

Annex to the ELBA method

Parameters for hydrocarbons including substituted cyclic compounds

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1. The ELBA Method

The basic guideline for developing the ELBA method was that the accuracy of the prediction should not be compromised by imposing a limit to the number of parameters but the physical meaning of these parameters should be as clear as possible and easy to identify. Regarding the optimization procedure, it was decided that after the addition of any new family to the database all the parameters should be reoptimized. The multiparameter regression analysis was made using the Microsoft[®] Office Excel 2003 SP3 Solver Tool. The estimates were made by the tangent method and forward derivatives with Newton search.

For each compound any property (e.g. the gas- and liquid-phase standard molar enthalpies of formation, the standard molar enthalpy of atomization or the specific heat) were expressed as a sum of parameters depending on the bond types and non-bonded interactions involved. For each one of those properties a specific set of parameters was defined. The description of these parameters is described in this note.

2. CH Compounds Parameters

2.1 Alkanes, Alkenes, and Alkynes

For the parameterization of the alkanes four different types of carbon atoms were considered: carbon atoms bonded to one, two, three or four carbons (Figure 1). Thus, ten different C–C bond types can be defined, from C1C1 to C4C4 (C1C1 being a bond between two type 1 carbons and C4C4 the bond between two type 4 carbon). For the C–H bonds, the hydrogen atom can be bonded to a carbon that is bonded to zero, one, two or three carbons (C0H to C3H), leading to four different types of C–H bonds.

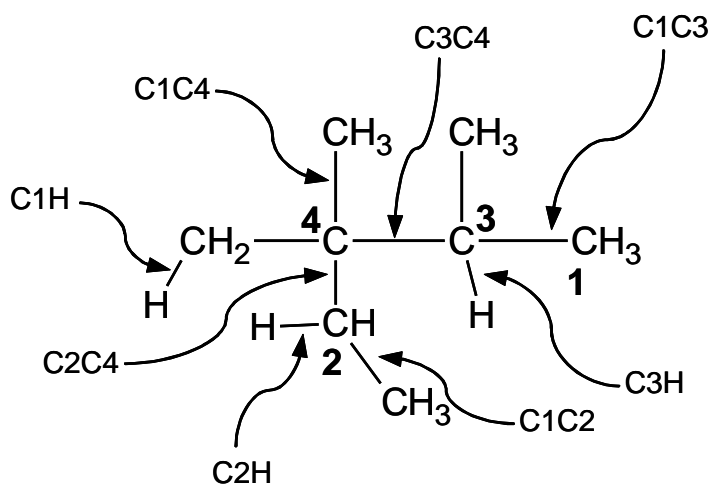


Figure 1 - The four different types of carbon atoms in alkanes (bold) and several C-C and C-H bond types.

Also a parameter Z15 (Figure 2), which takes into account steric hindrance in very bulky alkanes was defined. Therefore, 15 parameters were defined for the alkanes (Table 1). These parameters take into account all the possible

combinations of bonds in alkanes. Two of the parameters are only used in one compound: C1C1 in ethane and C0H in methane.

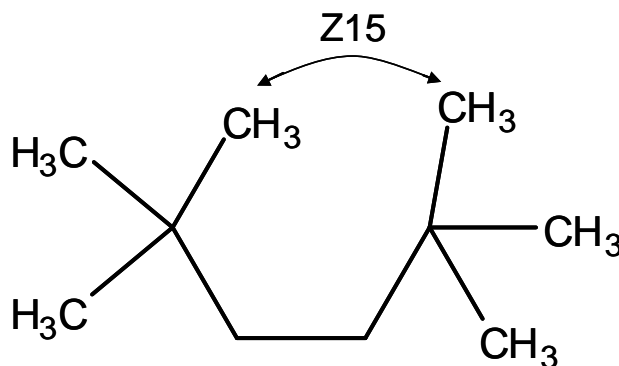


Figure 2 - The Z15 parameter for alkanes.

For the parameterization of alkenes three different types of sp^2 carbon atoms were considered: carbon atoms connected to one, two or three carbons (Figure 3). Thus, six distinct C=C double bond types (D1D1 to D3D3) and eight C–C single bonds involving an sp^2 carbon (C1D2 to C4D3) can be defined (Table 1 and Figure 3). For the C–H bonds, the hydrogen atom can be bonded to a carbon only involved in a double bond (D1H) or to a carbon involved in a C–C and a C=C bond (D2H). These parameters, together with those already defined for alkanes, take into account all the possible combinations of bonds in alkenes.

Table 1. The Laidler parameters for alkanes, alkenes, and alkynes.

C–C bonds	C=C bonds	C≡C bonds	C–C bonds with an <i>sp</i> ² carbon	C–C bonds with an <i>sp</i> carbon	C–H bonds	Non- bonded parameters
C1C1	D1D1	T1T1	C1D2	C1T2	C0H	Z11
C1C2	D1D2	T1T2	C1D3	C2T2	C1H	Z14
C1C3	D1D3	T2T2	C2D2	C3T2	C2H	Z44
C1C4	D2D2		C2D3	C4T2	C3H	Z15
C2C2	D2D3		C3D2		D1H	
C2C3	D3D3		C3D3		D2H	
C2C4			C4D2		T1H	
C3C3			C4D3			
C3C4						
C4C4						

However, in some alkenes there are also non-bonded interactions, known as 1,4 interactions, which should be considered. They occur when two groups of atoms exist in the same side of a double bond (Figure 3). To take this into consideration three extra parameters were considered (Z11, Z14, Z44). At a first glance, it could seem that more parameters would be required to account for all possible situations. However, it is easily concluded that due to the internal rotation of single C–C bonds, the interactions are identical when methyl, ethyl, and isopropyl groups are involved. Only the *tert*-butyl group cannot avoid having a methyl group turned to its neighbor and thus yields a different interaction. Table 2 summarizes the possible non-bonding interactions in alkenes.

