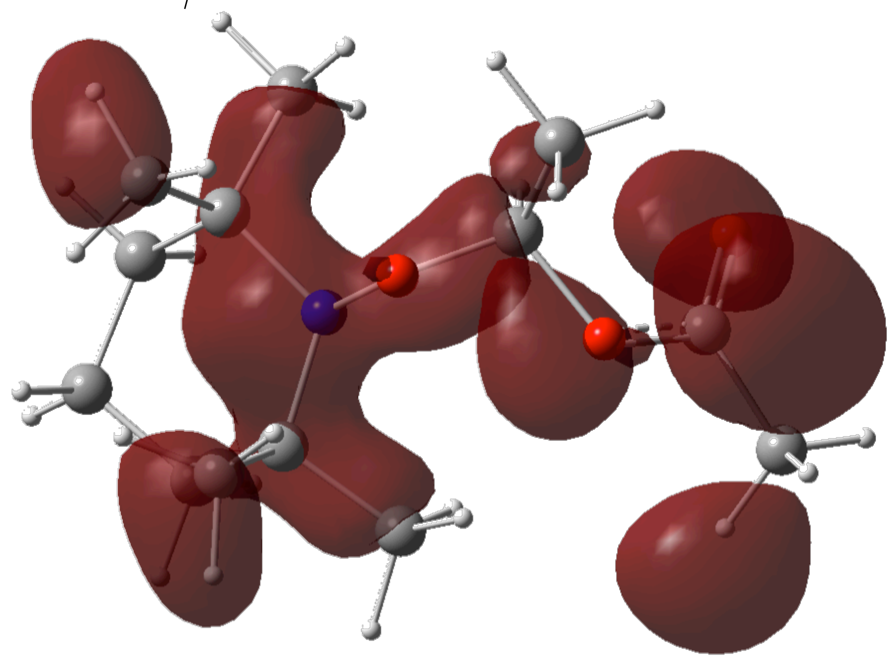




Anomeric effect







$$\begin{matrix} R' \\ R'' \end{matrix} \!\!> N\text{-}O^{\bullet} + R^{\bullet} \underset{}{\overset{K}{\rightleftharpoons}} \begin{matrix} R' \\ R'' \end{matrix} \!\!> N\text{-}OR$$

$$\log(K) = -0.10IP - 0.177RSE - 0.130RSE_{nxd} + 38.3$$

Hodgson, Lin, Coote, Marque, Matyjaszewski, *Macromolecules* **2010**, *43*, 3728.

Resonance / Conjugation

with single and double bonds

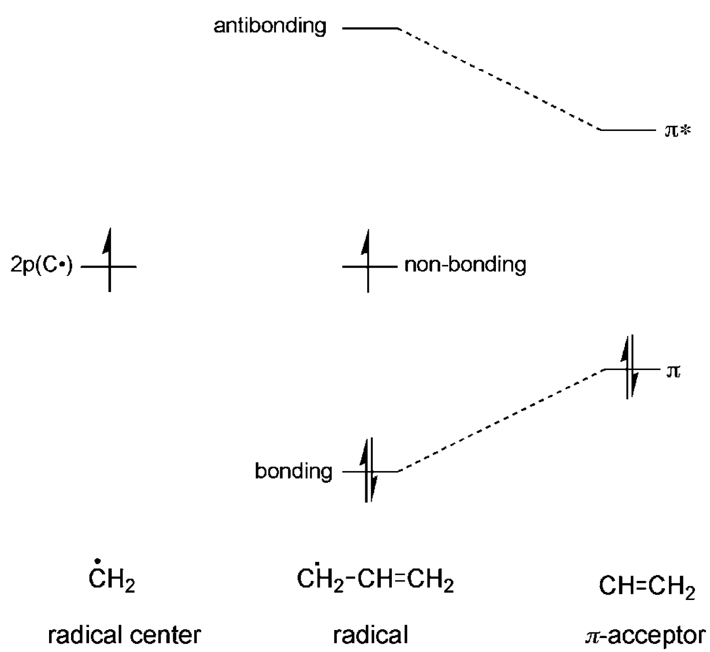


Figure 6. Orbital interaction diagram showing the three-electron interaction between the orbitals of the π acceptor group and the unpaired electron at a carbon radical center.

with π-orbitals on adjacent atom

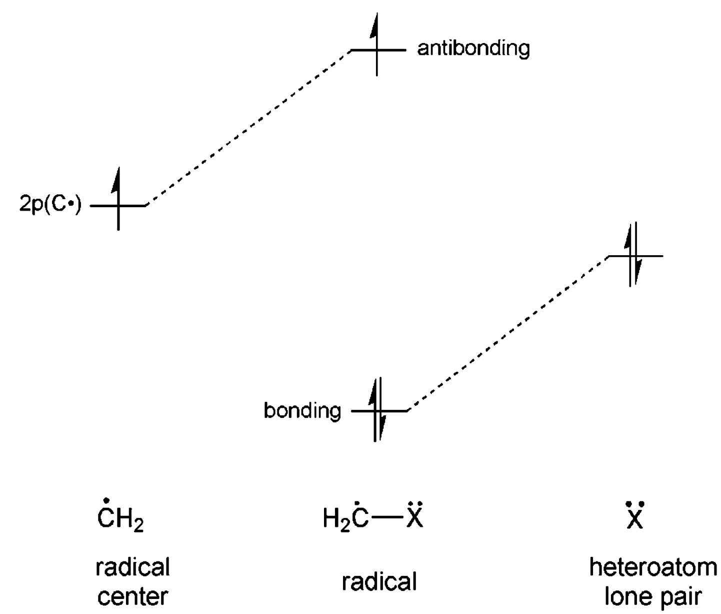
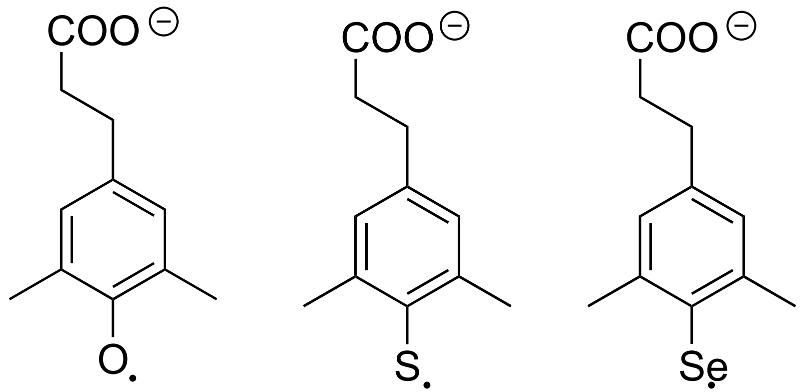


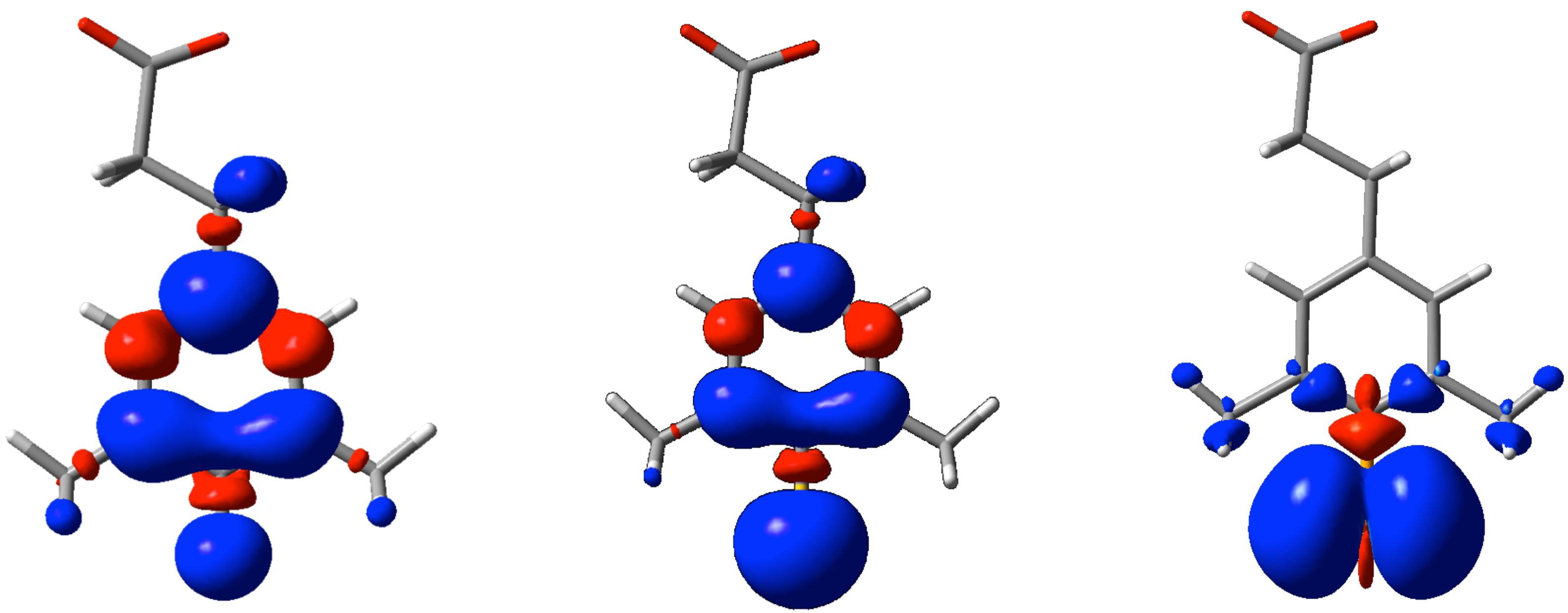
Figure 5. Orbital interaction diagram showing the three-electron interaction between the lone pair of a heteroatom and the unpaired electron at a carbon radical center.

Coote, Henry, *Macromolecules* **2005,** *38,* 1415.

Resonance / Conjugation



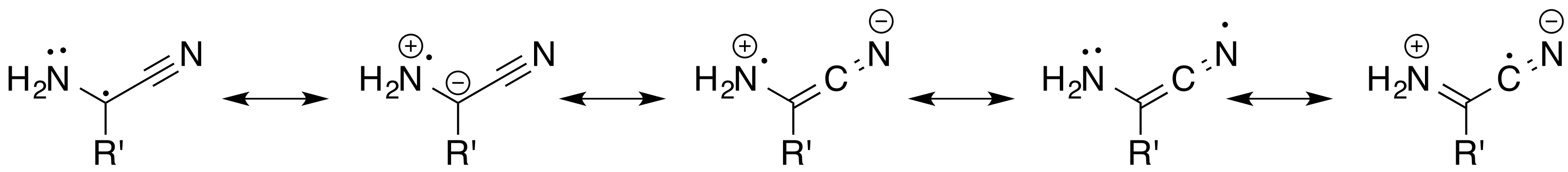
Orbital energies & sizes

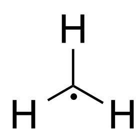


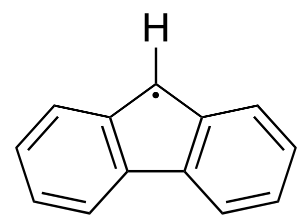
Gryn'ova, Coote, *J. Am. Chem. Soc.* **2013**, *135*, 15392.

