



Universitat d'Alacant
Universidad de Alicante

Departament de Química Orgànica
Departamento de Química Orgánica

LESSON 4

STEREOCHEMISTRY AROUND BONDS WITH RESTRICTED ROTATION

4.1. Introduction

4.2. Stereochemistry in cyclic systems

4.3. Stereochemistry in double bonds

4.4. *cis-trans* Isomerism: enantiomers and diastereomers

4.5. *cis-trans* Isomerism: nitrogenated compounds

4.6. Problems



cis-trans ISOMERISM

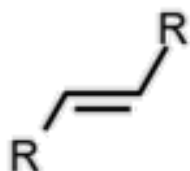
Stereoisomerism in alkenes or cyclic compounds due to the different relative position of substituents with respect to a reference plane

cis Isomer: groups on the same side of the plane

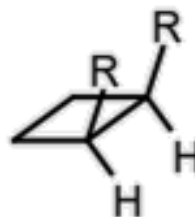
trans Isomer: groups on opposite sides of the plane



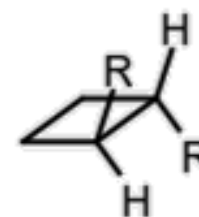
cis



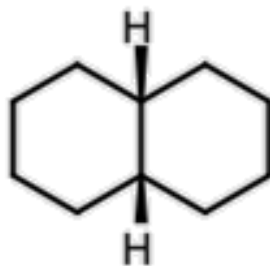
trans



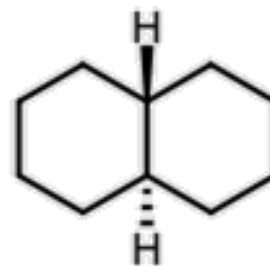
cis



trans



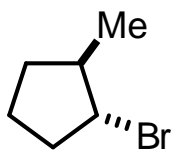
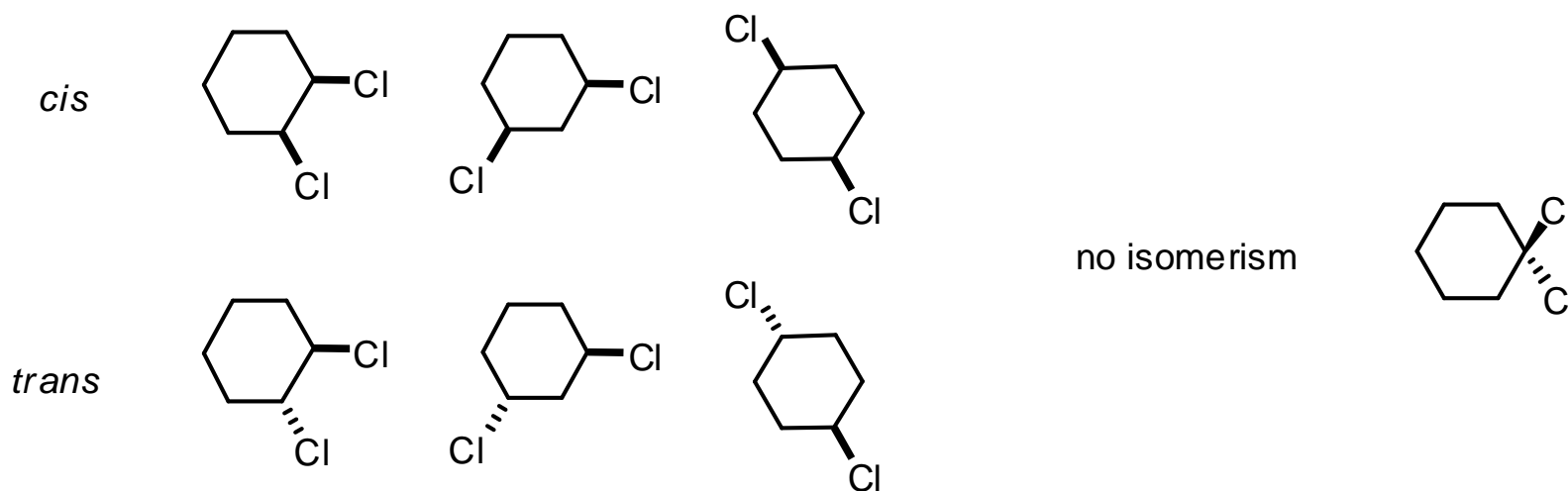
cis



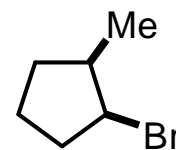
trans

***cis-trans* NOMENCLATURE**

Two substituents in a cycle can be on the same side (*cis*) or in opposite sides (*trans*)