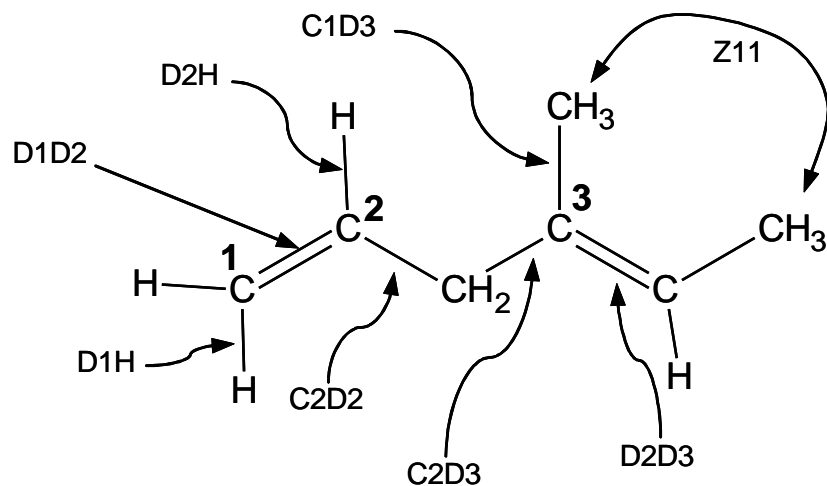


Figure 3 - The three different types of sp^2 carbon atoms in alkenes (bold) and several C–C, C=C, and C–H bond types and steric parameters.

Table 2. Non-bonding interactions in alkenes.

Group 1	Group 2	Interaction
H	H	
CH ₃	CH ₃	Z11
CH ₃	C ₂ H ₅	Z11
CH ₃	<i>i</i> -C ₃ H ₇	Z11
C ₂ H ₅	C ₂ H ₅	Z11
C ₂ H ₅	<i>i</i> -C ₃ H ₇	Z11
<i>i</i> -C ₃ H ₇	<i>i</i> -C ₃ H ₇	Z11
CH ₃	<i>t</i> -C ₄ H ₉	Z14
C ₂ H ₅	<i>t</i> -C ₄ H ₉	Z14
<i>i</i> -C ₃ H ₇	<i>t</i> -C ₄ H ₉	Z14
<i>t</i> -C ₄ H ₉	<i>t</i> -C ₄ H ₉	Z44

For the parameterization of alkynes it is noted that a *sp* carbon atom may or may not be bonded to another carbon atom (in addition to the one in the triple bond). Therefore, two different types of carbon atoms should be assumed, leading to three C≡C bonds (T1T1, T1T2 and T2T2) and four C–C bonds involving an *sp* carbon (C1T2 to C4T2) (Figure 4 and Table 1). For the C–H bonds only one parameter, T1H, is required. These eight parameters, together with those defined for alkanes and alkenes; take into account all the possible additional combinations of bonds in alkynes.

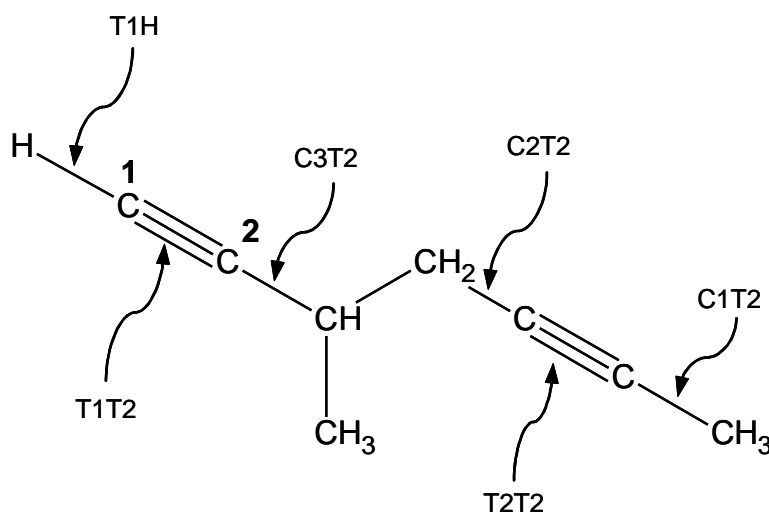


Figure 4 - The two different type of *sp* carbon atoms (bold) and several C–C, C≡C and C–H bond types.

All the above parameters (22 C–C, 6 C=C, 3 C≡C, 7 C–H bonds, and 4 non-bonded parameters) were compiled in Table 1.

