Fundamentals of Stereochemistry

Fundamentals of Stereochemistry

By

Sudhir Chandra Pal

Cambridge
Scholars
Publishing

Fundamentals of Stereochemistry

By Sudhir Chandra Pal

This book first published 2025

Cambridge Scholars Publishing

Lady Stephenson Library, Newcastle upon Tyne, NE6 2PA, UK

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN: 978-1-0364-4253-8
ISBN (Ebook): 978-1-0364-4254-5

In memory of

my Brother-in-law

Dr. Sankar K Saha

Table of Contents

Foreword

It is a pleasure to write to this foreword for the book "FUNDAMENTALS OF STEREOCHEMISTRY" by Professor Sudhir C Pal. The book is intended for college undergraduates majoring in chemistry and also to some extent to the post-graduate students as well. Although the stereochemistry has been an integral part of the undergraduate and postgraduate organic syllabus, and has been exclusively covered by many text books, newer books are always welcome to meet the requirements of the present generation of students and teachers. Professor Pal has exercised his 35 years of teaching experience to articulate the contents of the book. The coverage of the essentials of stereochemistry is thoughtful and beyond traditional approaches.

The author has rightfully focused on the symmetry elements and their applications in examining chirality of wide-ranging molecules. The topic of the conformational analysis is particularly informative and educational. It is likely to provide insightful understanding of the nature of the molecules. I personally like the exercises given at the end of each chapter of the book, which would provide enormous opportunities for refinement of thoughts and knowledge.

Congratulations to Professors Pal for an outstanding contribution to the chemistry fraternity. Hopefully, this book serves to give better opportunities to learn the stereochemical features of the complex organic molecules. For the teachers, the book would be a handy one.

Dipakranjan Mal, FRSC
Formerly Professor and Head
Indian Institute of Technology Kharagpur, INDIA
31st May, 2024

Acknowledgements

I am indebted to my parents who constantly worked hard and took pains for the continuation of my studies. I am proud of my two daughters, Sutanuka and Suchismita, the two sons-in-law (Avik and Saswata) and the two Grandsons (Shreyan and Aahan) who form a pleasing and cheerful environment around me. I am grateful to my loving wife who stood by me in times of crisis and all along my life.

I acknowledge the direct or indirect help of my close associates: Gourisankar Maiti, Nabin K Ghosh, Samik Nanda, Nirmal K Hazra, Sankar C Bhunia, Anirban Bhunia, Gopal Chandra Maity, Prof. Bimal Mahapatra, Late Prof. Anup K Dasmahapatra, Dr. Jayasree Laha (Principal) and Late Prof. Sudhansu S Pahari, and many others.

I am grateful to all the teachers of my student life. I am thankful to my research guide Prof. Avijit Banerji for arousing interest in the topic and organic chemistry in general.

Finally, I take this opportunity to thank M/s Cambridge Scholars Publishing to publish the work in print and in electronic media.

Sudhir C Pal

Preface

During my teaching days I found many bright students of chemistry who tried to avoid stereochemistry as far as practicable. This topic is not only a part and parcel of organic chemistry but undoubtedly a most interesting and important part of the subject.

These days there is a rapid growth of research in the field of stereoselective syntheses especially enantioselective syntheses. It is better that the students acquire the basic knowledge of stereochemistry in order to get the essence of such research and get motivated in this field. The present attempt is aimed to this direction. A large number of problems and their solution are given for the benefit of the learners. Moreover, some multiple-choice type questions (with answers at the end) are given to help the students in facing different competitive examinations.

This volume discusses mostly the basic aspects of stereochemistry. The application of these aspects / principles (dynamic stereochemistry) will be covered in a separate volume.

The work would be successful if at least a few students who are reluctant in the subject become inspired and find interest in this subject.

In spite of the best efforts some errors may creep in. I shall appreciate and be grateful if learned readers bring these errors to the notice of the author. Their suggestions in improving the quality of the book in any respect are most welcome.

Sudhir C Pal
Flat 3A, CD - 61
Street No. – 262, CD Block, Newtown Action Area 1C,
Kolkata – 700156
West Bengal, INDIA

CHAPTER 1

M. F., bonding, structure and naming of the molecules

1.1 Introduction

Before coming to the subject of stereoisomerism some relevant topics need to be discussed. The present chapter deals with these topics in brief.