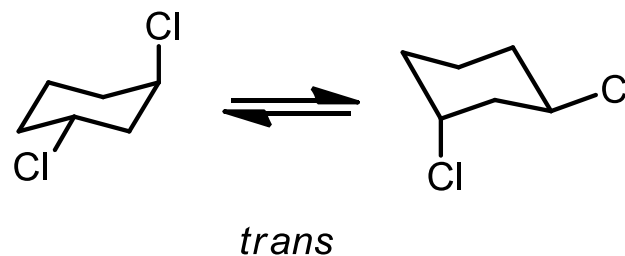
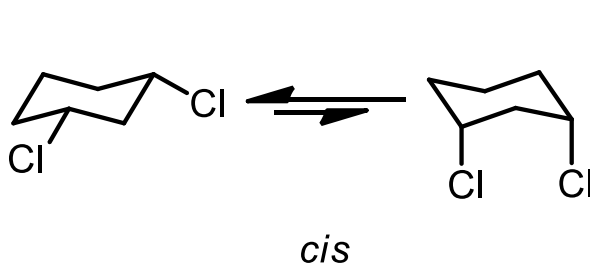
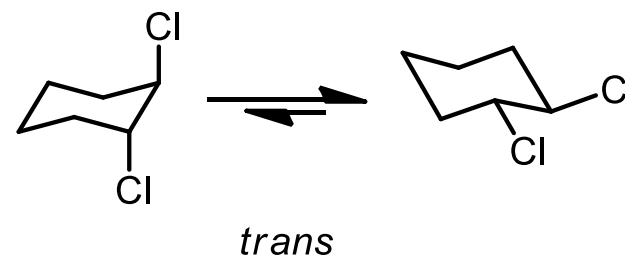
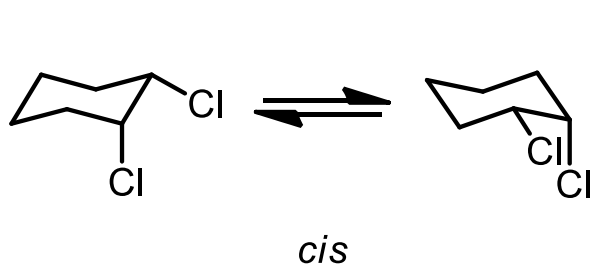
trans-1-bromo-2-methylcyclopentane



cis-1-bromo-2-methylcyclopentane

cis-trans NOMENCLATURE

Cyclohexanes: chair conformation

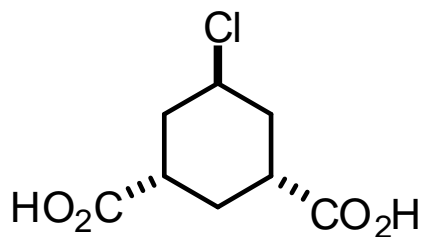


what about the 1,4-disubstituted?

cis-trans NOMENCLATURE

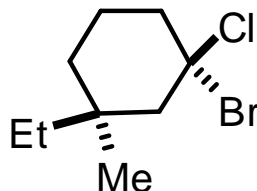
If there are three substituents on different carbon atoms:

(*r*) For the reference atom with the lowest position number; (*c*) if the substituent is *cis* with respect to (*r*) or (*t*) if *trans* with respect to (*r*)



t-5-chlorocyclohexane-*r*-1,*c*-3-dicarboxylic acid

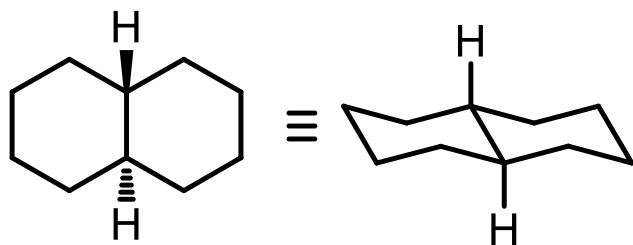
In the case of two possible references, the CIP rules are applied



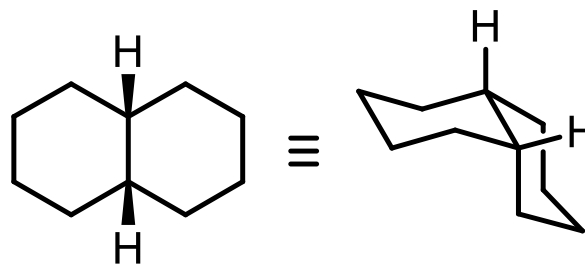
r-1-bromo-1-chloro-*t*-3-ethyl-3-methylcyclohexane

cis-trans NOMENCLATURE

It is also applied to fused cyclic systems



trans-decalin

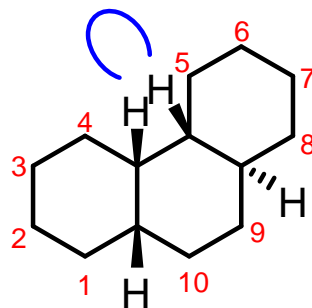


cis-decalin

cis-trans NOMENCLATURE

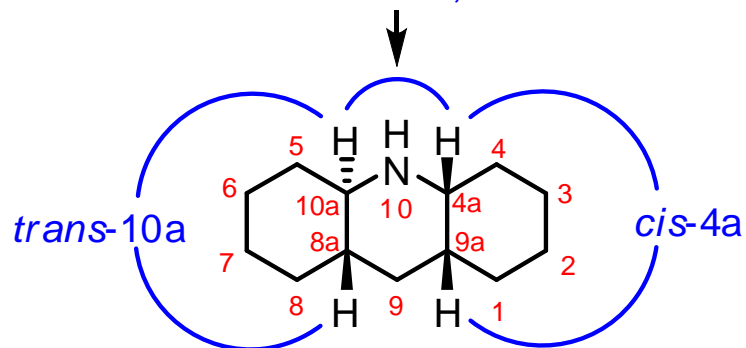
cisoid and *transoid* are used for more than two fused cyclic systems