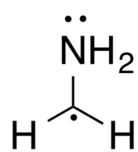
Resonance / Conjugation

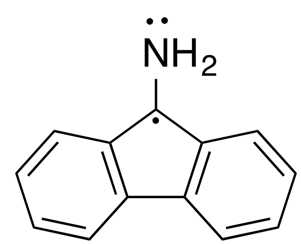
Captodative, or push-pull



0.0 

 0.0

43.1 

 62.8

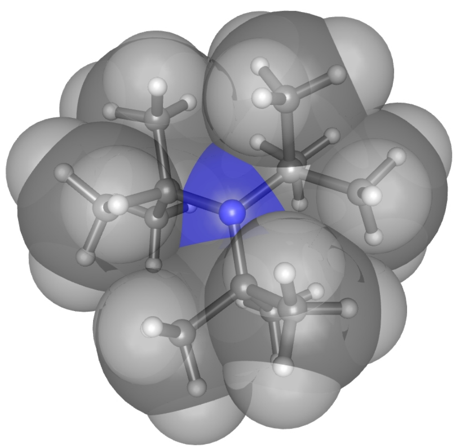
Bordwell, Lynch, *J. Am. Chem. Soc.* **1989**, *111*, 7558.

Steric effects

Shielding *Hindrance*

Amine basicity

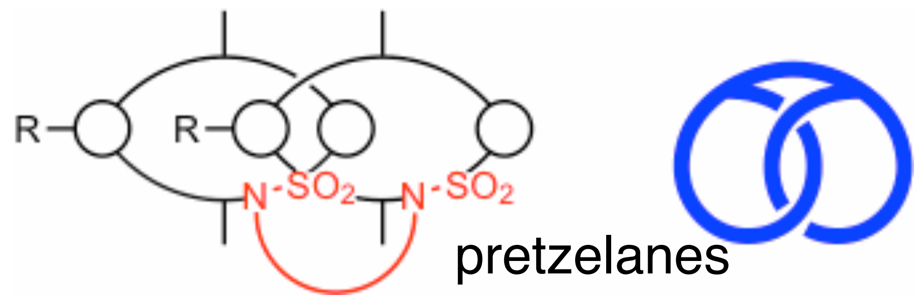
$NH_3 > NR_3 > NH_2R > NHR_2$



S_N2 reaction kinetics

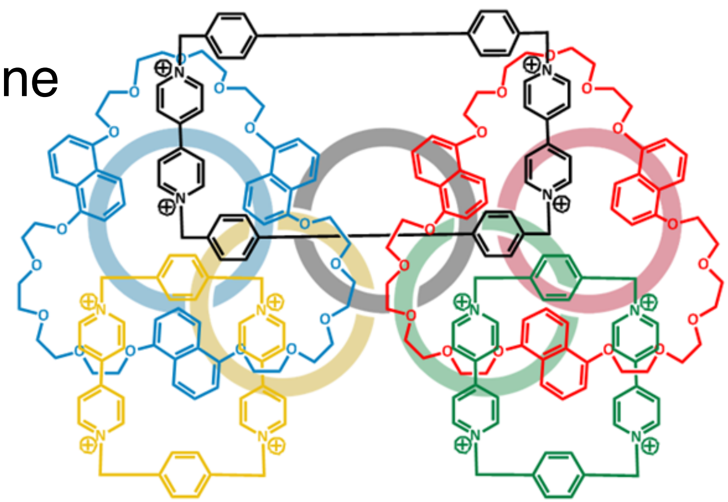
Chain crossing

Mechanically-interlocked molecular architectures (rotaxanes, catenanes)



pretzelanes

Olympiadane

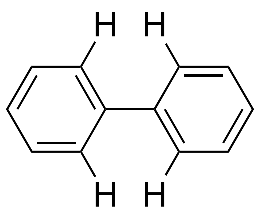


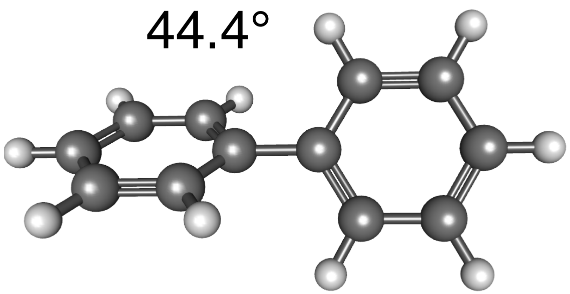
Amabilino, Ashton, Reder, Spencer, Stoddart, *Angew. Chem. Int. Ed.* **1994**, *33*, 1286.

Steric effects

Repulsion

Biphenyl





Torsional barrier for 0° and 90° are 8.0 and 8.3 kJ/mol, respectively

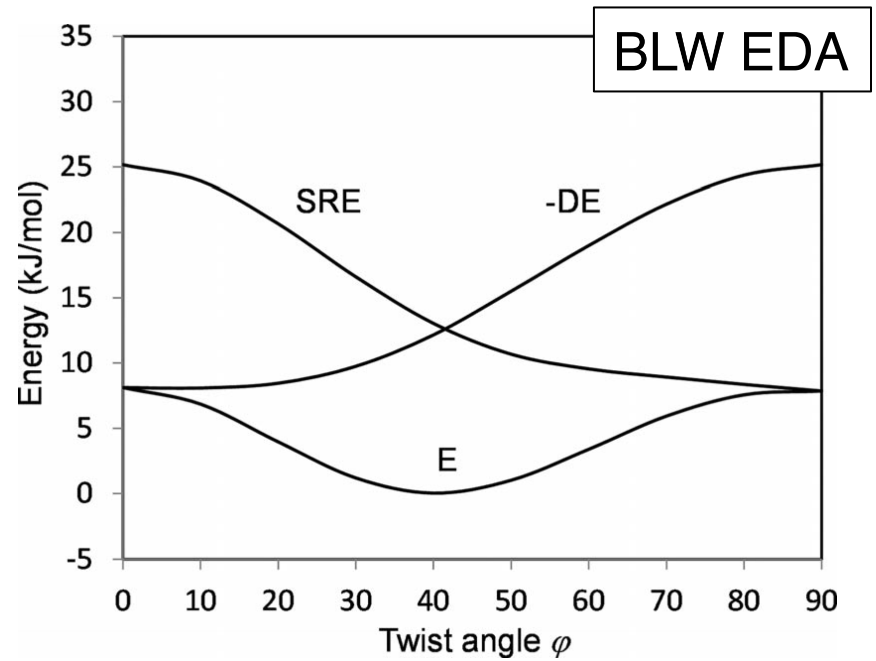


Figure 2. Variations in the energy components and the total energy with rotation around the central $C^1–C^{1'}$ bond in biphenyl.

Johansson, Olsen, *J. Chem. Theory Comput.* **2008**, *4*, 1460.

Jia, Wu, Chen, Mo, Eur. J. Org. Chem. **2013**, 611.

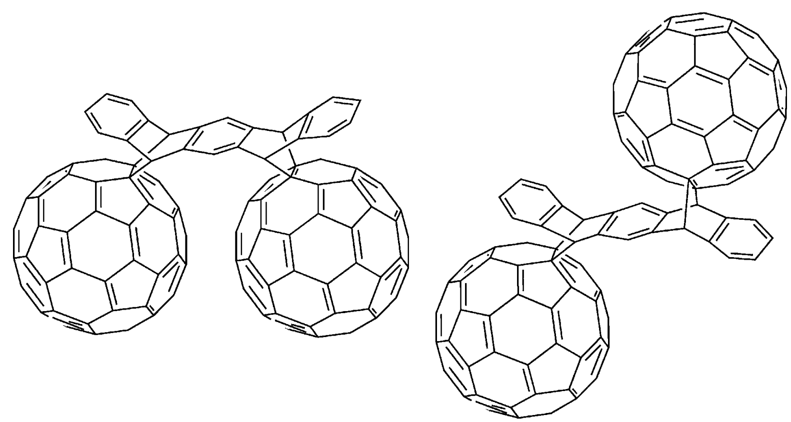
Steric effects

Repulsion

vs Dispersion

ΔG(syn-anti) = +1.15 kJ/mol using TPSS (no dispersion)

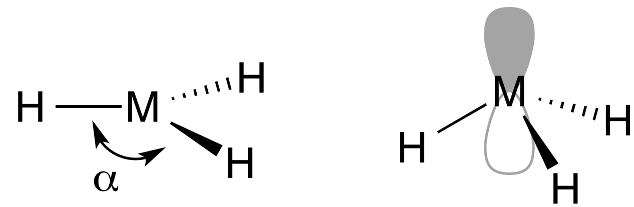
ΔG(syn-anti) = -26.6 kJ/mol using TPSS-D3 (dispersion corrected)



syn-1   *anti*-1

Scheme 1. Double C_{60} adducts of pentacene.[5]

Why is $\bullet CH_3$ planar?



minimised steric repulsion   maximised orbital overlap

M = C, Si, Ge, Sn

α = 120.00, 112.66, 112.44, 110.56

M–Cl BDE: 81.7, 105.6, 96.2, 93,6

C to Si – increased electronegativity difference (Cl 3.16, C 2.55, Si 1.90, Ge 2.01, Sn 1.96)

Si-Ge-Sn – increased bond length related to orbital overlap and vdW radii

Zhang, Dolg, *Chem. Eur. J.* **2014**, *20*, 13909.   Bickelhaupt, Ziegler, Schleyer, *Organometallics* **1996**, *15*, 1477.

Persistent Radicals

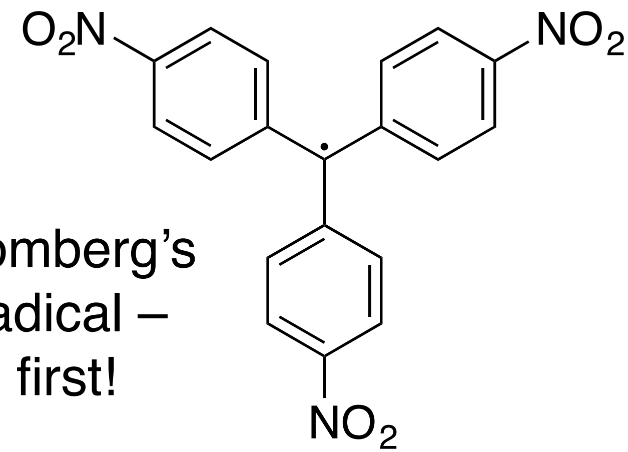
Carbon-centered

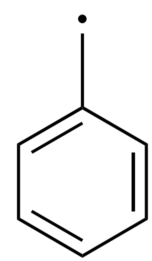
$$2R^{\bullet} \underset{}{\overset{k_d}{\rightleftharpoons}} \text{dimer}$$

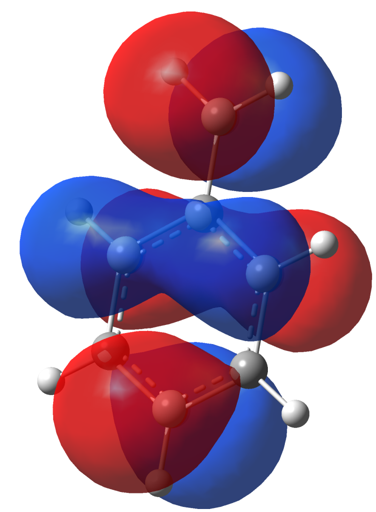
$$\tau_{1/2} = \frac{1}{k_d}$$

Persistent radical – $\log(t_{1/2})$ is > –3

Gomberg's radical – first!







Griller, Ingold, *Acc. Chem. Res.* **1976**, *9*, 13.