2.2 Allenes, Dienes, and Polyenes.

The only new type of carbon needed for the parameterization of allenes is the one that sits in the middle of two double bonds, leading to four new types of bonds (D1Dd, D2Dd, D3Dd, and DdDd) (Figure 5). For dienes and polyenes, new parameters will be needed only in the case of conjugated double bonds (C–C bonds between two double bonds): Cd2Cd2, Cd2Cd3, and Cd3Cd3 (Figure 6). These new parameters were presented in Table 3.

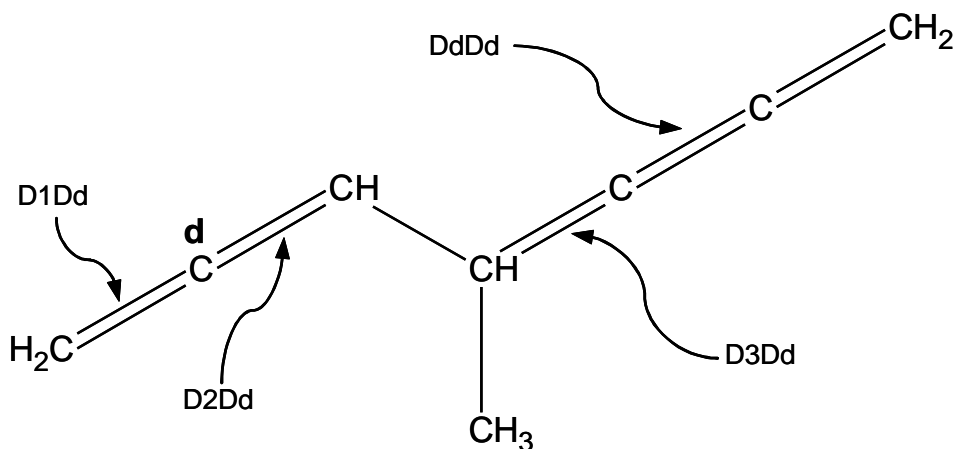


Figure 5 - The new type of carbon in allenes (bold) and the new C=C bond types.

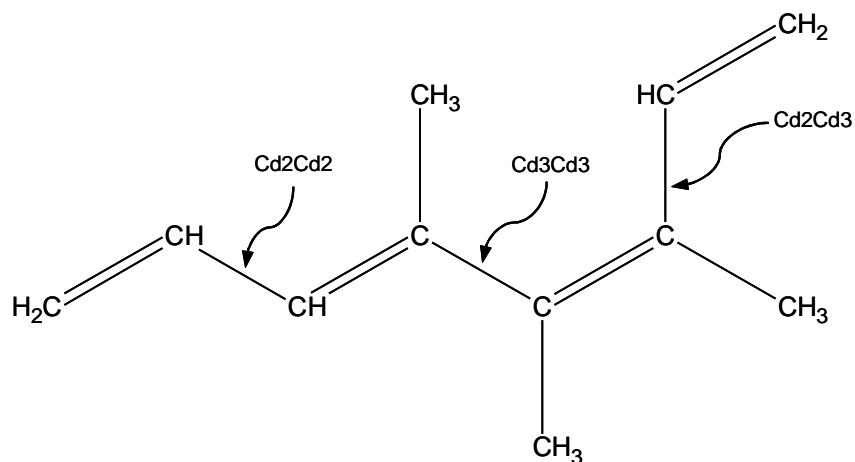


Figure 6 - The three new bond types in conjugated polyenes.

Table 3. Laidler parameters for allenes, dienes, and polyenes.

C=C adjacent bonds	C-C bonds between two C=C bonds
D1Dd	Cd2Cd2
D2Dd	Cd2Cd3
D3Dd	Cd3Cd3
DdDd	

2.3 Diynes, and Alkenynes.

For diynes and alkenynes, there is the possibility of a single bond between two triple bonds (Ct2Ct2) or between a triple and a double bond (Cd2Ct2 and Cd3Ct2) (Figure 7). These parameters are compiled in Table 4.

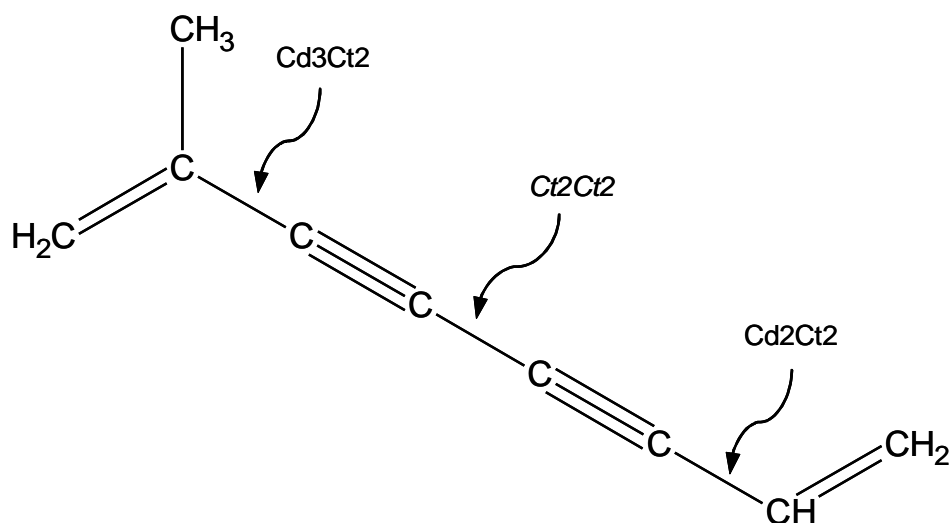


Figure 7 - The three different types of bonds in diynes and alkenynes.