1.2 Molecular formula

The saturated acyclic hydrocarbons (paraffins ≡ little affinity / poor chemical reactivity) have the general formula

$$C_nH_{2n+2} \ (n = \text{the number of tetravalent atom})$$

In a straight chain hydrocarbon (containing n Cs) each C is linked to two Hs (2n) except the two terminal carbons which are bonded to one extra H each (+2). For the branched chain hydrocarbons, the C at the branch point will have one H less but the same is increased due to one more terminal of the branched group. The general formula remains the same (see **Fig. 1.1:** C_6H_{14} for all hexane isomers).

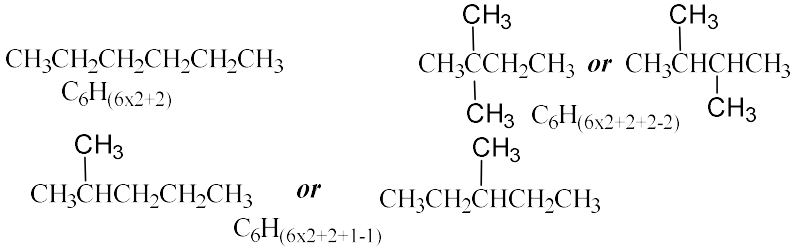


Fig. 1.1

In a compound having the monovalent atom(s) other than Hs e.g., halogens, the number of H will be lessened by an equal number of such atoms. The M.F. for such a compound would be

$C_nH_{2n+2-x}X_x$ (where x = number of the monovalent atoms X)
or C_nX_{2n+2} (now X represents monovalent atoms including H)

1.2.1 Cyclic and multiple-bonded compounds

The two non-adjacent carbons (or heteroatoms) in an acyclic compound can be linked together to form a ring compound. The linked atoms lose one H each so that M.F. of a monocyclic saturated compound will have two hydrogen atoms less than the corresponding acyclic compound. The same thing happens when the compound contains one double bond (e.g., C=C, C=O, N=N, C=S, etc.); the H atoms being eliminated from a pair of the adjacent carbons or heteroatoms. One ring is thus equivalent to a double bond in this respect.[1] The general M.F. of the monocyclic saturated or 'mono-unsaturated'[2] compounds takes the form

C_nH_{2n} (Hydrocarbon)
or C_nX_{2n} (where X = monovalent atoms including H)

A triple bond (e.g. alkyne or nitrile) or two double bonds (e.g., an alkadiene or alkenone) or two rings (e.g., indane or decalin) or one double bond plus a ring (e.g., a cycloalkene or cycloalkanone) will have four H/monovalent atoms less in their M.F. in comparison to the saturated acyclic analogue. The general formula for them is then,

C_nH_{2n-2} (Hydrocarbon)
or C_nX_{2n-2} (where X = monovalent atom including H)

A bivalent singly bonded heteroatom (e.g., -O- / -S-) can be inserted into a C—C or C—H/X bond without a change anywhere in the molecule. This will not affect the C : X (X is any monovalent atom) ratio. Thus, the general molecular formula of the different types of compounds having the bivalent atom(s) (Y; y in number) will take the form as shown in **Fig. 1.2**.

---

[1]A mono-unsaturated alcohol / ether, a cycloalkanol, a cyclic ether, a ketone and an aldehyde can become isomers of each other (i.e. same M.F.); so are a carboxylic acid, a keto-alcohol, and a mono-unsaturated diol.

[2]here signifies compounds with a double bond.

	Saturated acyclic	Mono-'unsaturated' acyclic or monocyclic	Doubly unsatd., /Triple bonded acyclic or bicylic or cyclic 'monounsaturated'
General M.F:	$C_nX_{2n+2}Y_y$	$C_nX_{2n}Y_y$	$C_nX_{2n-2}Y_y$

Fig. 1.2

When the compound contains a tervalent element (Z; usually *N*) it may be regarded as the insertion of ZH or ZX in the formula. The respective compounds will have the general formula as given in **Fig. 1.3**.

	Saturated acyclic	Mono-'unsaturated' acyclic or monocyclic	Doubly 'unsaturated' or triple bonded acyclic or bicylic or cyclic mono-'unsaturated'
M.F:	$C_nX_{2n+2+z}Z$	$C_nX_{2n+z}Z_z$	$C_nX_{2n-2+z}Z_z$
M.F:	$C_nX_{2n+2+z}Y_yZ_z$	$C_nX_{2n+z}Y_yZ$	$C_nX_{2n-2+z}YZ_z$

y and z are the numbers of Y and Z in the molecule.