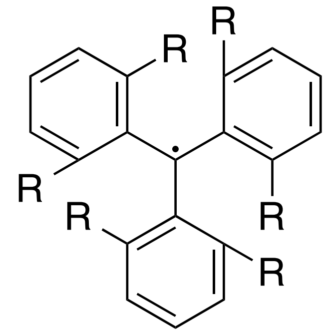
Persistent Radicals

Carbon-centered

$$2R^{\bullet} \underset{}{\overset{k_d}{\rightleftharpoons}} \text{dimer}$$

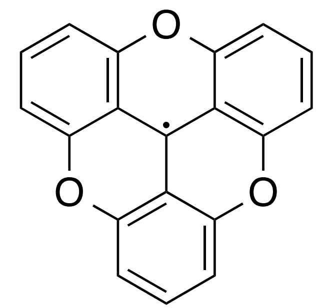
$$\tau_{1/2} = \frac{1}{k_d}$$

Persistent radical – $\log(t_{1/2})$ is > –3



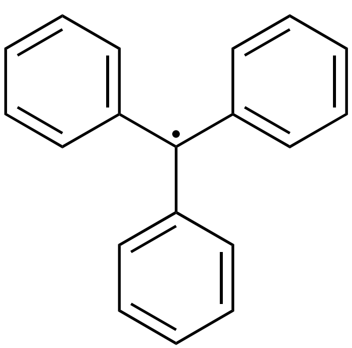
R = OMe

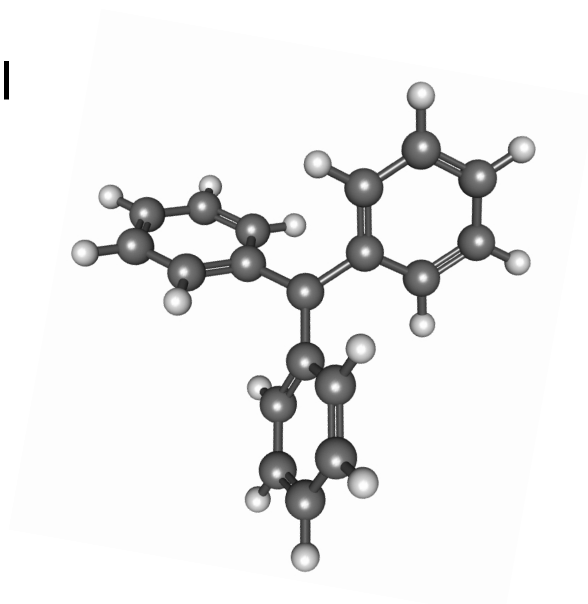
does not dimerize



mostly a **dimer** in solution

Triphenylmethyl





Persistence arises largely in steric hindrance, not so much in electronic effects (resonance)

Griller, Ingold, *Acc. Chem. Res.* **1976**, *9*, 13.

Persistent Radicals

Carbon-centered

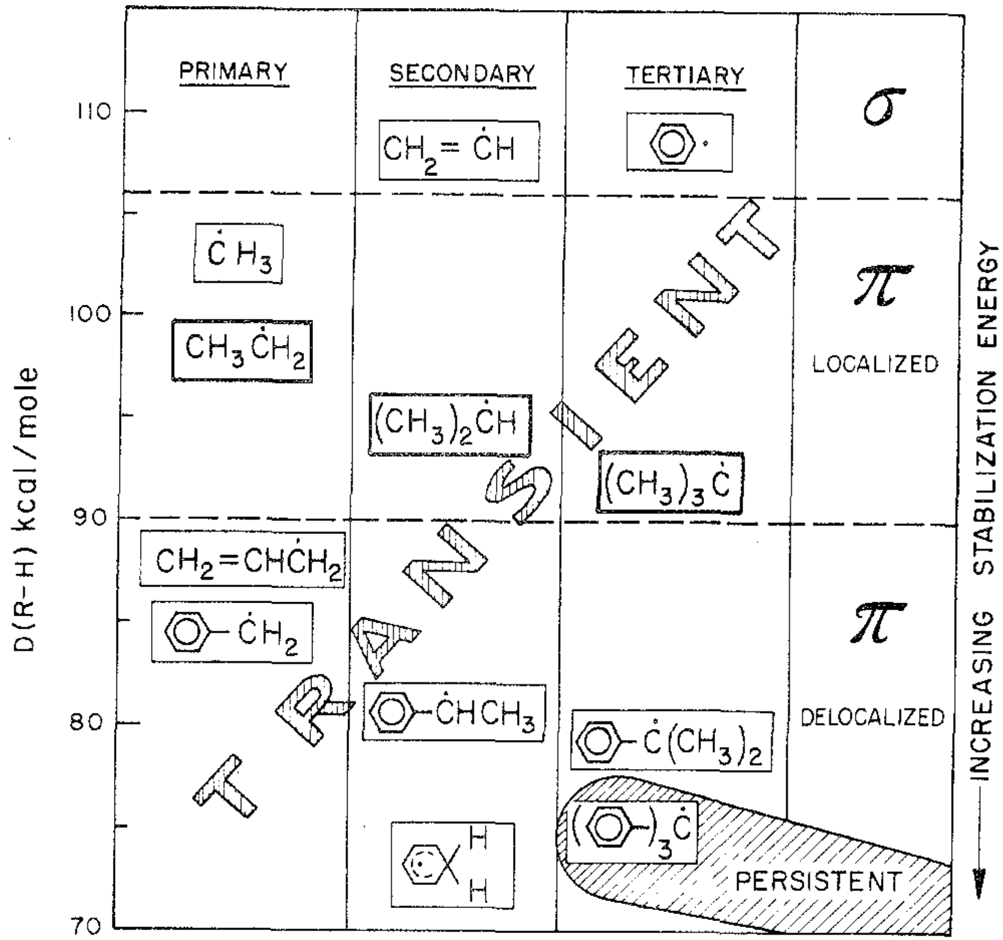
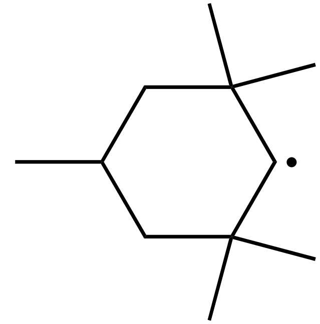
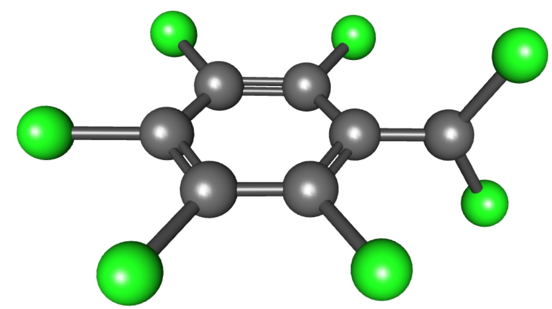


Figure 1. Some representative carbon-centered radicals ranked in terms of their stabilization energy and type. Destabilized radicals are of the σ type and have their unpaired electron in a localized orbital with considerable s character. Radicals that are not stabilized are of the π type and have their unpaired electron in a localized p orbital. Stabilized radicals are also of the π type, but the unpaired electron can be delocalized into adjacent systems of π bonds.



$\log(t_{1/2}) = 2.4$

perchlorobenzyl

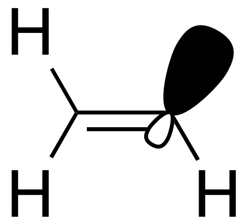


Persistence arises largely in steric hindrance, not so much in electronic effects (resonance)

Griller, Ingold, *Acc. Chem. Res.* **1976**, *9*, 13.

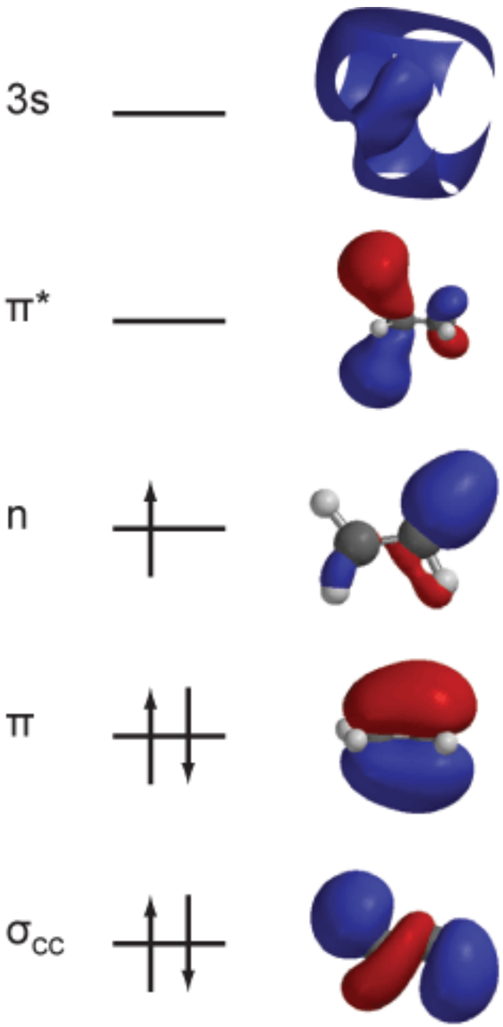
Persistent Radicals

Sigma radicals

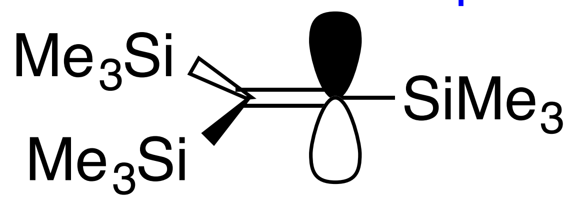


vinyl radical

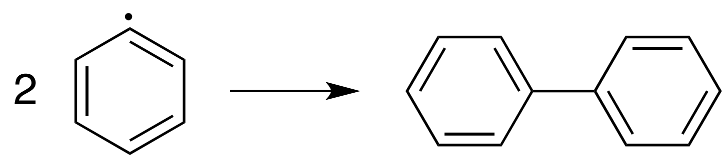
transient



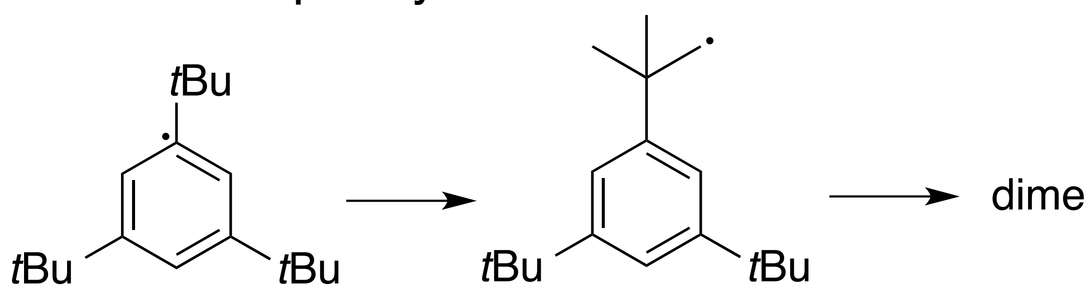
persistent



transient



phenyl



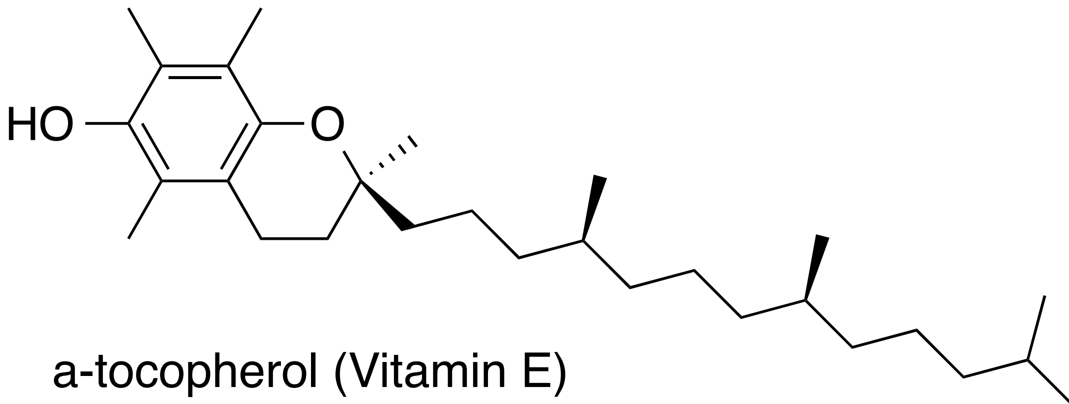
$\log(\tau_{1/2}) = -2.2$

persistent

Griller, Ingold, *Acc. Chem. Res.* **1976**, *9*, 13.