Table 4. Laidler parameters for diynes, and alkenynes.

C-C bonds between C=C and C≡C bonds	C-C bonds between two C≡C bonds
Cd2Ct2	Ct2Ct2
Cd3Ct2	

2.4 Cycloalkanes and Cycloalkenes.

The approach for cycloalkanes and cycloalkenes was not, as usually, to define several ring strain parameters depending on the size of the ring. A completely different approach was followed in this work: Instead of considering a strain parameter for each ring, a strain parameter is defined for each atom of the ring. At first sight, this difference may not seem relevant, but it allows a simpler expansion of the method to substituted cyclic compounds and, in the future, with

the introduction of heteroatoms in the ring, the new approach will be rather important.

Three strain parameters were considered for cycloalkanes, according to the fact that the carbon atom in the ring can be secondary, tertiary or quaternary ($ZSnC2$, $ZSnC3$, and $ZSnC4$, n = size of the ring) (Figure 8). A new strain parameter ($ZSnD3$, n = size of the ring) is also introduced for up to six-atom rings, to be considered when a double bond is connected directly to the ring.

In addition to those general parameters, new corrective parameters must be introduced in some cases. For example, it was found that in the case of three-atom rings compounds the strain produced by one methyl group is different from the strain produced by higher alkyls. It was also noted that one or two methyl groups bonded to the same ring atom produce different strain. Therefore, three new strain parameters were defined ($ZS3C3m$, $ZS3C4m$, and $ZS3C4mm$) for this family of compounds (Figure 9).

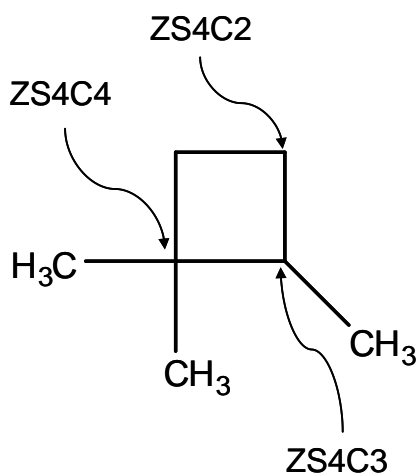


Figure 8 - Atomic strain parameters for cycloalkanes,
illustrated for a cyclobutane.

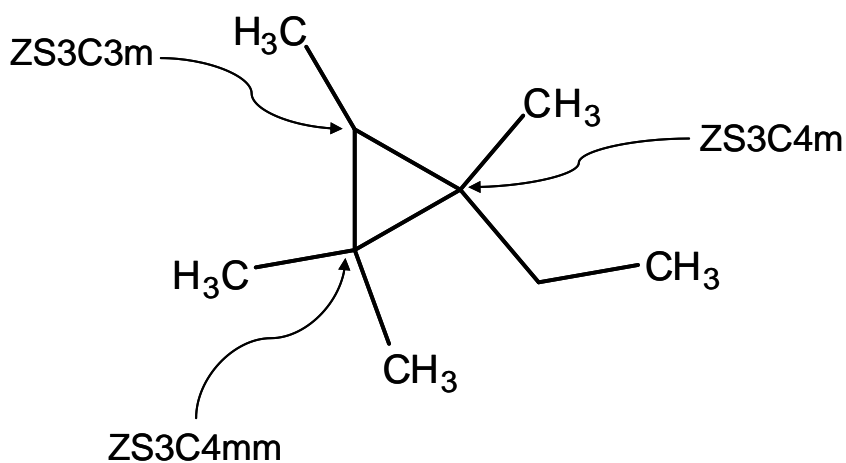


Figure 9 - Non-bonded parameters for cyclopropanes.

In small rings (three to six atoms) it was found that some additional non-bonded parameters were required to account for interactions between ring substituents. For three- to five-atom rings there is a non-bonded interaction between *cis*-1,2-substituents (*Znc12*, $n = 3$ to 5) (Figure 10).

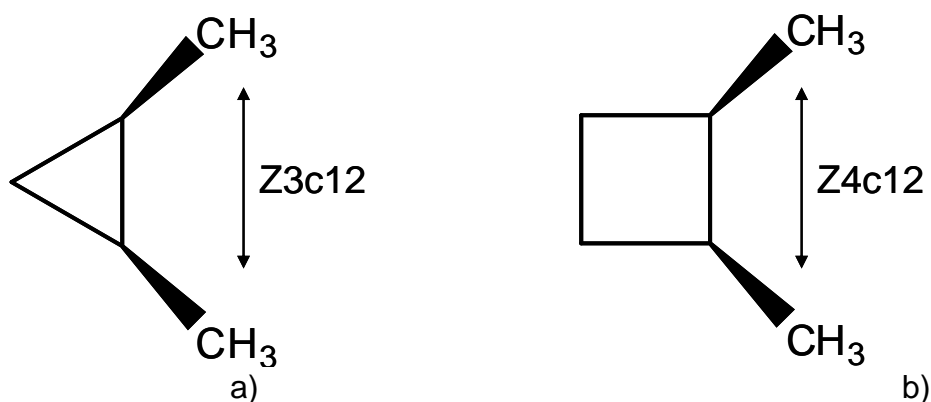


Figure 10 - Two examples of the ZnC12 interaction:

(a) Z3c12. (b) Z4c12.

