Computational and Theoretical study of Dienone-Phenol rearrangement and compare the reaction mechanism with different migratory substituents

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Abstract:

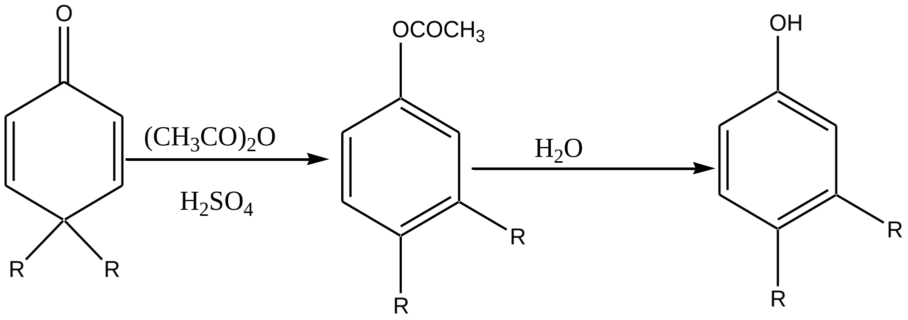
The dienone-phenol rearrangement studied explain the net thermodynamic profile for the rearrangement of dienone through the 1,2-migration of various groups (H , Me, Et, i-pro, t-but, Phenyl) and the enthalpy changed for successive steps in their migration pathways and these are calculated at the level of AM1, HF and B3LYP level of theory and the results are compared and analyzed . The effects of different substituents upon the rearrangement can be deliberated by migratory Aptitudes of the groups, geometry of the transition states (TS) and relative positions of the transition states in the context of the Hammond postulate.

Keywords: Dienone-phenol, 1, 2 shifts, AM1, HF, DFT.

Introduction

Rearrangement Via 1,2- shift in carbocation is studied extensively. But it is not easy to predict which substituent will migrate when there is a competition between two similar groups. The results of such studies are usually expressed as relative migratory aptitudes (RMA), which describe migration of one group in preference to another. Thus this rearrangement is an intramolecular comparison method. Cyclohexadienones may exist as 2,4- dienones or as 2,5- dienone. The prominent among reaction associated with the cyclohexa-2,5- dienone system is the dienone-phenol rearrangement, where the substrate undergoes an intramolecular 1,2-shift of a group R situated at the C-4 position to finally form a 3- substituted phenol as shown in fig. Cyclohexa-2,4- dienone can also undergo dienone – phenol rearrangements along similar lines, R situated at the C-6 position to form a 5–substituted phenol. Both these reactions are acid catalyzed and are actually isomerizations involving carbocationic intermediates [1]. The key steps in these reactions is the 1, 2 - shift of a group within the intermediate cation . The driving force for the rearrangement reaction in both 2,4- and 2,5- dienones is the gain of aromaticity as the non-aromatic dienone substrate rearranges to the aromatic product[2] .

When Dienones are treated commonly in acetic anhydride solution with a little sulphuric acid at room temperature, aryl acetate product is usually hydrolyzed to the phenol either with a base or by boiling with the aqueous acid as shown in figure 1. The dienone substrate achieve rapid equilibrium with their conjugate acids (benzonium ions), where the migratory aptitude of the migrating group is determined by the ability of the group to stabilize the carbocationic centre[3]. Cyclohexadienone system is studied here as substrate for the dienone-phenol rearrangement reaction are substituted cyclohexa 2,4- and 2,5- dienone which are disubstituted at the C-4 and the C-6 position respectively[3] .



Dienones treated in acetic anhydride solution to form phenol

Methodology

Gaussian software package was used to calculate the gradient – corrected electron density functions, geometries, energies and frequencies of the dienone system at the level of AM1,HF and DFT[4]. In some sample cases of the key migration step, the carbo-cationic II and the rearranged cationic IV were subjected to conformational analysis to yield the most stable conformer of both. The transition state III was located for each case by the SADDLE key word of the MOPAC package, invoking a reverse search strategy with interpolation between the equilibrium geometries of the reactant and product (both in their lowest energy conformers) to arrive at the saddle point or transition state . Once located, the transition state was verified as such by diagonalising the Hessian matrix to yield one and only one negative Eigen value [5].

The approach of this study involves studying the successive steps of the dienone – phenol rearrangement incorporated here in the manner described below. Energy minimized heats of formation were calculated for each of the molecular species involved in the reaction mechanism, and used as the basis for calculating the energy profile for the reaction pathway in each cases as well as for calculating the enthalpy changes for each successive steps in the reaction. Special attention was paid to the key step of the 1,2 – migration in the initial carbocation species leading to the formation of the rearranged carbocation , where the transition state was located and confirmed for each case, and the activation enthalpy barrier estimated . The geometry of the transition state was then examined in relation to the Hammond postulate, which states that, a transition state and an unstable intermediate occur consecutively during a reaction process and have nearly the same energy content. Their interconversion will involve only a small reorganization of the molecular structure.

Results and discussion

The theoretically calculated heats of formation for the various species involved at each step along the mechanistic pathway (including water or the hydronium ion) are the basis for the energy level at each stage along the rearrangement pathway, where the initial stage of substrate plus a hydronium ion H_3O is arbitrarily set at a Zero energy level, which rearranges by 1,2 – migration and the enthalpy of this 1,2 – migration step is denoted by ΔH_r . The various migrating groups were compared with regard to kinetic facility of undergoing the 1,2 – migration step by comparing the calculated values of the activation energies (Ea) which is the enthalpy difference between the transition state and the reactant for this step. The calculation of various reaction mechanisms by using different substituents gave us the following observation as follows.