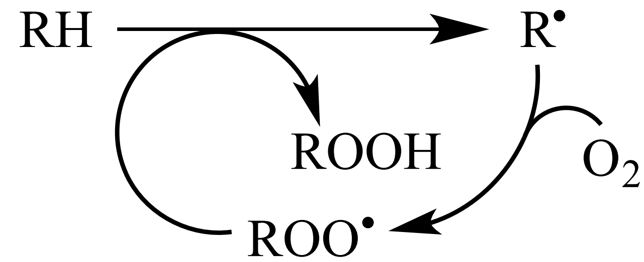
Persistent Radicals

Non carbon-centered

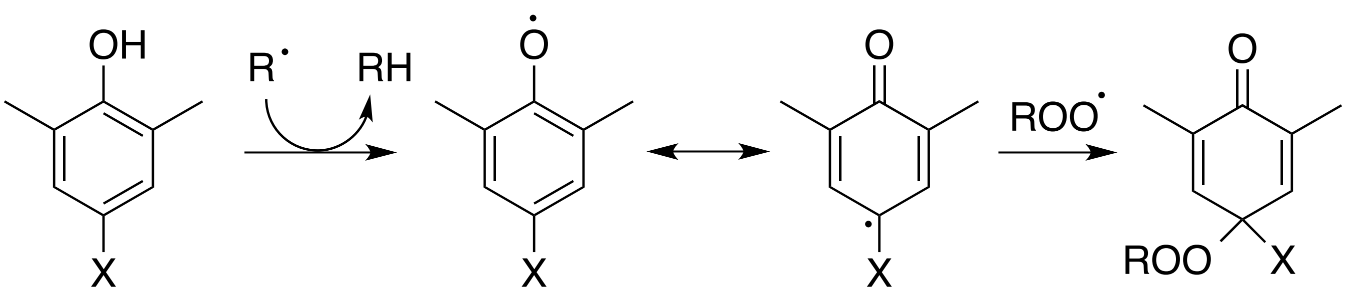


a-tocopherol (Vitamin E)

Autooxidation:



Antioxidant:

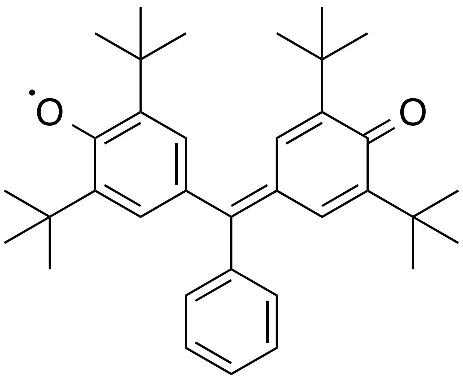


Gryn'ova, Hodgson, Coote, *Org. Biomol. Chem.*, **2011**, *9*, 480.
Gryn'ova, Ingold, Coote, *J. Am. Chem. Soc.*, **2012**, *134*, 12979.

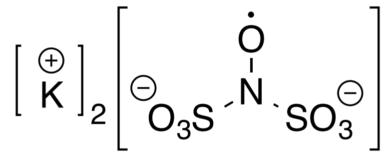
Persistent Radicals

Non carbon-centered

Galvinoxyl



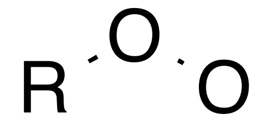
Free radical inhibitor



Frémy's salt

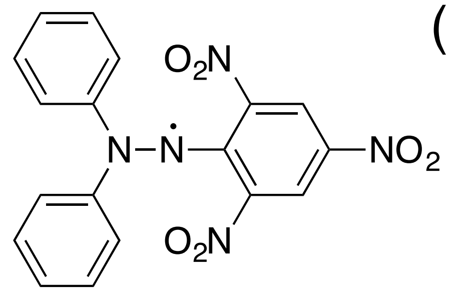
Strong oxidizing agent

Peroxyl



Radical damage

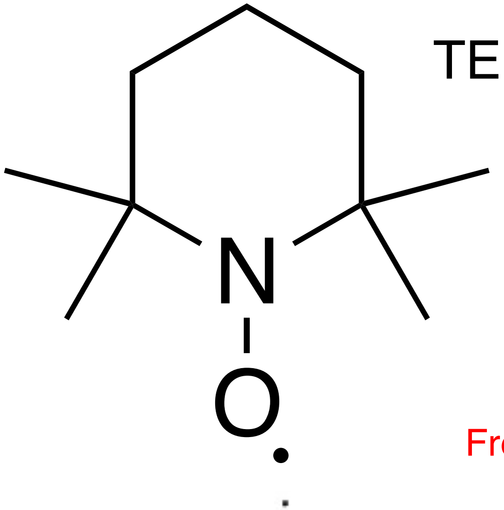
Diphenylpicrylhydrazyl (DPPH)



Monitor of chemical reactions involving radicals, most notably it is a common antioxidant assay;
Standard of the position and intensity of electron paramagnetic resonance signals.

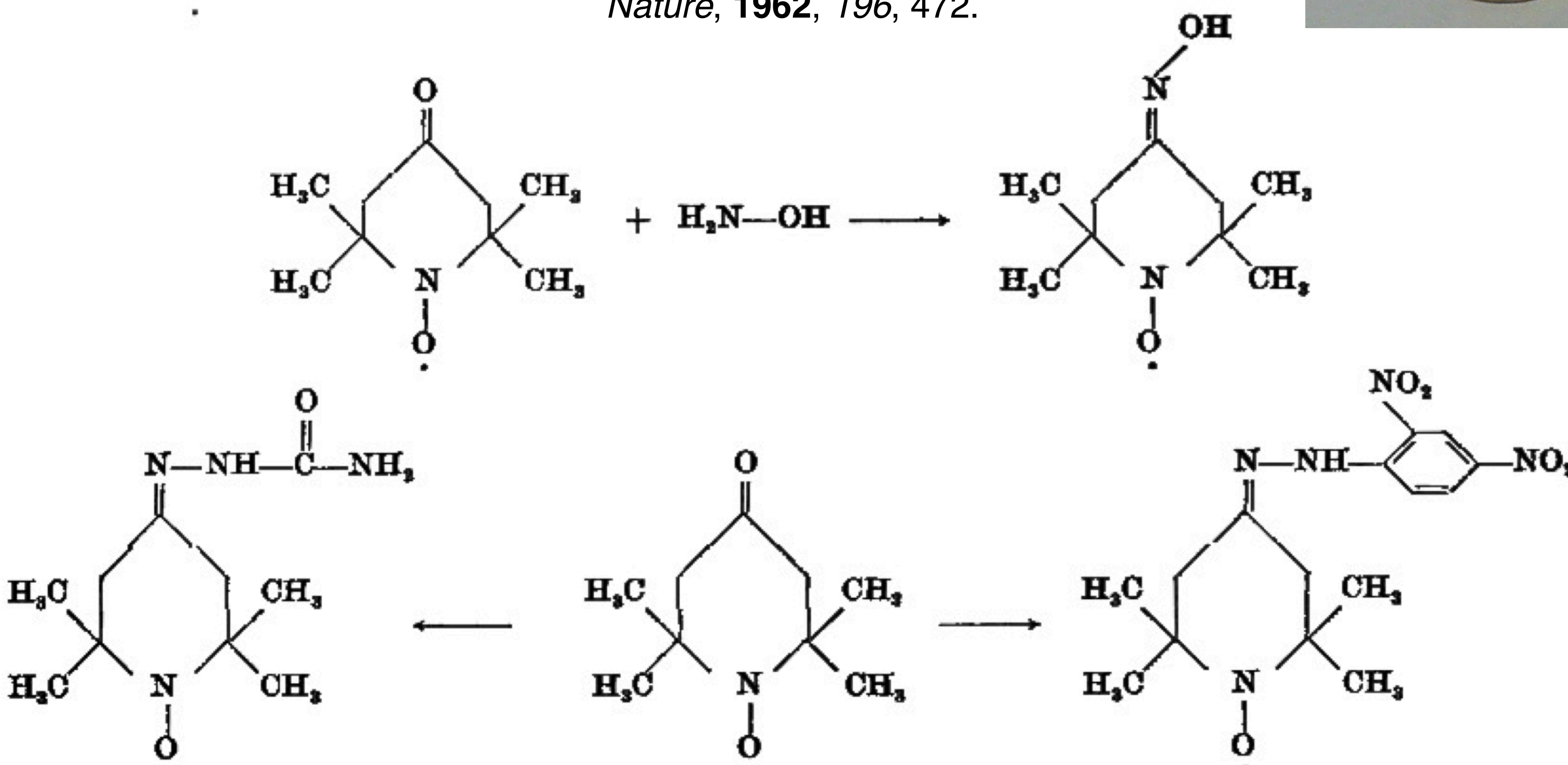
Persistent Radicals

Nitroxides



TEMPO

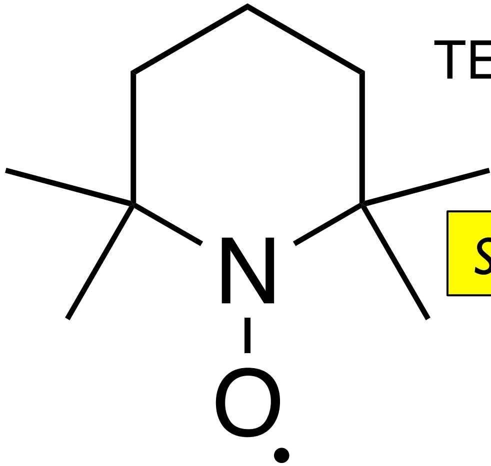
Neiman, Rozantzev, Mamedova,
Free radical reactions involving no unpaired electrons,
Nature, **1962**, *196*, 472.