Fig. 1.3

It may be noted in this connection that the odd number of the monovalent atoms in the formula ensures the presence of one or any odd number of *N* (or any tervalent atom, Z), and even number of the monovalent atoms indicates an even number / zero *N* in the compound.

1.2.2 D.B.E. or I.H.D.

D.B.E. (double bond equivalent) or
I.H.D. (index of hydrogen deficiency) = the number of double bonds + twice the number of triple bonds + the number of rings.

This can easily be determined from the given M.F. The number of the monovalent atoms is compared with that of the corresponding saturated acyclic compound (**Fig. 1.4**). The factor ½ is due to the fact that for every two H/X short D.B.E would be 1.

M. F. of the compound	M. F. of saurated acyclic compound	D.B.E. (calculated)
$C_nX_xY_y$ [y = 0 or any integer]	$C_nX_{2n+2}Y_y$	$(2n + 2 - x) / 2$
$C_nX_xY_yZ_z$	$C_nX_{2n+2+z}Y_y$	$(2n + 2 + z - x) / 2$

Fig. 1.4

The conclusion that can be drawn from a **D.B.E**. are given in **Fig. 1.5**. As seen, the number of the possibilities (ring / multiple bonds) increases largely as D.B.E. is increased. It is to be noted that a D.B.E. of 4 (or higher) is indicative (not certain) of the existence of a benzenoid ring in the molecule.

D.B.E.	Conclusion
0	No 'unsaturation' (acylic saturated compound)
1	One double bond *or* a ring
2	Two double bonds *or* two rings *or* one triple bond *or* 1 double bond plus 1 ring
3	Three double bonds *or* three rings *or* two double bonds plus a ring *or* one double bond plus two rings *or* one triple bond plus a double bond *or* one triple bond plus a ring

Fig. 1.5

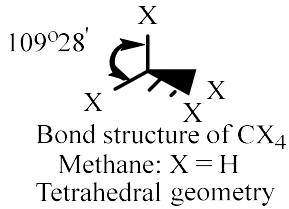
1.3 Hybridisation of C orbitals and structure of molecules

The energetically close atomic orbitals are assumed to mix up and then generate a new set of the equal number of orbitals with 'averaged' energy (degenerate) and the same total electron capacity. This concept is known as **hybridisation**.[3] The bonding capacity of the hybrid orbitals (or the degree of overlap) is higher (and hence stronger bonds are formed) than the unhybrid orbitals. This is the reason for forming bonds using the hybrid orbitals.

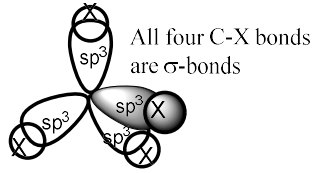
The hybrid orbitals are highly directional in characteristics (i.e., overlap of the orbitals are higher in a particular direction). This gives rise to a specific geometry to the molecules for the particular type of hybridisation.

For C, three types of hybridisations namely the sp^3, sp^2 and the sp hybridisation are recognised. The four (the 2s and three 2p), three (the 2s and two 2p) and two (the 2s and one 2p) orbitals are hybridised in the respective cases. The geometry, the bond angles and the orbital pictures of some simple molecules, as examples, are presented in **Figs. 1.6a - d**.

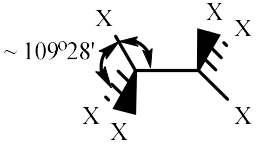
[3]The concept was introduced by **Linus Pauling** (1901 – 1994). He (a two-time Nobel laureate) was among the first scientists to work in the fields of the quantum chemistry and molecular biology.