Also, in five-atom rings with 1,3-substituents, an additional non-bonded interaction exists in one of the *cis-trans* isomers. For the *cis* isomer, the most stable arrangement is an envelope conformation (see example in Figure 11a) with the 1,3-substituents in the equatorial positions (numbered as in Figure 11a). When the substituents change to a *trans* arrangement, as in the case of *trans*-1,3-dimethylcyclopentane, the most stable conformation forces the ring to assume an half-chair arrangement (Figure 11b) with the two 1,3-substituents in the equatorial positions (numbered as in Figure 11b). An extra parameter (Z5t13) had to be defined for this last case.

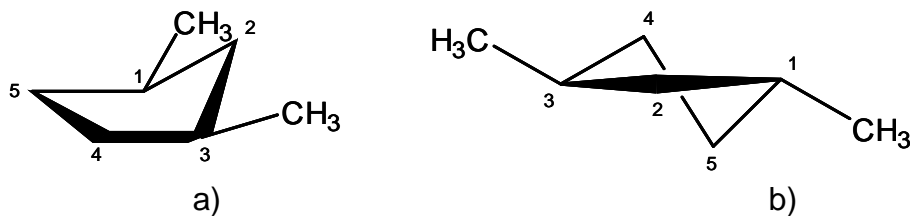


Figure 11 - The most stable conformational arrangements of the 1,3-dimethylcyclopentane isomers. (a) cis isomer in a 1,3-diequatorial envelope conformation. (b) trans isomer in a 1,3-diequatorial half-chair conformation.

In six-atom rings with only one substituent, the molecule will preferentially assume a conformation with that substituent in an equatorial position, but with two substituents in *cis*-1,2, *trans*-1,3 or *cis*-1,4 positions it is not possible to avoid one of them to be in axial position. The presence of at least one substituent in axial position in six-atom rings produces a destabilizing interaction between those substituents and the ring carbon atoms (Z6ax) (Figure 12). Also, with 1,3,5-substituents the α,α,α isomer has the more stable conformation with all the substituents in an equatorial position, but in the α,α,β isomer it is not possible to avoid one of the substituents to be in axial position.

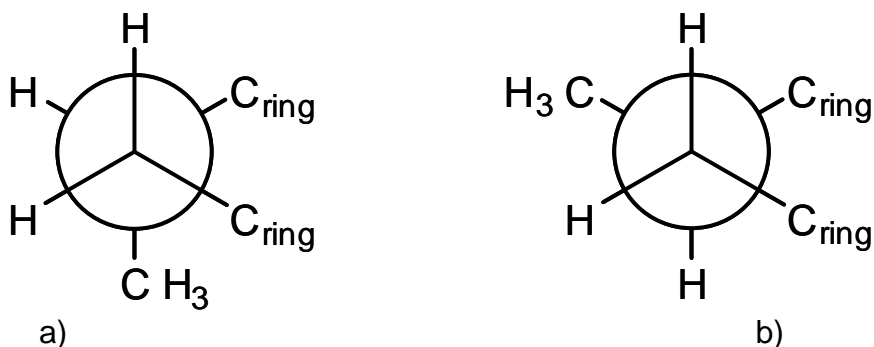


Figure 12 - There are three situations where a six-atom ring with two substituents is forced to have at least one of them in the axial position: *cis*-1,2, *trans*-1,3, and *cis*-1,4. The fact that one of them is in the axial position (b), yields an extra non-bonded interaction when compared with a substituent in an equatorial position (a).

In the cases of a double bond connected to a ring, a non-bonded interaction could exist between the substituents of the double bond, like in any other alkene. This interaction is, however, different from the cases of single alkyl substituents and therefore a new parameter (Z1cy) was introduced (Figure 13).

In the stable cyclodecane conformation, one may discern two kinds of C–H bonds: those that point out from the ring (extra-annular) and those that point into the ring (intra-annular). Groups other than hydrogen in intra-annular positions would clearly be in a highly strained situation. To take this problem into account, a steric term (Z10int) was defined for the cases of disubstituted ten-atom rings in any of the 2, 3, 5, 7, 8 or 10 positions.