Persistent Radicals

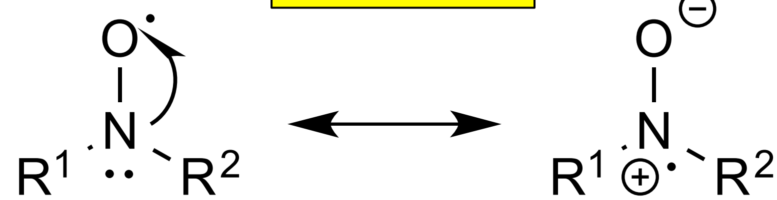
Nitroxides

TEMPO



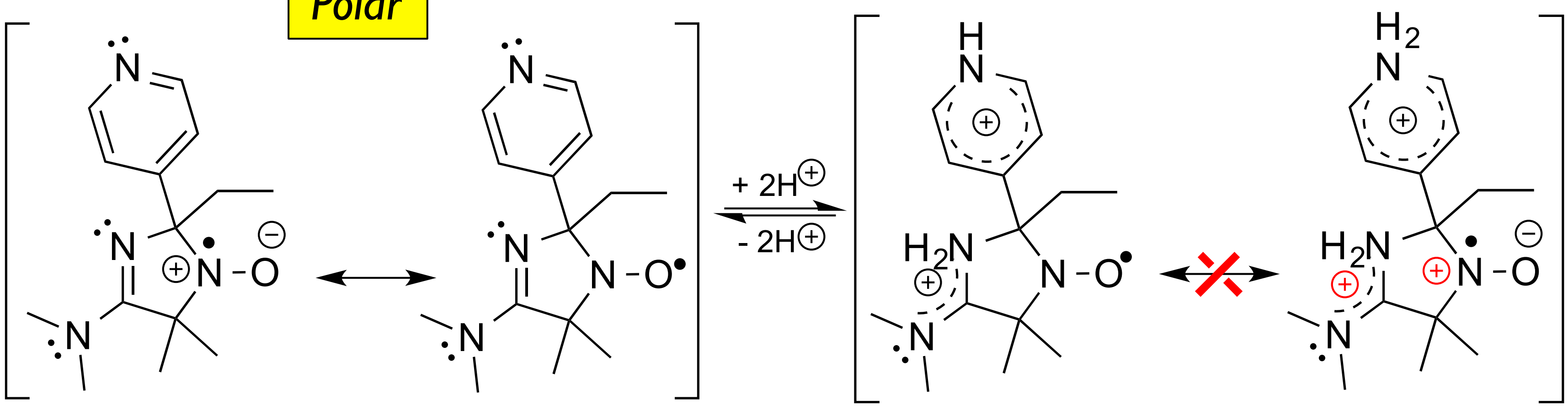
Steric

Resonance



I **II**

Polar



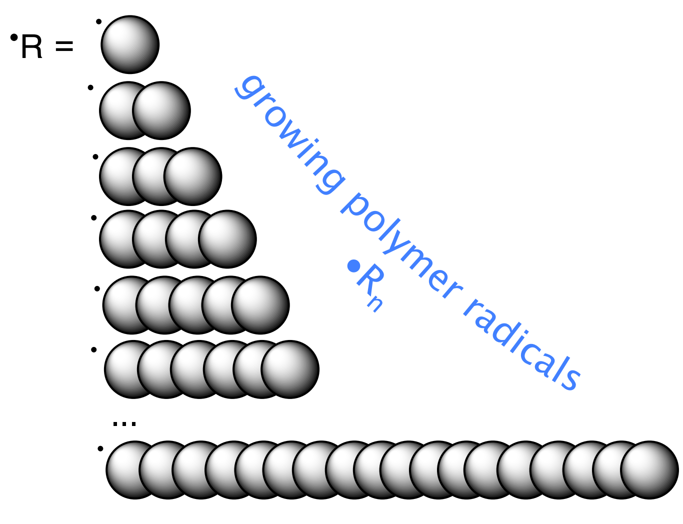
Edeleva, M. V. Kirilyuk, I.A., Zhurko, I. F., Parkhomenko, D.A. Tsentalovich, Y.P. and Bagryanskaya, E. G. *J. Org. Chem.* **76**, 5558 (2011)

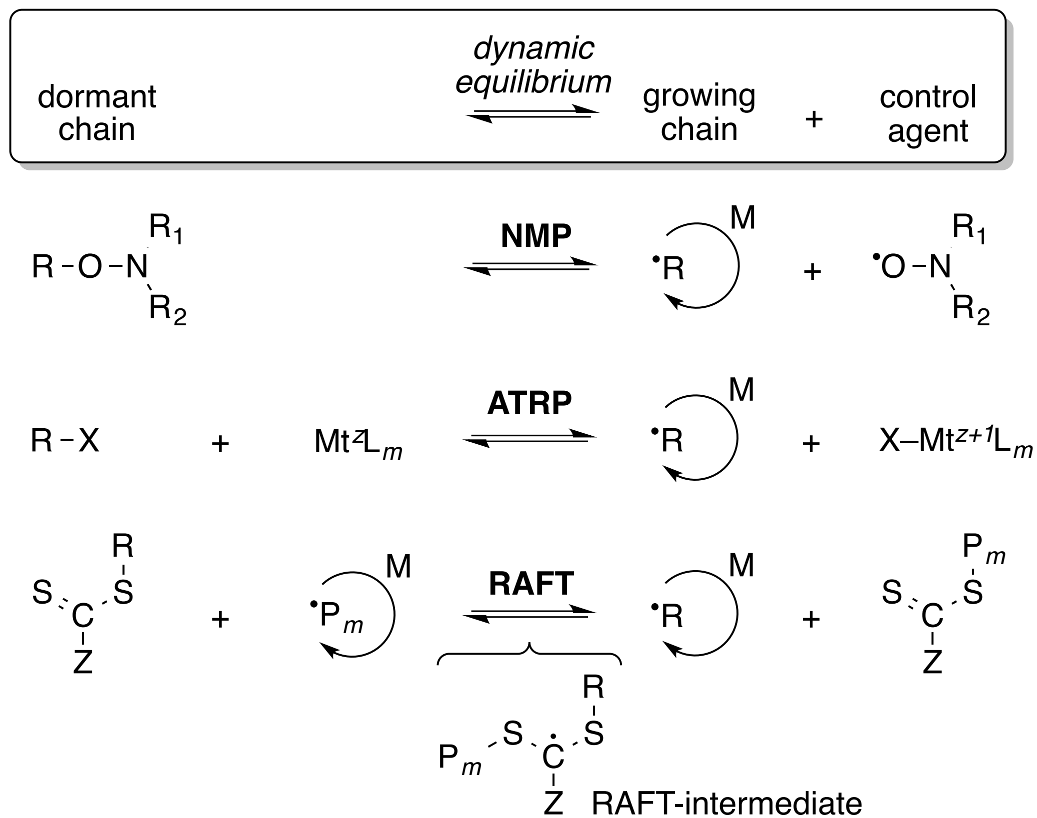
Persistent Radicals

Radical Polymerizations

- Desired length and structure of the polymer chains
- High conversion and low polidispersity
- Complex polymer architectures and customizable end groups

- Mild polymerization conditions





Georges, Veregin, Kazmaier, Hamer, *Macromolecules*, **1993**, *26*, 2987.
Moad, Anderson, Ercole, Johnson, Krstina, Moad, Rizzardo, Spurling, Thang, *ACS Symp. Ser.* **1998**, *685*, 332.
Hawker, Bosman, Harth, *Chem. Rev.* **2001**, *101*, 3661.

Spin multiplicity

Multiplicity is the number of possible orientations of spin angular momenta

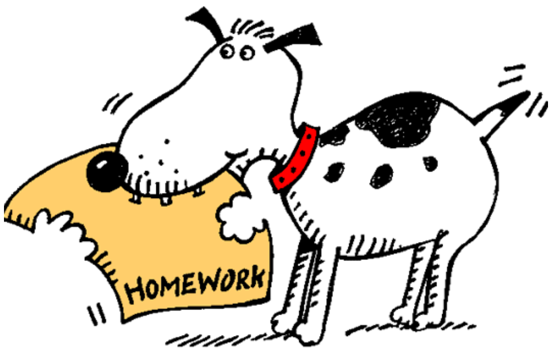
Multiplicity = 2S +1

where S = ±½

Spin contamination

$$\langle S^2 \rangle_{exact} = (\frac{N_\alpha - N_\beta}{2})(\frac{N_\alpha - N_\beta}{2} + 1)$$

Spin multiplicity



Multiplicity is the number of possible orientations of spin angular momenta

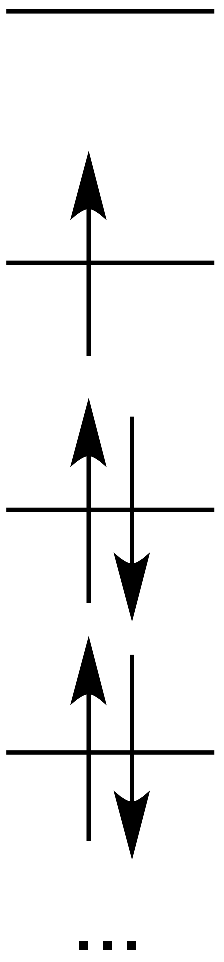
Multiplicity = 2S +1
where S = ±½

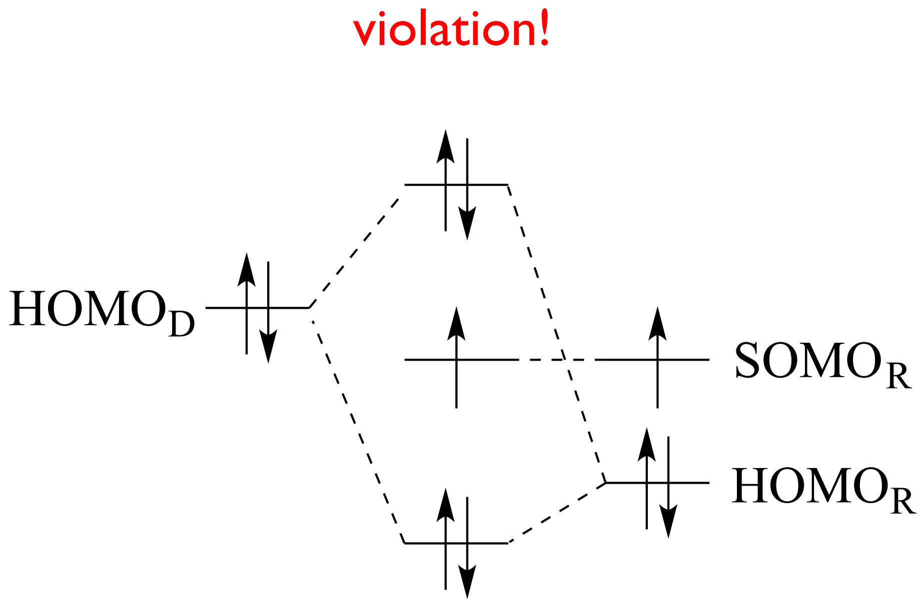
Spin contamination

$$\langle S^2 \rangle_{exact} = \left(\frac{N_\alpha - N_\beta}{2}\right)\left(\frac{N_\alpha - N_\beta}{2} + 1\right)$$

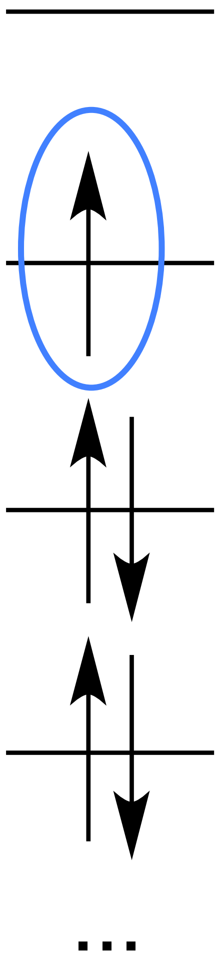
Closed-shell vs Open-shell
Even-electron vs Odd-electron
Singlet vs Doublet vs Triplet vs …

aufbau principle

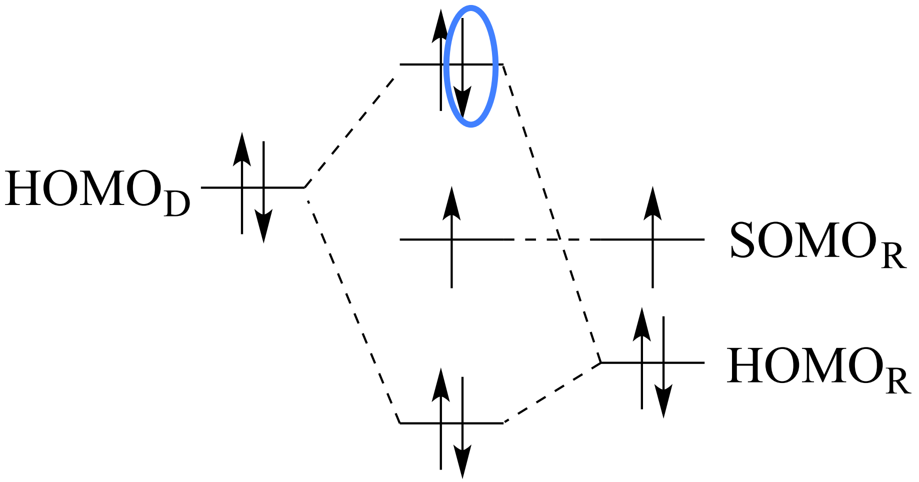




aufbau principle

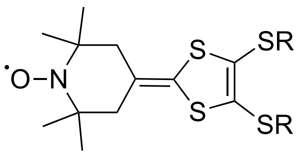


violation!