cisoid



cis-4a-cisoid-4a,4b-trans-4b-perhydrophenanthrene

transoid-4a,10a



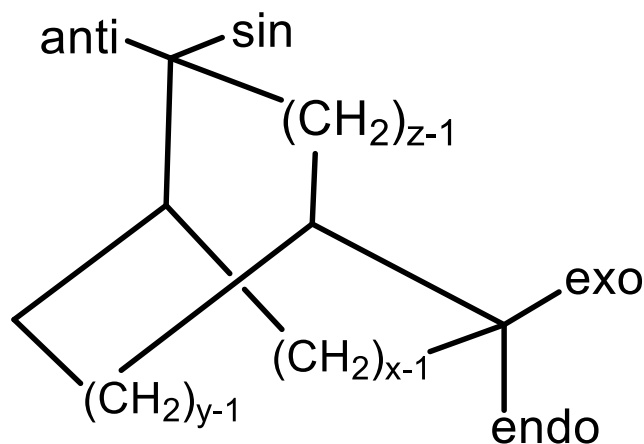
cis-4a-transoid-4a,10a-trans-10a-perhydroacridine

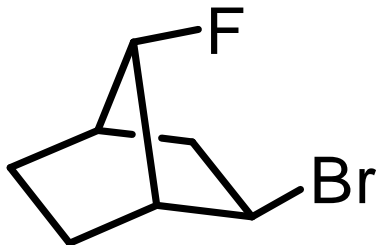
endo-exo, sin-anti NOMENCLATURE

These stereodescriptors are used for the relative position of substituents on the cycle branches

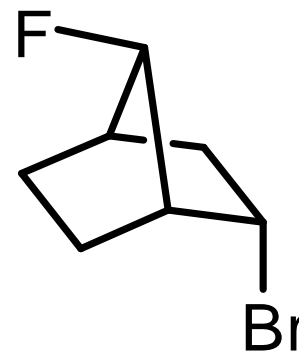
General formula: bicyclo[x.y.z]alkane

where $x \geq y \geq z > 0$



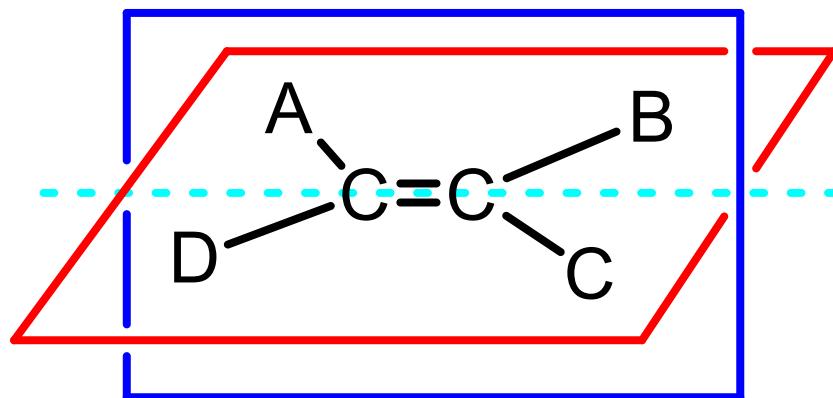
***endo-exo, sin-anti* NOMENCLATURE**

2-*exo*-bromo-7-*sin*-fluoro
bicyclo[2.2.1]heptane

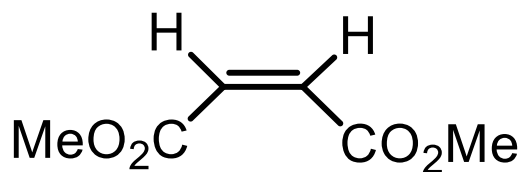


2-*endo*-bromo-7-*anti*-fluoro
bicyclo[2.2.1]heptane

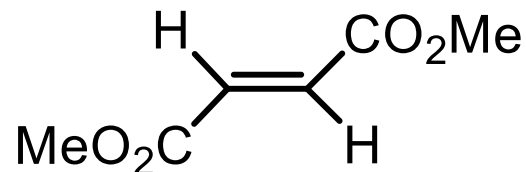
Z / E NOMENCLATURE



cis / trans can be used when two substituents are identical



cis



trans

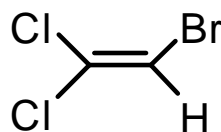
Z / E NOMENCLATURE

The stereodescriptors used to specify a double bond are:

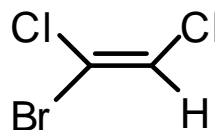
Z (zusammen = together)

E (entgegen = opposite)

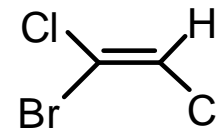
Priorities are established according to the CIP rules



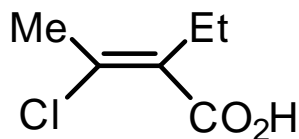
without isomerism



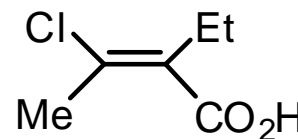
E



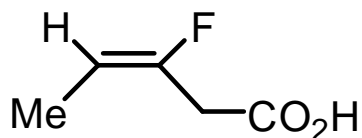
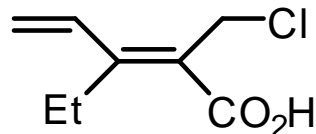
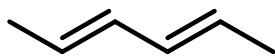
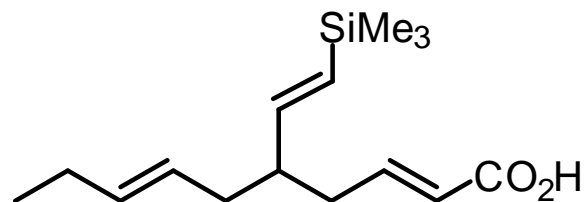
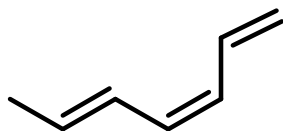
Z

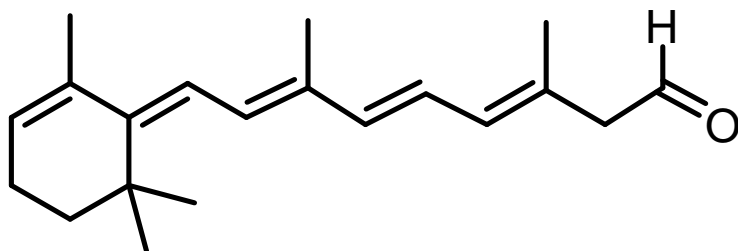


(*Z*)-3-chloro-2-ethylbut-2-enoic acid



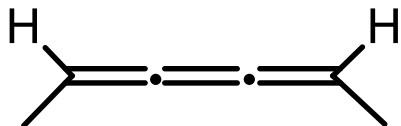
(*E*)-3-chloro-2-ethylbut-2-enoic acid

Z/E NOMENCLATURE*(E)*-3-fluoropent-3-enoic acid*(Z)*-2-(chloromethyl)-3-ethylpenta-2,4-dienoic acid*(2E,4E)*-hexa-2,4-diene*(2E,7E)*-5-[(*E*)-2-(trimethylsilyl)vinyl]deca-2,7-dienoic acid*(3Z,5E)*-hepta-1,3,5-triene

Z/E NOMENCLATURE

(3*E*,5*E*,7*E*)-3,7-dimethyl-9-[(*E*)-2,6,6-trimethylcyclohex-2-enylidene]nona-3,5,7-trienal