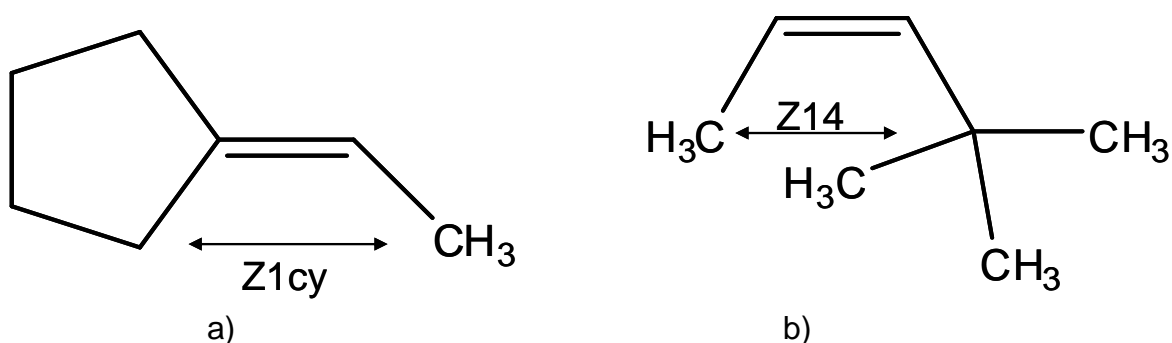


Figure 13 - (a) Interaction between a ring and other substituent in a double bond. (b) Interaction between substituents in a double bond not involving a ring.

All strain, and non-bonded parameters (with the exception of Z1cy, which is valid for rings of any dimension) defined for cycloalkanes are presented in Table 5.

Table 5. Strain and non-bonded parameters for cycloalkanes.

3-atom ring	4-atom ring	5-atom ring	6-atom ring	<i>n</i> - (7 to 17) atom ring ^a	10-atom ring
ZS3C2	ZS4C2	ZS5C2	ZS6C2	ZSnC2	Z10int
ZS3C3	ZS4C3	ZS5C3	ZS6C3	ZSnC3	
ZS3C3m	ZS4C4	ZS5C4	ZS6C4	ZSnC4	
ZS3C4	ZS4D3	ZS5D3	ZS6D3		
ZS3C4m	Z4c12	Z5c12	Z6ax		
ZS3C4mm		Z5t13			
ZS3D3					
Z3c12					

^a ZSnD3 parameter for $n \geq 7$ is not given because there are no experimental values for a compound with a double bond connected to a $n \geq 7$ ring.

For cycloalkenes it was necessary to define several conformational parameters to take into account the distortion caused by the presence of one or more double bonds in the ring, in addition to the strain parameters with a similar meaning to those defined for cycloalkanes. The new parameters for cycloalkenes are represented by ZD_nD_m ($n = 3$ to $10, 12$, and $m = 2, 3$, $n =$ size of the ring, and $m =$ number of atoms connected to the carbon atom under consideration) and $ZD10Cd$. An example of the first group of parameters is shown in Figure 14 and the parameter $ZD10Cd$ is illustrated in Figure 15.

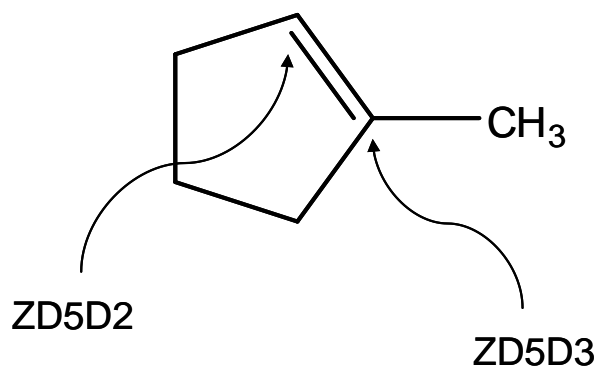


Figure 14 - General strain parameters for cycloalkenes:
example for a five-atom ring.

For five-atom rings, when the ring is unsubstituted, independent of the number of double bonds, the system seems to have a high ability to find a more stable conformation and a supplementary parameter ($Z5$) was introduced to account for that. For six-atom rings having one or two double bonds, two

additional parameters (Z6 and Z6s) were defined and used according to the compound structure. Reliable experimental data are scarce for compounds involving this type of unsaturated rings, affecting the correct parameterization.

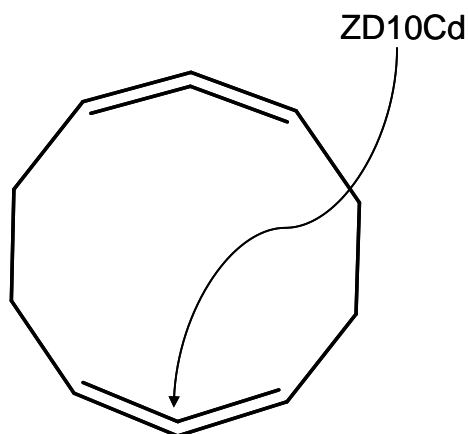


Figure 15 - The ZD10Cd strain parameter defined for a ten-atom ring compound containing two consecutive double bonds.

The parameter Z6s was needed as an additional correction to Z6 for molecules that have the isopropenyl substituent in their structure (e.g., (R)-1-methyl-4-(1-methylethenyl)cyclohexene). In the particular case of a six-atom unsubstituted ring, with two unconjugated double bonds (e.g., 1,4-cyclohexadiene), it was found that no correction is necessary. Once again due to the scarcity of experimental data, the corrections for this type of substituted unsaturated ring are unknown. For compounds with one double bond in the ring, the term Z6 is multiplied by two both in the absence and in the presence of one substituent (e.g., cyclohexene, 1-methylcyclohexene), or by four when two

substituents are present (e.g., (R)-1-methyl-4-(1-methylethenyl)cyclohexene). If the compound has two conjugated double bonds in the ring, the term Z6 is multiplied by eight in the absence of substituents (e.g., 1,3-cyclohexadiene), or by five in the presence of one or two substituents (e.g., 2-methyl-1,3-cyclohexadiene, 5-isopropyl-2-methyl-1,3-cyclohexadiene).