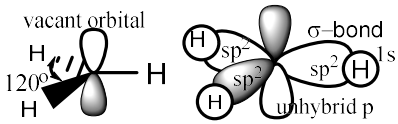
Bond structure of CX_4
Methane: X = H
Tetrahedral geometry



Orbital picture of CX_4

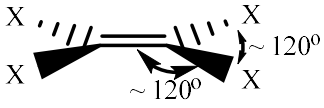


Staggerd form of X_3C-CX_3
(X=H: ethane)

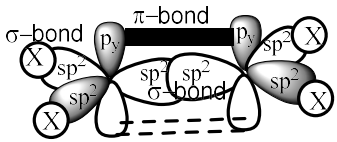


Bond structure and orbital picture
of methyl carbocation [$^{+}CH_3$] (planar)

Fig. 1.6a: Molecules having sp^3 C

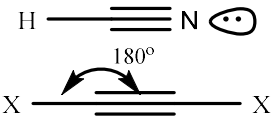


C_2X_4 (Planar geometry)
[X = H: ethene]

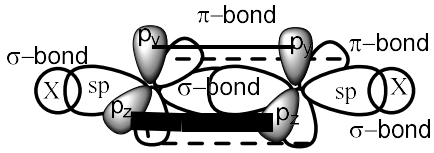


Orbital picture of X_2C=CX_2

Fig. 1.6b: Species/molecules with sp^2 hybrid C

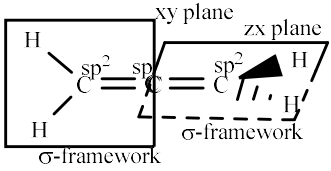


Bond structures of HCN & C_2X_2
Linear geometry

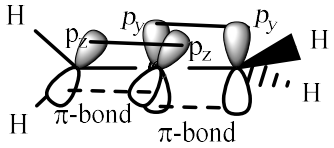


Orbital picture (X = H: ethyne)

Fig 1.6c: Molecules having sp hybrid C



Two terminal sp^2 Cs are in
mutually perp. planes



Orbital picture: only π-bond
orbitals are shown

Fig 1.6d: Allene having both sp^2 and sp hybrid Cs

The following features are noteworthy:
(i) The orbitals are all equi-spaced around the C for a maximum separation to minimise the inter-electronic repulsions. The respective bond angles are accordingly 109º28′, 120º and 180º respectively for the sp^3, sp^2 and sp hybrid carbons.
(ii) The overlap capacity of the orbitals is in order sp > sp^2 > sp > p (**Fig. 1.7**) and so the strength of the different C—H bonds: C_{sp3}—H (~500 kJ mol^{-1}), > C_{sp2}—H (~436 kJ mol^{-1}) > C_{sp}—H (~425 kJ mol^{-1}). However, the total energy of the four σ-bonds of a sp3 C > energy of the three σ- and one π-bond of an sp^2C > energy of the two σ- and two π-bonds of an sp C. So, where permissible C forms bonds via the sp^3 hybridisation and never forms bonds from the unhybrid state.[4]

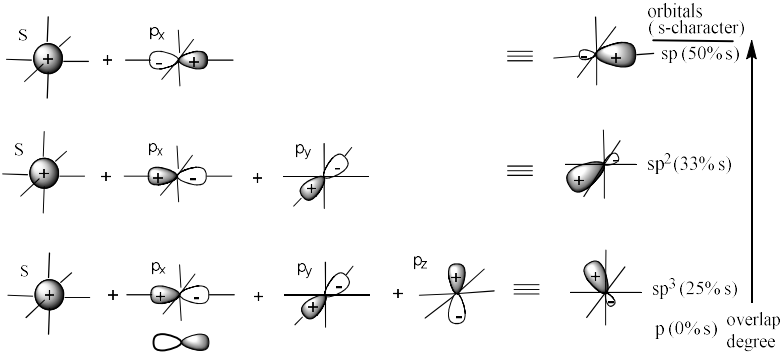


Fig 1.7

(iii) When the number of the ligands falls short C changes strategy[5] to undergo the sp^2 or even the sp hybridisation. The carbons satisfy some of the valencies between themselves by lateral overlap of the unhybrid p-orbitals forming the pi-bonds.
(iv) The rotation about the C—C bond (a σ-bond: cylindrically symmetrical) is almost 'free' (the degree of overlap of the orbitals is not affected).[6] This internal rotation (one C fixed, the other rotated) creates the different arrangements that are called **conformations**.

[4]Even in CO and in carbenes carbons form bonds in unhybrid states.
[5]A business policy, indeed!
[6]See **Chapter 7** for exceptions.