It is also applied to systems with similar geometry



(*Z*)-hexa-2,3,4-triene

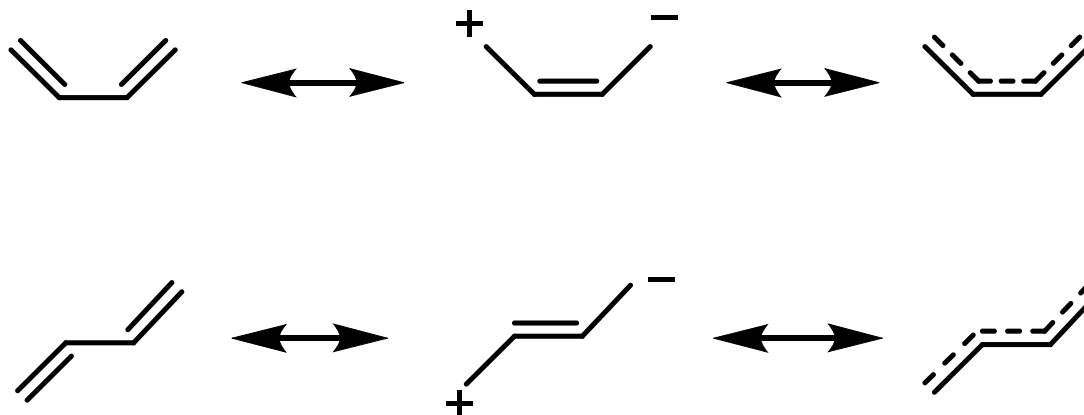


(*E*)-3,6-diethylidencyclohexa-1,4-diene

STRUCTURES WITH PARTIAL DOUBLE BONDS

1,3-Dienes

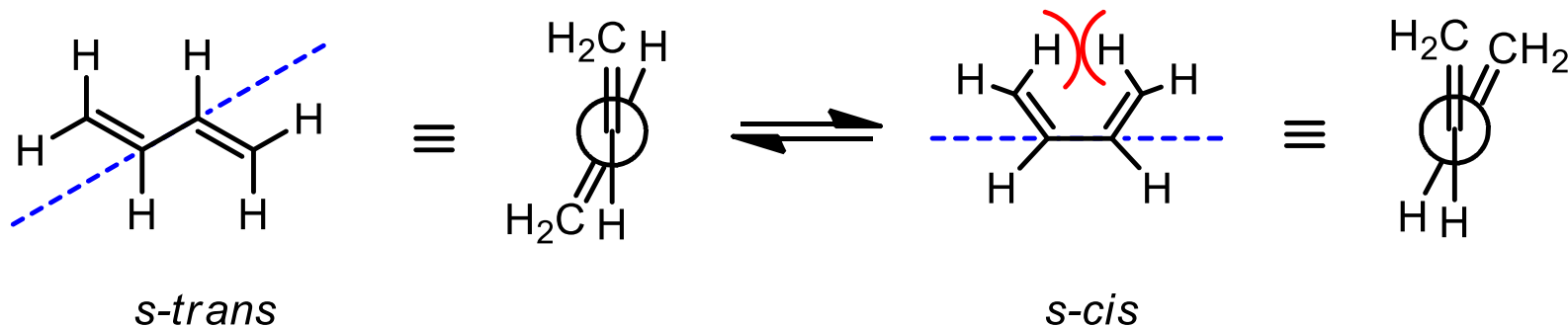
Electron delocalization increases the bond order between two double bonds



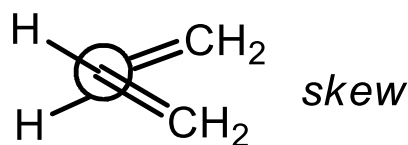
STRUCTURES WITH PARTIAL DOUBLE BONDS

1,3-Dienes

There are two main in-plane conformations: *s-trans* and *s-cis*
 One main out-of-plane conformation: *skew*.



$$\Delta H = 1.5\text{--}2.6 \text{ kcal/mol}$$



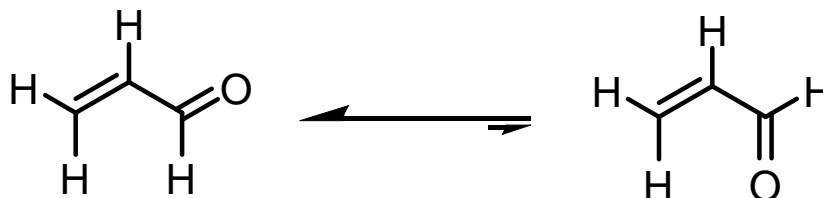
$$E_{s\text{-trans}} < E_{skew} < E_{s\text{-cis}}$$

STRUCTURES WITH PARTIAL DOUBLE BONDS

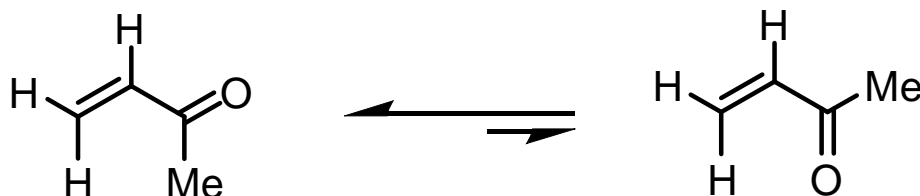
α,β -Unsaturated carbonyl compounds

The conformations are governed by substituent and π interactions

acrolein



methyl vinyl ketone



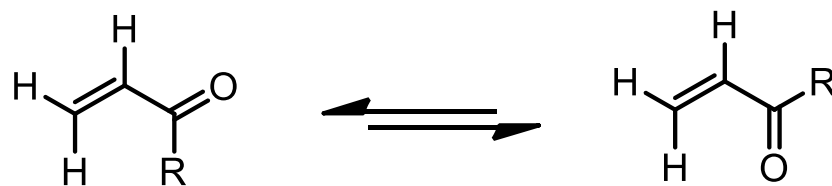
73 %
s-trans

27 %
s-cis

STRUCTURES WITH PARTIAL DOUBLE BONDS

α,β -Unsaturated carbonyl compounds

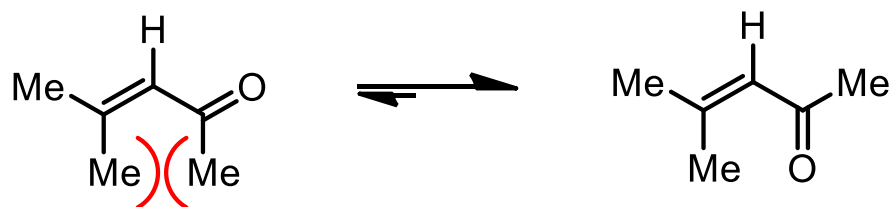
The presence of other substituents can affect the equilibrium