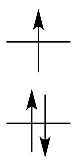


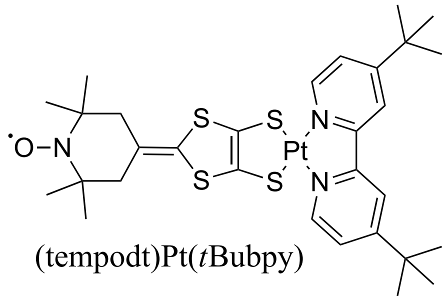
1-electron oxidation

aufbau principle

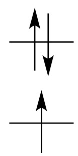


tempodt

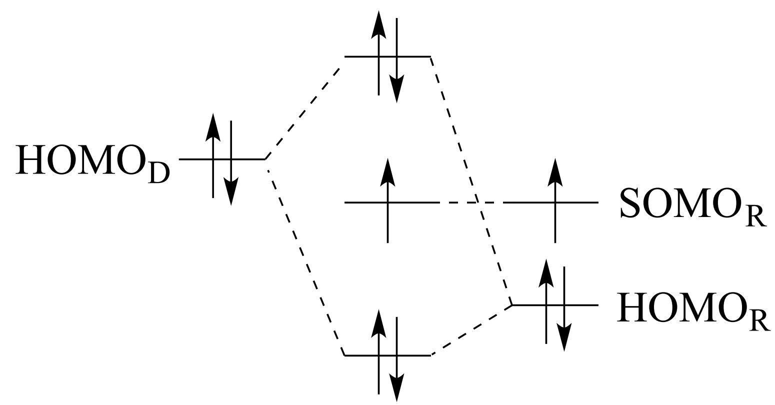


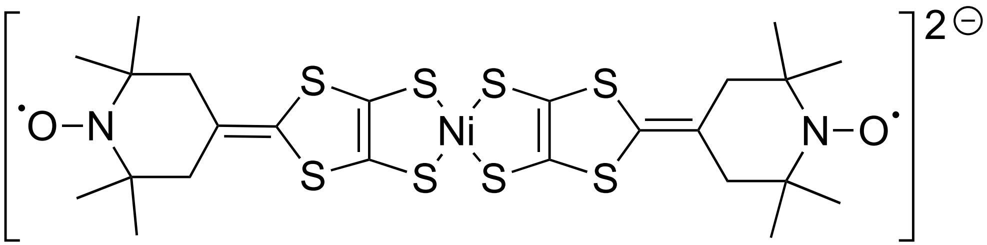


(tempodt)Pt(*t*Bubpy)

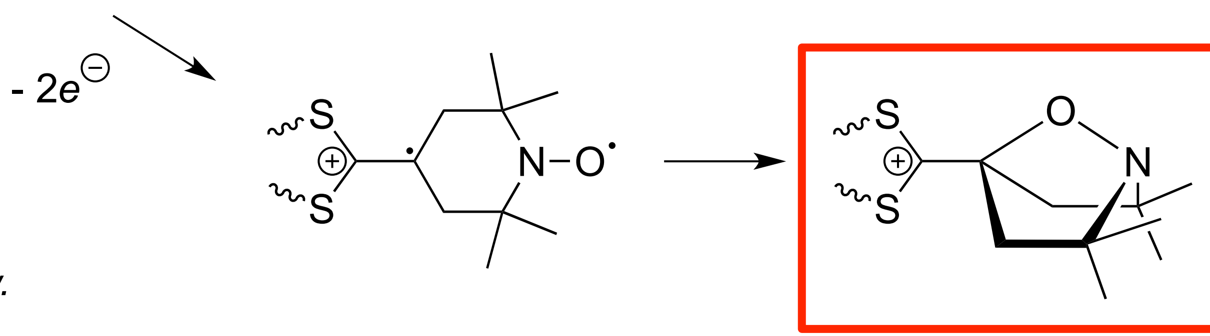


violation!





1-electron oxidation

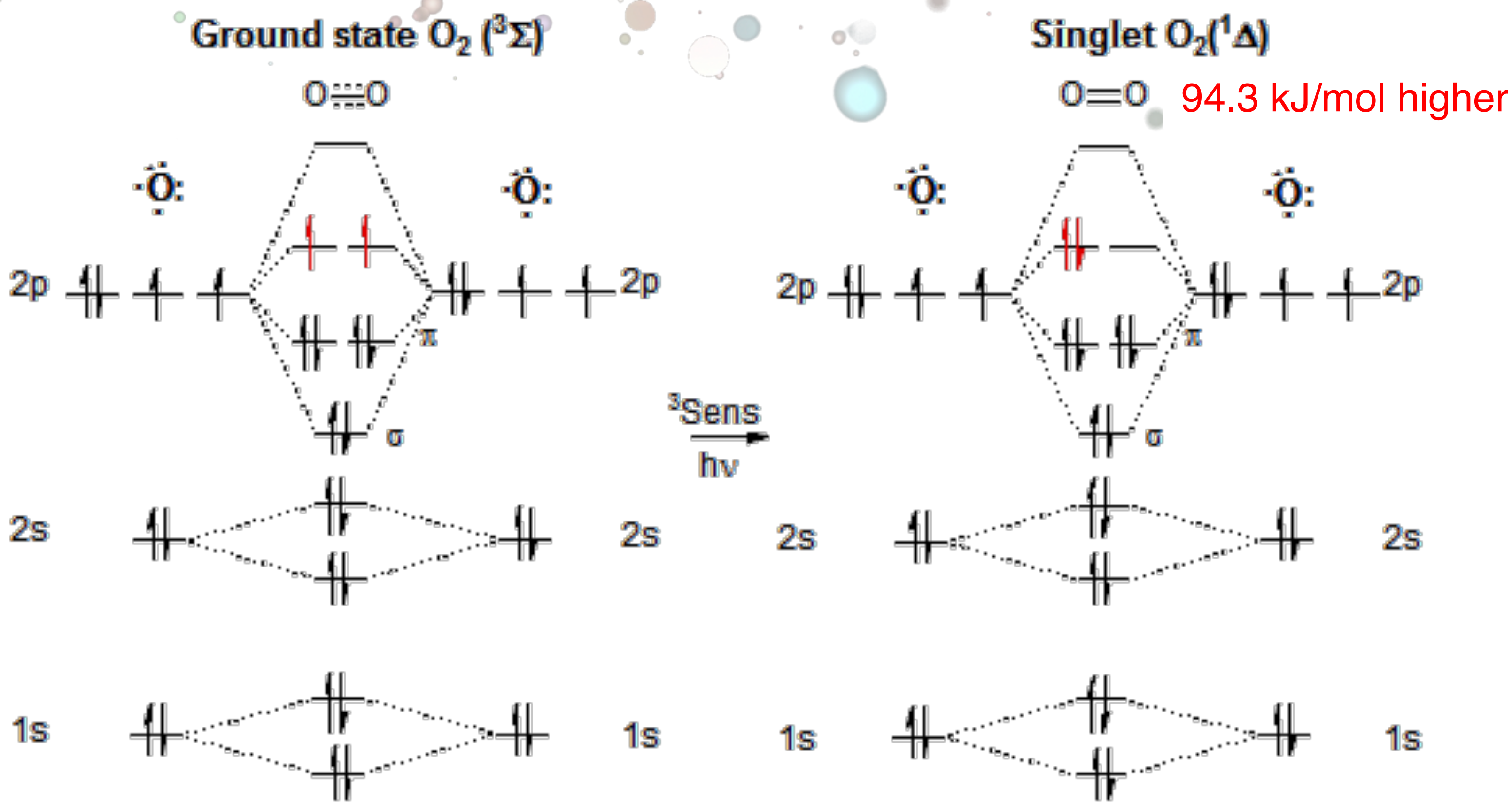


Kusamoto, Kume, Nishihara, *Angew. Chem. Int. Ed.* **2010**, *49*, 529.

Hund's rule of maximum multiplicity

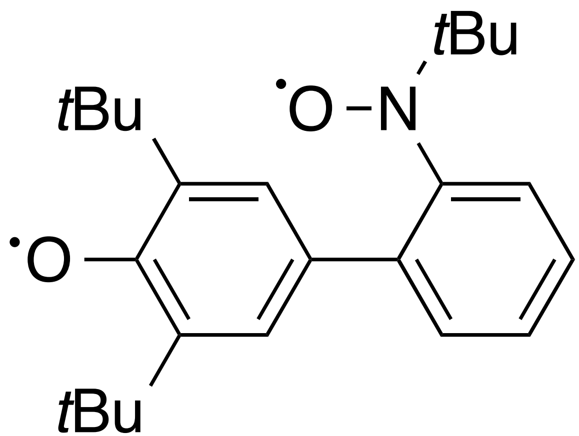
Oxygen

paramagnetic *diamagnetic*



Biradicals

An even-electron molecular entity with two (possibly delocalized) radical centres which act nearly independently of each other