(v) As long as all the four ligands (X) in CX_4 are identical the structure remains a regular tetrahedron. This regularity is disturbed when the ligands are made different. When all the four are different the structure becomes asymmetric, and Cabcd type molecule can exist in the two non-superposable mirror image structures (called **enantiomer** of each other).[7] See **Chapter 3** for details.

(vi) A π-bond does not allow the internal rotation (under normal circumstances). So, the ethylenic molecules like abC=Cab / abC=Cbd / abC=Cde can exist in the non-superposable structures. These are **cis-trans** or ***E-Z*** isomers. See **Chapter 6** for details.

So long as the ligands (a,b,d,e) are achiral the alkenes cannot exhibit the chirality / enantiomerism.

(vii) In respect of the stereochemistry (in 3D) the triple-bonded (with sp-hybrid C) compounds (linear geometry) are not important. But, the sp C in the cumulated polyenes e.g., allenes are of stereochemical interest.

The central C in an allene uses its two different p-orbitals (perpendicular to each other) to form the two π-bonds. This gives rise to the molecule an elongated tetrahedron shape (**Fig. 1.6d**). The distortion of the geometry in abC=C=Cab / abC=C=Cbd / abC=C=Cde type molecules results in a dissymmetric or an asymmetric shape. These compounds exhibit **enantiomerism**.[8]

1.3.1 Hybridisation of tri- and tetra-coordinated N, P, As

The group III elements like *N, P* and *As* also form bonds in the tri- and tetra-coordinated compounds using their hybrid orbitals. One of the four sp^3 hybrid orbitals is occupied by a lone pair of electrons in the tri-coordinated compounds so that the geometry (decided by the nuclei) becomes a trigonal pyramid. The distortion of the regular pyramidal structure in **:**Xabc type (X = *N/P/As*) molecules can result in enantiomerism. For the simple un-bridged compounds, however, facile pyramidal inversion restricts their separation. This inversion barrier (**Fig. 1.8)** increases from *N* to *P* to *As*. The chiral arsenic compounds can be resolvable from the racemic form. The carbanions, formed at the stereocentre, changes the configuration due to the low barrier of their pyramidal inversion (see **Chapter 8**).

---

[7]This is one proof for the tetrahedral configuration of saturated C (see **Section 3.2**).
[8]This is factorised as **axial chirality**. See **Chapter 7** for details.

Compounds	Inversion barrier, in kJ mol^{-1}
NH_3	~24.0
$(PhCH_2)_2NC_2H_5$	~28.0
PH_3	132.0
AsH_3	~184

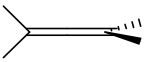
Fig. 1.8: Pyramidal inversion barrier

This inversion barrier for the *N* is much higher in the aziridines (15 – 20 kcals mol^{-1}), and is further increased when an electron-withdrawing substituent is present in the ring. In those cases, resolution of the enantiomers is possible.

The tetra-coordinated *N, P* and *As* in their sp^3 state of hybridisation give tetrahedral compounds e.g., amine oxide, phosphine oxide etc. When asymmetrically substituted these would become chiral. These are separable from the racemic modifications (see **Chapter 3** for examples).

1.3.2 Polyenes

The polyenes with isolated double bonds have no special stereochemical characteristics. The conjugated polyenes also can exhibit the cis-trans isomerism like the simple alkenes (see **Chapter 6**). The cumulated polyenes are typical; those with an odd number of the double bonds exhibit the cis-trans isomerism (the ligands at the two termini are in common plane) and those with an even number of the double bonds show enantiomerism (the termini ligands are in perpendicular planes) (**Fig. 1.9**).

Constituion (a&b different)	**Geometry**	**Isomerism**	**Structure pattern**
$ab(C=)_{2m+1}Cab$	Planar	Diastereomeism (cis-trans)	
$ab(C=)_{2m+2}Cab$	Elongated tetrahedron	Enantiomerism	

[m is 0 or any integer; n = 2m+1 / 2m+2]

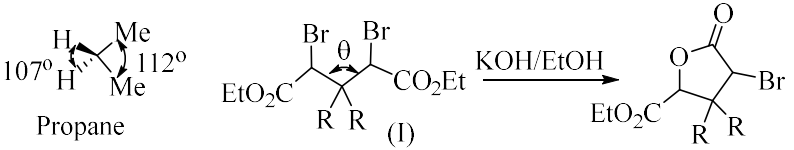
Fig. 1.9

With an increase in the number of the double bonds the configurational stability of the cumulenes is diminished. The bond order of the 'double bonds' is lowered resulting in the easier (barrier[9] lessened) interconversion between the isomers. The barrier (192 – 197 kJ mol^{-1}) in allene is however sufficient to enable resolution of the isomers.