s-trans

s-cis

R = Me	73	27
R = <i>i</i> -Pr	55	45
R = <i>t</i> -Bu	0	100



28 %

s-trans

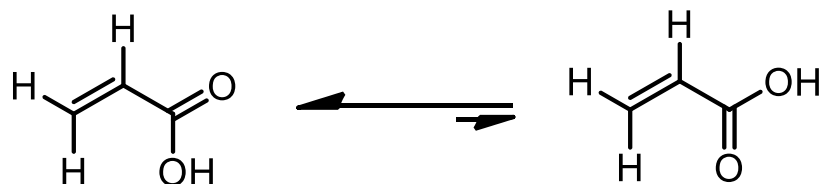
72 %

s-cis

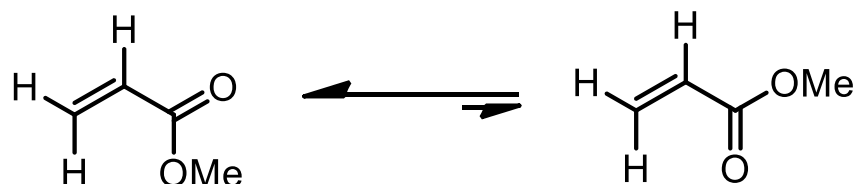


STRUCTURES WITH PARTIAL DOUBLE BONDS

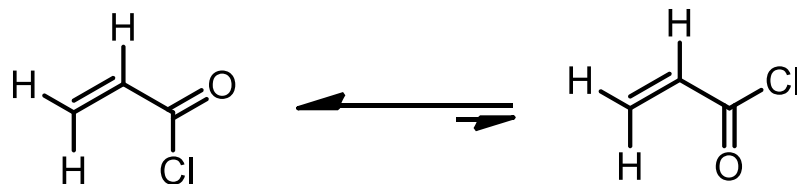
Other α,β -unsaturated compounds



$$\Delta H = 0.17 \text{ Kcal/mol}$$



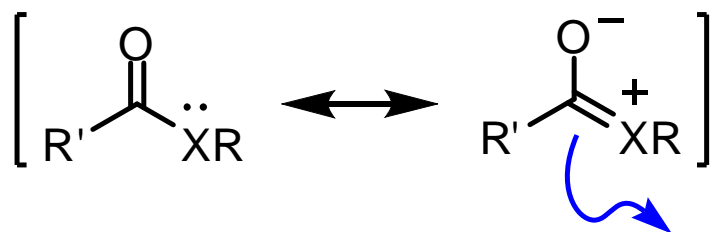
$$\Delta H = 0.31 \text{ Kcal/mol}$$



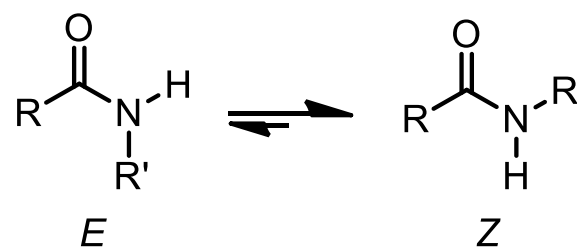
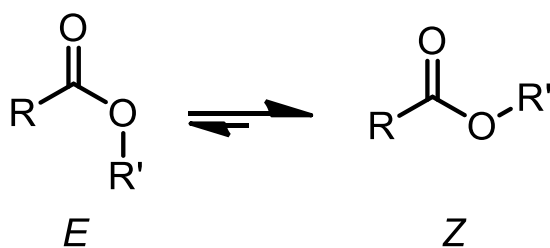
$$\Delta H = 0.25 \text{ Kcal/mol}$$