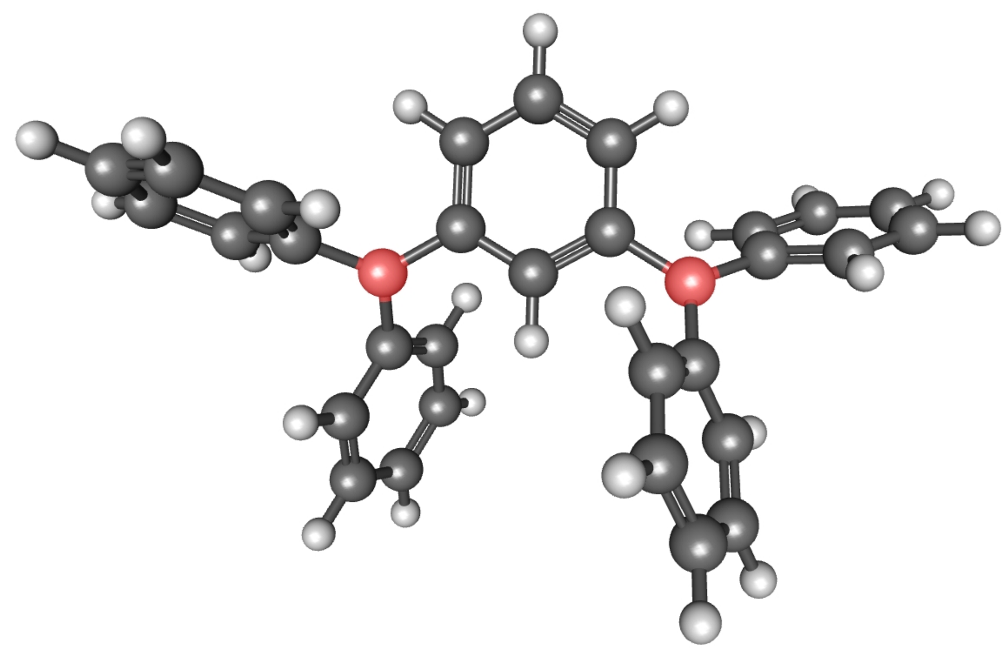


Stable for weeks even in air

Diradicals

Molecular species with two electrons occupying two degenerate molecular orbitals

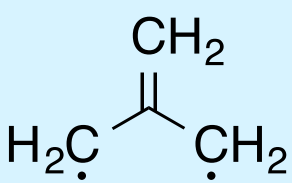
Schlenk-Brauns hydrocarbon

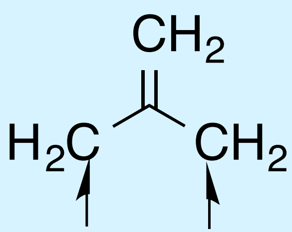


Biradicals

A *non-Kekulé molecule* is a conjugated hydrocarbon that cannot be assigned a classical Kekulé structure

Longuet-Higgins formula

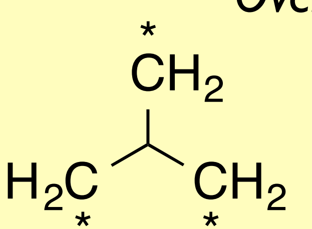




$$S = \frac{n}{2}$$

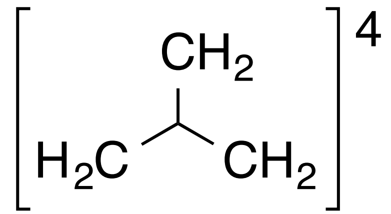
n is a number of non-bonding electrons

Ovchinnikov's formula



$$S = \frac{N^* - N}{2}$$

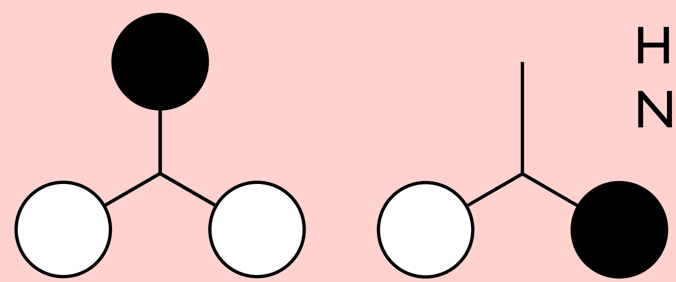
Diradicals



Trimethylenemethane (**TMM**)

triplet ground state

Borden-Davidson analysis



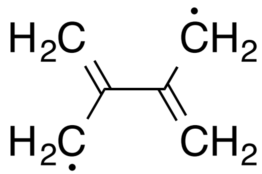
Huckel's NBMOs

non-disjoint – two electrons' motions are correlated to prevent them from occupying the same space (Pauli principle)

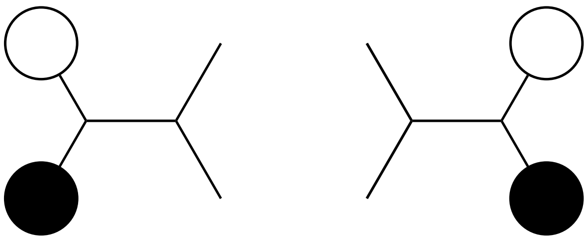
Biradicals

Diradicals

tetramethyleneethane (**TME**)



Borden-Davidson analysis



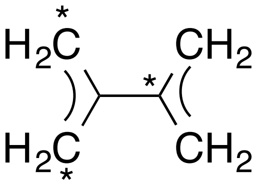
disjoint NBOs – singlet ground state

Longuet-Higgins formula

$$S = \frac{n}{2}$$

n is a number of non-bonding electrons

Ovchinnikov's formula



$$S = \frac{N^* - N}{2}$$

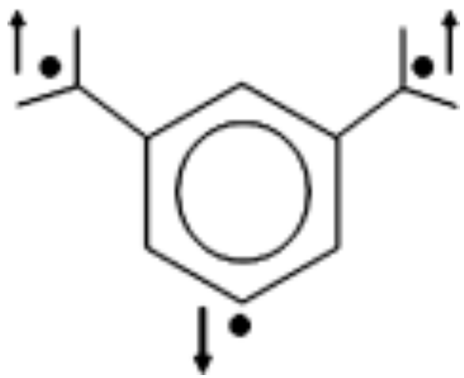
EXPERIMENT:

It's actually a triplet – and non-planar!

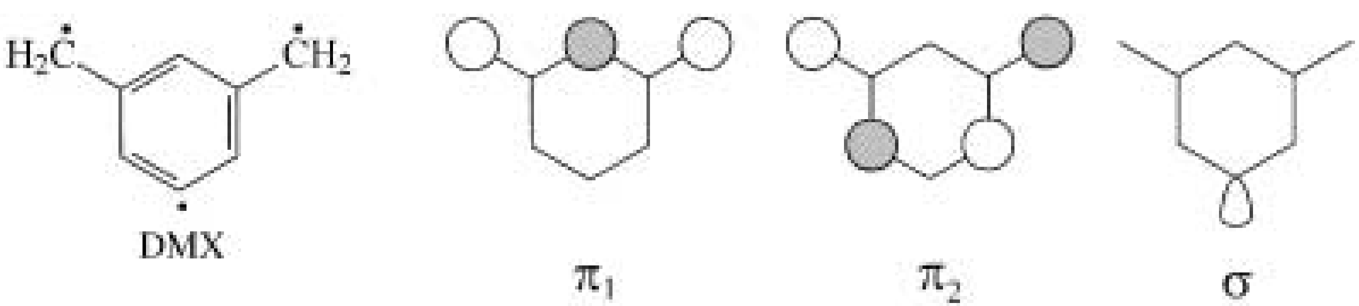
However, planar TME is a singlet.

Hund's rule of maximum multiplicity

violation!



DMX



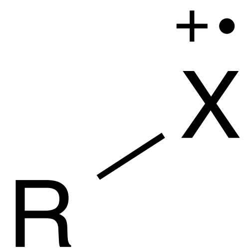
Slipchenko, Munsch, Wenthold, Krylov,

5-Dehydro-1,3-quinodimethane: A Hydrocarbon with an Open-Shell Doublet Ground State,

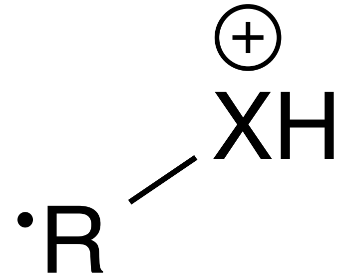
Angew. Chem. Int. Ed. **2004**, *43*, 742.

Radical ions

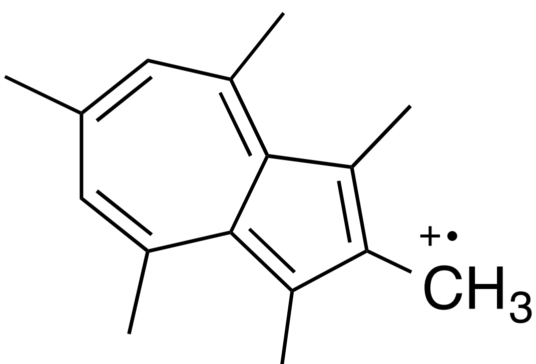
Classic (Conventional)

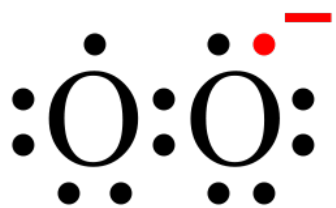


Distonic



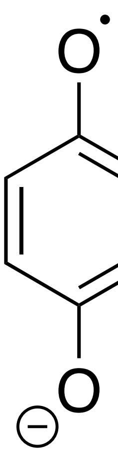
Reactive intermediates

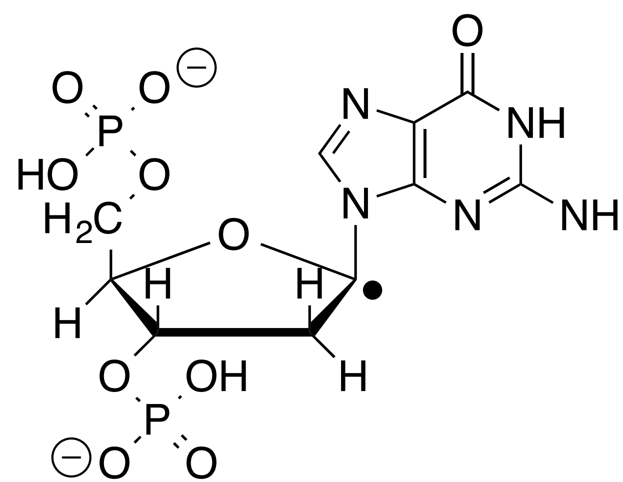




superoxide

Mass-spec gas-phase ions



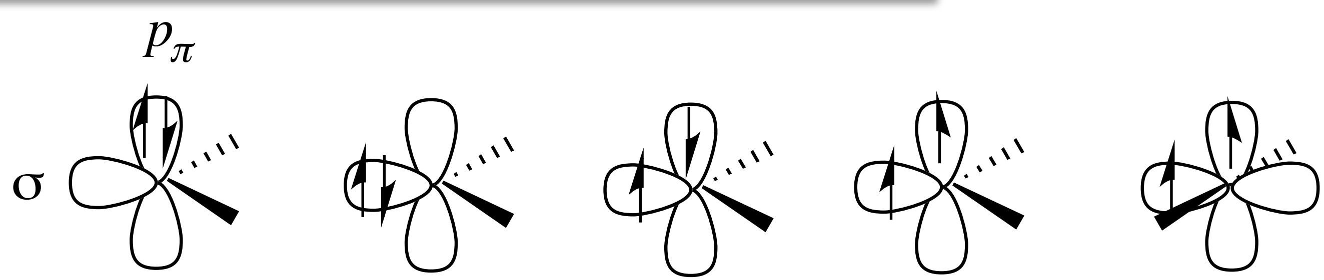


Carbenes

Carbene *is a molecule containing a neutral carbon atom with a valence of two and two unshared valence electrons*

R_1=R_2=H
methylene

R_1=R_2=Cl
dichlorocarbene

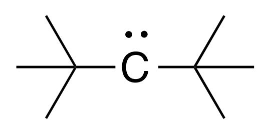


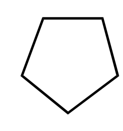
Most simple hydrocarbon carbenes – triplet is lower by ca. 33 kJ/mol.