Due to the several possible conformations of eight-atom rings having one or two double bonds, four new parameters become necessary. These rings can have the double bonds in (E) or (Z) conformations. For rings with only one double bond, when a (Z) conformation occurs no extra parameter is needed but for an (E) conformation the Z8uE parameter must be used. In the case of two double bonds in the ring, a total of three combinations are possible, which will be described by the parameters Z8uEE, Z8uZZ, and Z8uZE.

When rings have three or four double bonds, the conformational correction used is described by the parameter $ZnuABCD$, where $n = 7, 8$ or 10 is the size of the ring, and A, B, C , and D are the positions of the double bonds in the ring. A special case is the twelve-atom ring parameter Z12u159E, which is used when all the three double bonds in the ring are in (E) conformation.

The parameters proposed for cycloalkenes are presented in Table 6.

Table 6. Strain and conformational parameters for cycloalkenes.

<i>n</i> - (3 and 4) atom ring	5-atom ring	6-atom ring	7-atom ring	8-atom ring	9-atom ring	10-atom ring	12-atom ring
ZD _n D2	ZD5D2	ZD6D2	ZD7D2	ZD8D2	ZD9D2	ZD10D2	ZD12D2
ZD _n D3	ZD5D3	ZD6D3	ZD7D3	ZD8D3	ZD9D3	ZD10D3	ZD12D3
	Z5	Z6	Z7u13	Z8uE		ZD10Cd	Z12u159E
		Z6s	Z7u135	Z8uEE		Z10u1267	
				Z8uZZ			
				Z8uZE			
				Z8u136			
				Z8u1357			

2.5 Benzene Derivatives

For benzene and its derivatives some new parameters must be defined since an aromatic bond cannot be described by the parameters proposed so far. A carbon atom from a benzenic ring can be bonded to two other ring carbons and an hydrogen or to the ring carbons and another carbon atom. This defines three different types of bonds in the ring: A2A2, A2A3, A3A3 (Figure 16).

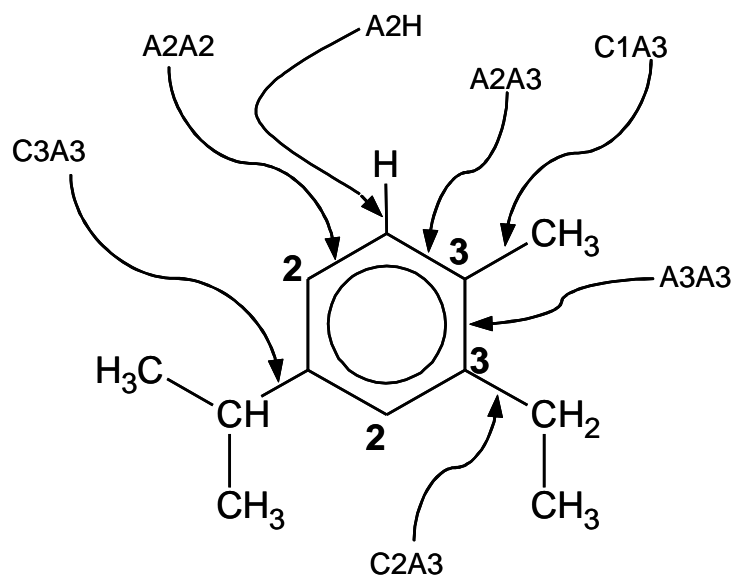


Figure 16 – The two different type of carbons in a benzenic ring (bold) and several carbon-carbon and carbon-hydrogen bond types.

Also, one parameter is needed for aromatic carbon-hydrogen bond (A2H) and four different parameters can be defined for the bond between a benzene ring carbon and a carbon from an alkyl group, depending on the number of carbons bonded to the sp^3 carbon: C1A3, C2A3, C3A3, and C4A3. For non-alkane substituents (with double and triple bonds), three new parameters must be defined (Figure 17 and Table 7).

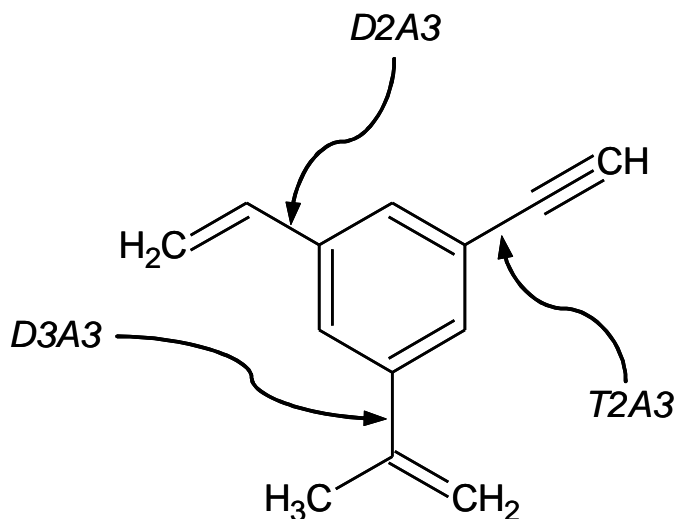


Figure 17 – Additional bond types between an aromatic ring and unsaturated substituents.