STRUCTURES WITH PARTIAL DOUBLE BONDS

Acids, esters and amides: resonance favours a plane conformation

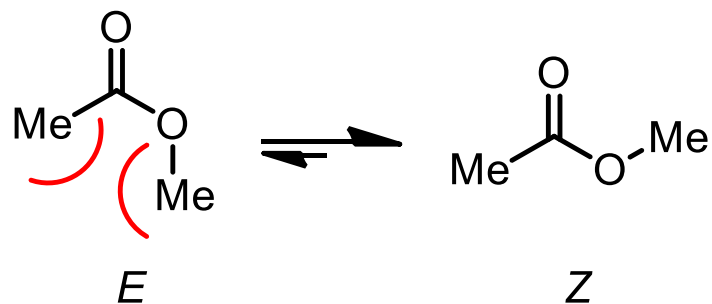


partial double bond, more pronounced for amides

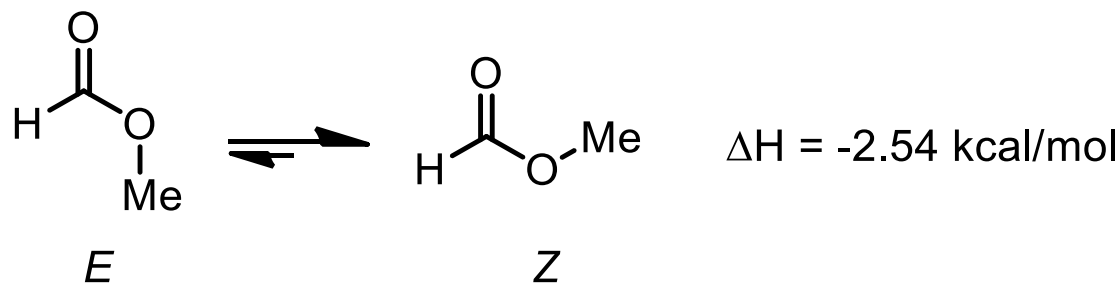


STRUCTURES WITH PARTIAL DOUBLE BONDS

Acids, esters and amides



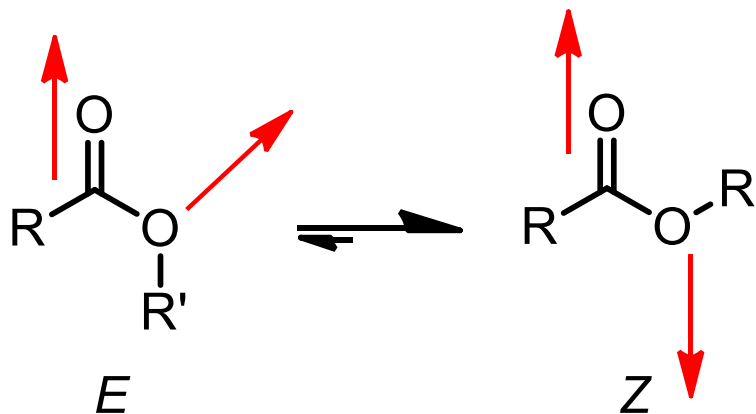
Not only steric factors are involved



STRUCTURES WITH PARTIAL DOUBLE BONDS

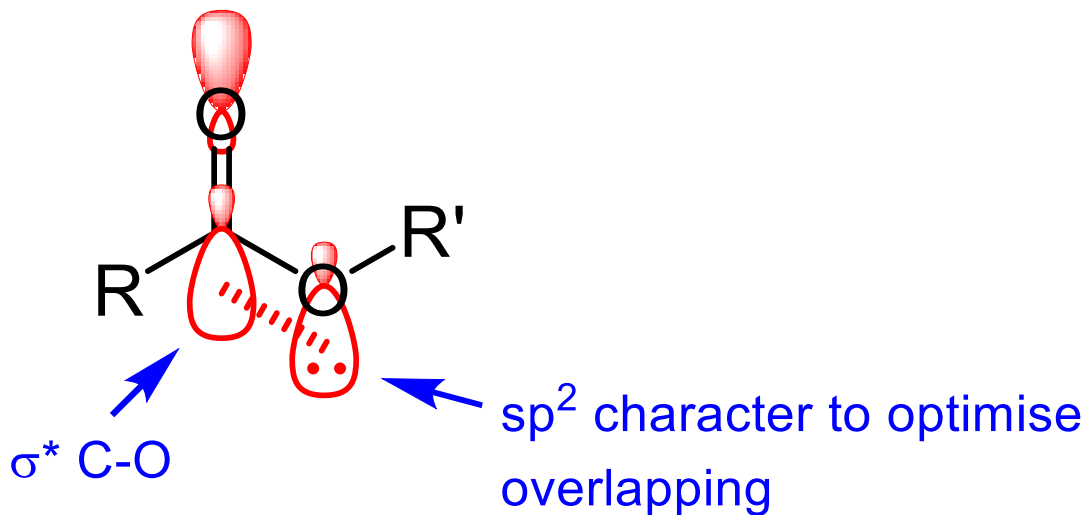
Justification

a) Dipole-dipole interactions, not favourable in the *E* conformation



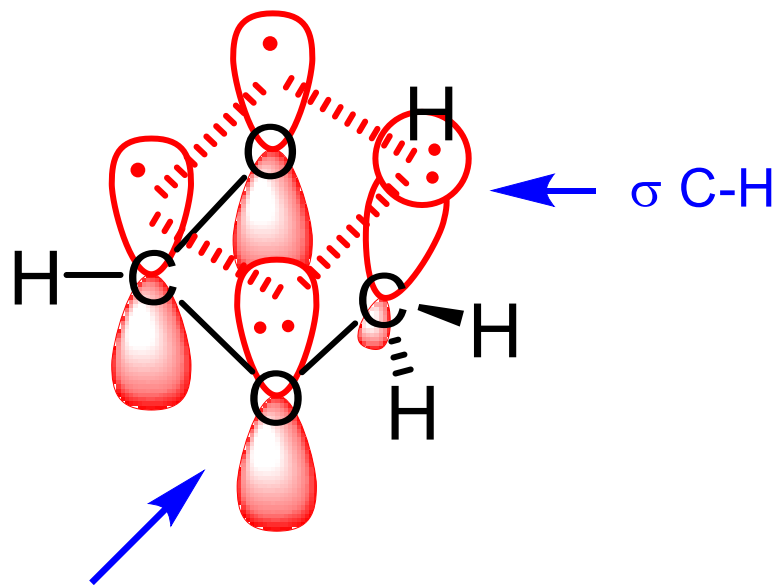
STRUCTURES WITH PARTIAL DOUBLE BONDS

b) $n-\sigma^*$ overlapping favourable in the Z conformation



STRUCTURES WITH PARTIAL DOUBLE BONDS

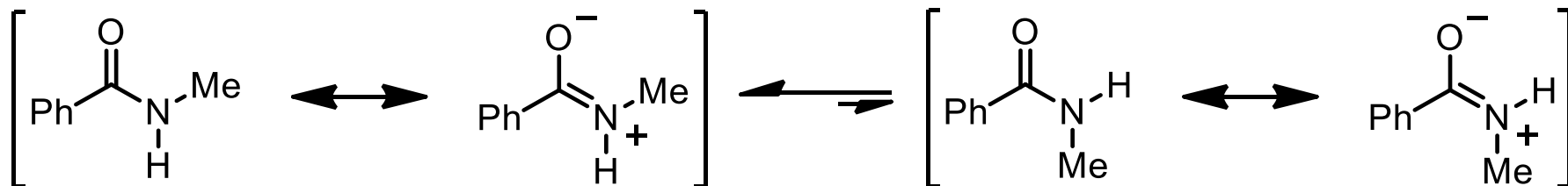
c) Formation of a 6 e⁻ π cyclic system (“aromaticity”)



sp² character to optimise overlapping

STRUCTURES WITH PARTIAL DOUBLE BONDS

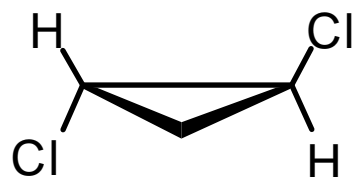
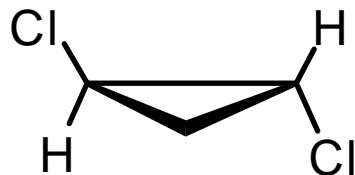