1.4 Bond angle

In the regular/perfect sp^3, sp^2 and sp, states of hybridisation of carbon (or other tetra-covalent element) the bond angles are 109°28', 120° and 180° respectively around it (see **Figs. 1.6a-d**). If all the ligands to the C are not equal the bond angles are changed somewhat.

In propane <C—C—C is increased (112°) and <H—C_2—H is decreased (107°) due mainly to the steric reasons. The geminal di-substitution (I: R = alkyl) facilitates the intramolecular reaction due to the reduction of the angle θ (shown in the structure I). This is known as the **Thorpe-Ingold effect**.



The 'imperfect' or 'non-ideal' hybridisation resulting in the disproportionate orbital character can explain the observed bond angles in the examples given in **Fig. 1.10.** The carbon uses a hybrid orbital with more p-characters to form a bond with the electronegative elements. This meets the higher electron demand of the latter. As such <H—C—Cl is less than 109°28′ in chloromethane. The same trend is observed in 1,1-dichloroethene; the <Cl—C—Cl is reduced from 120°. Conversely a lone pair orbital gets more s-character (takes more space) to reduce bond angles in NH_3, and more so in H_2O. There is also a generalisation that the lone pair – lone pair repulsion > lone pair – bond pair repulsion > bond pair – bond pair repulsion (VSPER theory). Both the electronegativity and size of the halogens are supposedly important to explain the observed bond angles in the trihalomethanes.

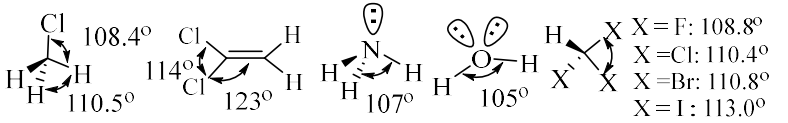
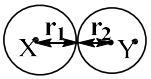


Fig. 1.10

[9]The approximate energy barrier ($\Delta G^{\#}$, kJ mol^{-1}): 260 (n = 1), 194 (n = 2), 132 (n = 3), 115 (n = 4), 80 (n = 5).

1.5 Bond Length

Bond length is the inter-nuclear distance of the two bonded atoms. It is effectively the sum of the covalent radii (r_1 & r_2) of two concerned elements (**Fig. 1.11**).



X--Y bond length = $\mathbf{r_1 + r_2}$

Fig. 1.11

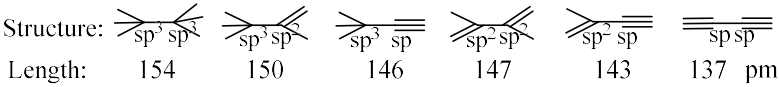
The following criteria are to be noted for the bond length variation:

(i) The bond order[10] remaining same, the bond length increases as the bond involves larger atom(s) (i.e., atoms of higher row elements): H—H < C—H < C—C < C—S; C=C < C=S.

(ii) With an increase of the bond order, the length decreases: C—X > C=X > C≡X (X = C, N). A conjugation can change the bond order to some extent and this is reflected in the bond length variation: (C=)C—C(=O) > C—C; C=C-(CN) < C=C, etc.

(iii) An increase of the p-character in the hybrid orbitals increases the bond length slightly: ≡C—C < =C—C < C—C.

(iv) Both the conjugation and % s-/p-character in the orbitals are needed to account for the variation of the C—C bond lengths in the following cases:



The lengths of some common bonds in organic compounds are noted in **Table 1.1**.

It needs mention that for a particular type of bond, the length is more or less constant e.g., C—C bond distances in ethane, propane, butane, cyclohexane, etc. are essentially the same.

1.6 Bond energy and Bond dissociation energy

Bond dissociation energy (B.D.E.) is the energy necessary to cleave the particular bond to the product radicals – both the reactants and products are in the gaseous states. For a compound like methane successive bond

[10]Bond order in MO terms, is defined as: (Number of electrons in bonding M.O. – number of electrons in ABMO) / 2.