As considered for alkenes, some non-bonding interactions must be considered for *ortho*-substituents. We have designated these terms as ZA11, ZA14 and ZA44. The meaning of these parameters is similar to the one described for alkenes. The number 1 applies to methyl, ethyl or isopropyl groups (primary, secondary, and tertiary carbons) and the number 4 applies to quaternary carbon substituents. When more than two substituents are present in adjacent positions, the internal rotation of some of them can be severely hindered and more terms are required (ZA1'1, ZA1'4, ZA1'1', ZA1'4', ZA4'1, and ZA4'4'), leading to a total of nine different non-bonding interactions in benzene rings (Figure 18 and Table 7). The number identified with a prime refers to a substituent in between two other substituents.

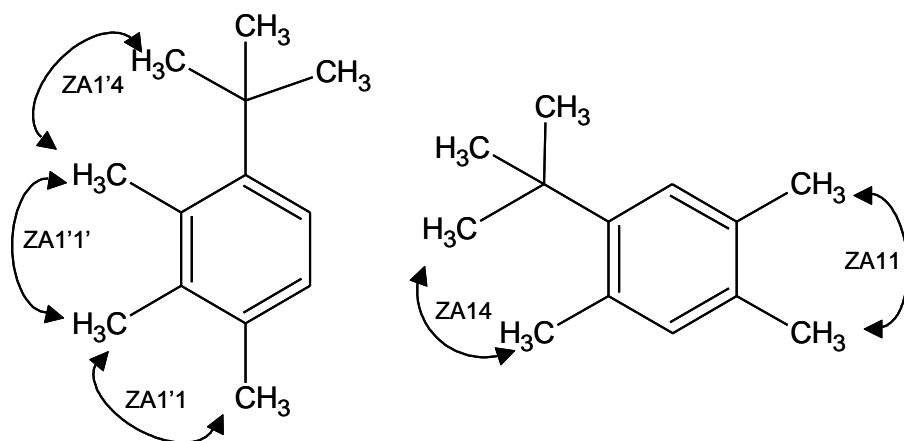


Figure 18 – Non-bonding interactions in benzenic rings.

Table 7. Parameters for benzene derivatives.

Bonds in benzene ring	Alkyl groups bonded to the benzene ring	Non-alkyl groups bonded to the benzene ring	Non-bonded parameters (neighbours repulsion)		
A2A2	C1A3	D2A3	ZA11	ZA11'	ZA1'4'
A2A3	C2A3	D3A3	ZA14	ZA1'4	ZA4'1
A3A3	C3A3	T2A3	ZA44	ZA1'1'	ZA4'4'
A2H	C4A3				

2.6 Bi and Polyphenyls

The only new parameter required to cover biphenyls is the one related to the bond between the aromatic rings, Ca3Ca3. However, two additional parameters were also defined to take in account the non-bonded interaction that occurs in some biphenyl and polyphenyl compounds. In biphenyls with a substituent in position 2, the repulsive interaction is described by the ZA1A parameter (Figure 19). For polyphenyls, a stabilizing interaction ZAA was found when two aromatic rings are near each other, out of plane (Figure 20).

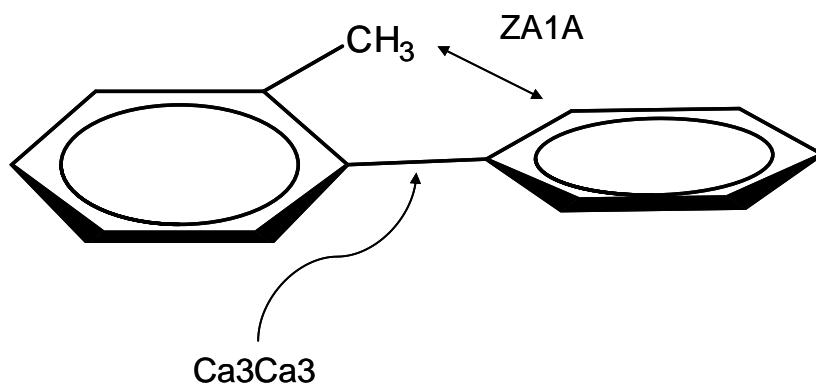


Figure 19 - New bond and non-bonded parameters for biphenyls.

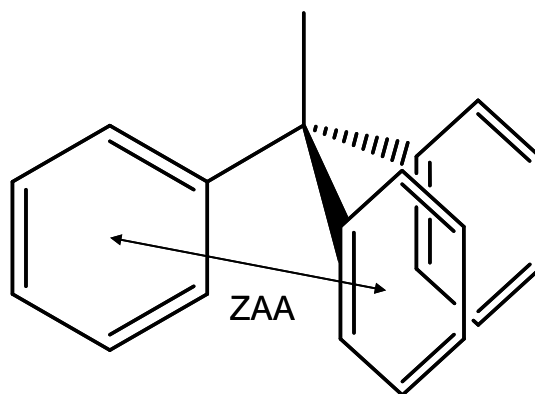


Figure 20 - The interaction between two aromatic rings in polyphenyls.