N-Alkyl-substituted amides: large delocalization effect and high rotation barrier between the conformations (20.8-25.4 kcal/mol)



Examples of enantiomers



(*E*)-cyclooctene



trans-1,2-dichlorocyclopropane

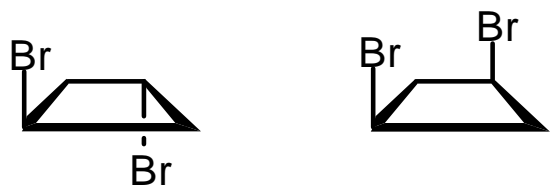
Examples of diastereomers (not all chiral)



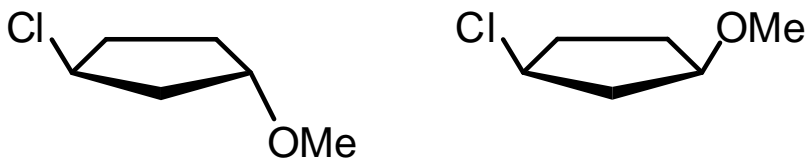
(*E*) and (*Z*)-but-2-ene



trans and *cis*-1,2-dibromocyclobutane



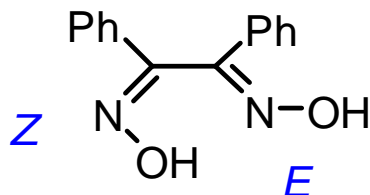
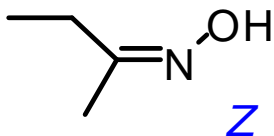
trans and *cis*-1,3-dibromocyclobutane



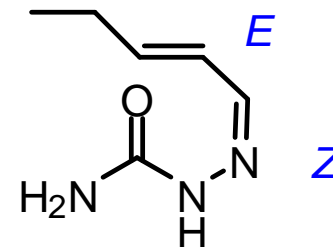
trans and *cis*-1-chloro-3-methoxycyclopentane

Nitrogenated compounds with *cis-trans* isomerism

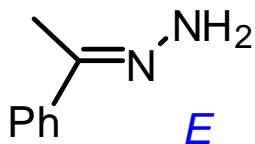
Oximes:



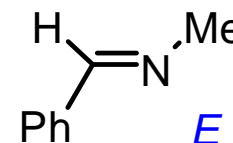
Semicarbazones:



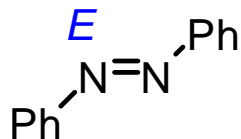
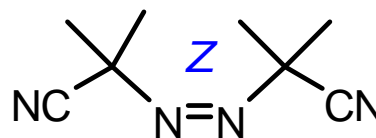
Hydrazones:



Imines:



Azo compounds:

*(E)*-azobenzene*(Z)*-AIBN

Predict the most stable conformation for butane-2,3-dione and (*Z*)-pent-3-en-2-one.