Inductive: +I substituents favour triplet, -I – singlet state

Mesomeric: +M substituents can donate electron pair and thus stabilise the triplet state

Steric: bulky groups favour linear = triplet state, strain favours singlet state

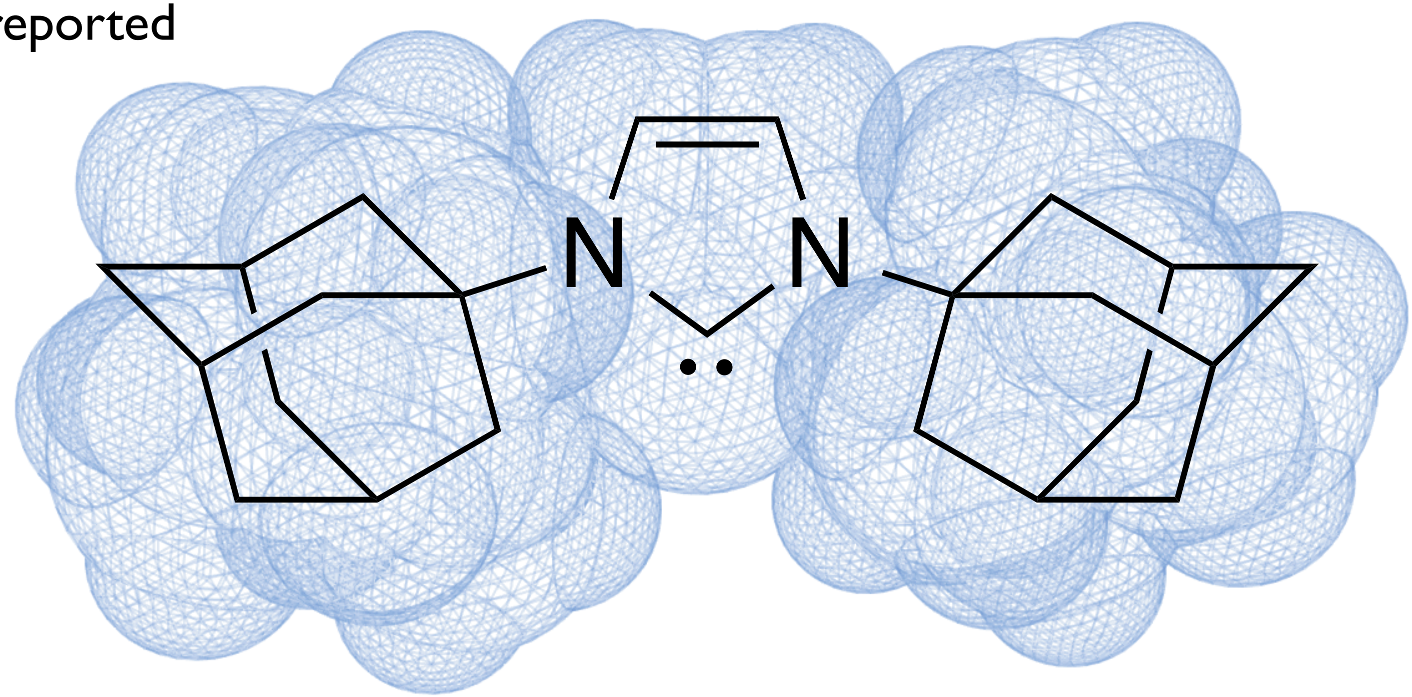




Bourissou, Guerrret, Gabbai, Bertrand, *Chem. Rev.* **2000**, *100*, 39.

Carbene Stability

IAd
– first stable (crystalline) carbene reported



Why?

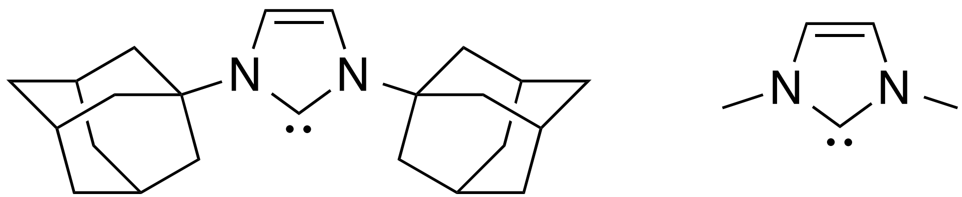
Because of steric or electronic factors?

Here…
stable = does not want to react, especially dimerize, happy as is

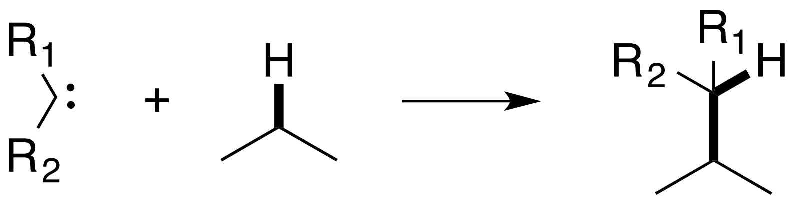
Arduengo, Harlow, Kline, *J. Am. Chem. Soc.* **1991**, *113*, 361.

Carbene Stability

Compare



in reaction of C–H insertion

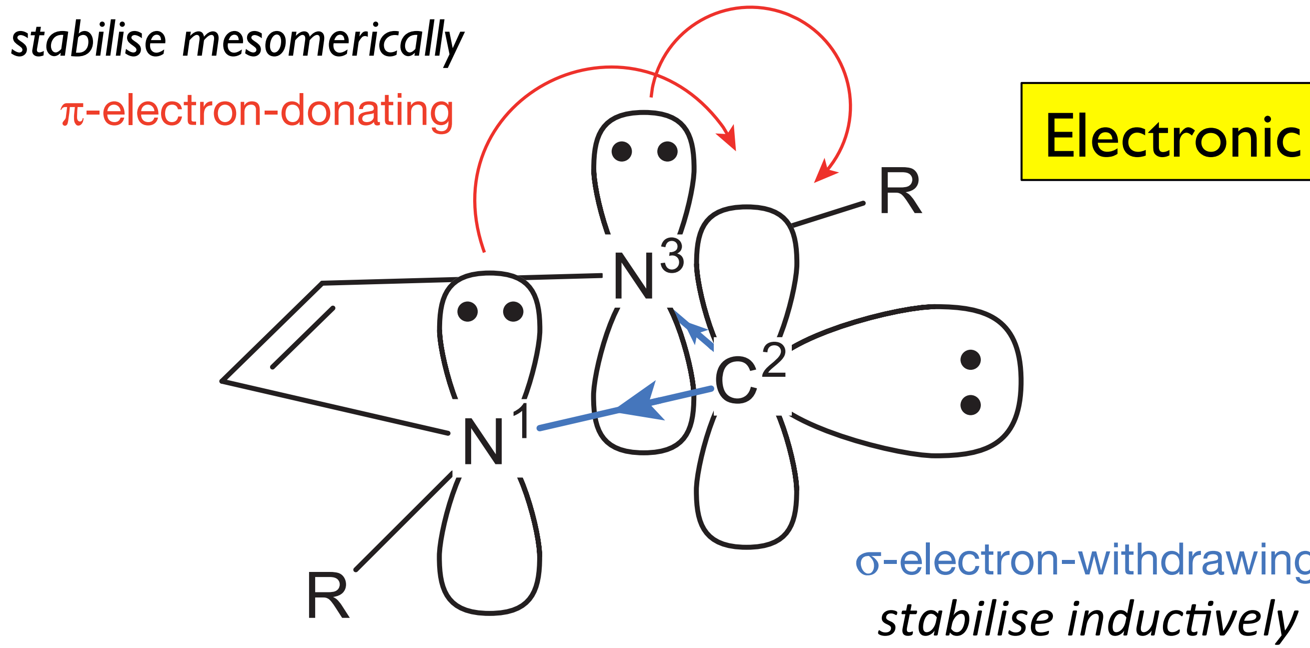


Reaction energies – same

Barrier heights – noticeably lower for dichlorocarbene than for imidazole carbenes, for which the barriers are similar to each other

Stability is due to **kinetics**
Stability is **not** due to **the steric effect**

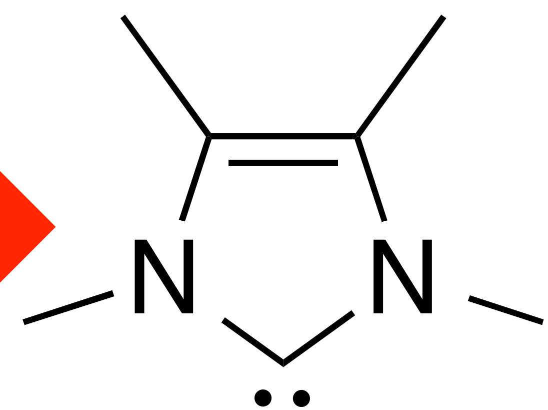
Carbene Stability



Electronic effect

M. N. Hopkinson, C. Richter, M. Schedler & F. Glorius, *Nature* **2014**, *510*, 486.

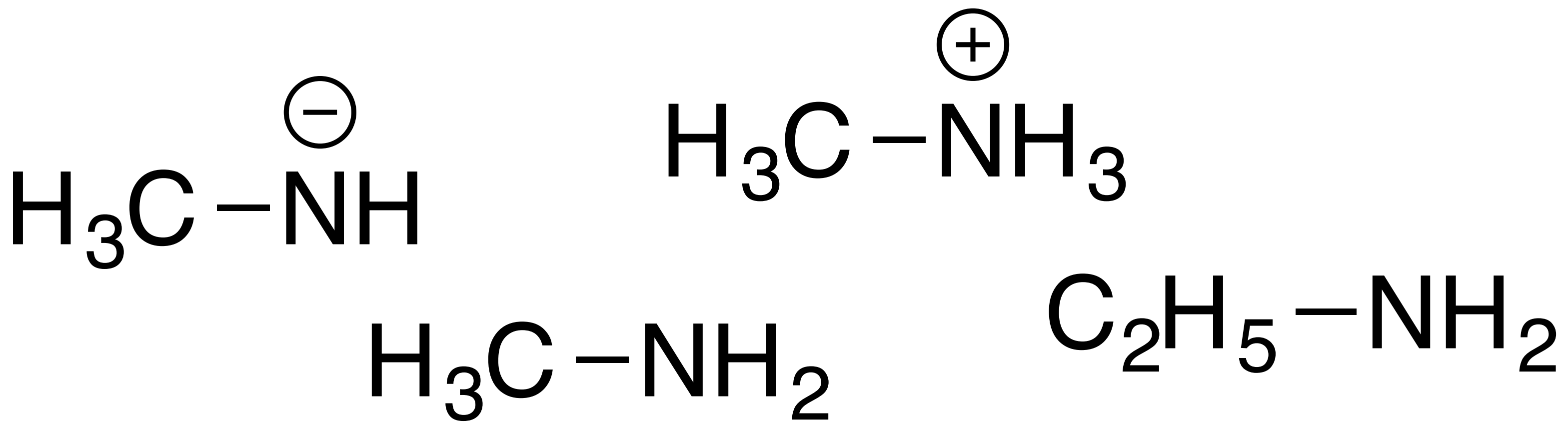
Experiment agrees:
an analogue lacking steric hindrance is also stable



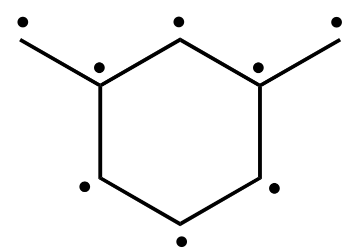
Arduengo, Dias, Harlow, Kline, *J. Am. Chem. Soc.* **1992**, *114*, 5530.

Mini Quiz

1. Arrange in the order of C–N BDE



2. Identify the spin state of the following alternant hydrocarbon



3. Arrange in the order of radical stability/persistence