Table-1: Energy profile for the successive steps of the dienone-phenol rearrangement (4,4-disubstituted cyclohexa-2,5-dienones with (R_1 =H, R_2 = R = H, Me, Et, Pr^i, Bu^t, Ph,) where migration of R is from the C-4 to the C-3 position for transition state III in AM1 calculation (sub set-A)

No	R	I	II	IV	III (TS)	V
1	H	-7.08	158.53	172.26	190.26	15.24
2	Me	-11.16	158.47	172.70	201.17	18.75
3	Et	-17.18	157.65	171.69	192.89	18.49
4	Pr^i	-20.44	156.90	171.01	184.30	19.18
5	Bu^t	-8.59	159.09	156.21	166.36	32.10
6	Ph	23.32	157.02	171.95	193.89	20.00

*All enthalpy terms in kcal/mol; Hessian eigenvalue in mdyn/angstrom

Table 2: Energy profile for the successive steps of the dienone-phenol rearrangement (4,4-disubstituted cyclohexa-2,5-dienones with (R_1 =H, R_2 = R = H, Me, Et, Pr^i, Bu^t, Ph,) where migration of R is from the C-4 to the C-3 position for transition state III in #HF/6-31G calculation (sub set-B)

No	R	I	II	IV	III (TS)	V
1	H	0	194.56	201.67	222.68	10.16
2	Me	0	135.70	202.93	223.94	11.91
3	Et	0	190.32	204.12	225.00	12.73
4	Pr^i	0	261.37	267.45	288.53	76.76
5	Bu^t	0	115.88	140.59	202.05	12.04
6	Ph	0	193.20	204.05	225.19	17.11

*All enthalpy terms in kcal/mol; Hessian eigenvalue in mdyn /angstrom

Table 3: Energy profile for the successive steps of the dienone-phenol rearrangement (4,4-disubstituted cyclohexa-2,5-dienones with (R_1 =H, R_2 = R = H, Me, Et, Pr^i, Bu^t, Ph,) where migration of R is from the C4 to the C3 position for transition state III in #B3LYP/6-31G calculation (sub set-C)

No	R	I	II	IV	III (TS)	V
1	H	0	197.22	206.88	222.68	13.76
2	Me	0	166.08	189.57	194.71	16.43
3	Et	0	199.42	210.14	225.50	17.05
4	Pr^i	0	206.63	211.89	226.63	18.06
5	Bu^t	0	193.27	131.00	209.32	16.36
6	Ph	0	204.37	208.69	225.56	19.56

*All enthalpy terms in kcal/mol; Hessian eigenvalue in mdyn/angstrom

Table 4: Geometry parameters of the transition states for the 1,2-migration step of the dienone-phenol rearrangement in (4,4-disubstituted cyclohexa-2,5-dienones with R_1 =H, R_2 = R = H, Me, Et, Pr^i, Bu^t, Ph,) including bond lengths, bond angles and dihedrals angle.

No	R	R_1	R_2	R_3	α	β	γ	φ_1	φ_2
1	H	1.416	1.246	1.4465	1.60	62.96	65.42	95.32	115.52
2	Me	2.019	1.905	1.426	64.49	73.60	42.50	100.86	44.16
3	Et	2.178	2.042	1.421	65.24	75.57	39.18	102.58	179.62
4	Pr^i	2.592	2.306	1.419	62.37	84.61	33.02	103.43	177.41
5	Bu^t	2.588	1.682	1.462	37.44	110.65	31.91	126.41	61.78
6	Ph	1.906	1.673	1.450	57.91	74.84	47.26	107.47	99.31

*All bond distances in angstroms; bond angles and dihedral angles in degrees

Table 5 Bond ratio, enthalpy with remarks showing the nature of the rearrangement in relation to the transition state along the reaction pathway for various species.

No.	**R**	R_2	R_1	R_2/R_1	ΔH_r
1	H	1.246	1.416	0.8799	13.73
2	Me	1.905	2.019	0.9435	14.23
3	Et	2.042	2.178	0.9375	14.04
4	Pr^i	2.306	2.592	0. 8896	14.11
5	Bu^t	1.682	2.588	0.6499	-2.88
6	Ph	1.673	1.906	0.8778	14.93

Enthalpy in Kcal/mol

Table 6: AM1 Energy of the reactions (AHr) and the activation energy (Ea) in Kcal/mol. for IV –II and III (TS) – II systems for each species (sub set-A)

Sl.No	R1	System	AHr	System	Ea
1	H	IV-II	13.73	III(TS)-II	31.73
2	Me	IV-II	14.23	III(TS)-II	42.75
3	Et	IV-II	14.04	III(TS)-II	35.24
4	i-Pro	IV-II	14.11	III(TS)-II	27.4
5	t-But	IV-II	-2.88	III(TS)-II	7.27
6	Phenyl	IV-II	14.93	III(TS)-II	36.87

Table 7: HF Energy of the reactions (AHr) and the activation energy (Ea) in Kcal/mol. for IV –II and III(TS) – II systems for each species. (sub set-B)

Sl.No	R1	System	AHr	System	Ea
1	H	IV-II	7.11	III(TS)-II	28.45
2	Me	IV-II	67.23	III(TS)-II	88.24
3	Et	IV-II	13.8	III(TS)-II	34.68
4	i-Pro	IV-II	6.08	III(TS)-II	27.16
5	t-But	IV-II	24.71	III(TS)-II	86.17
6	Phenyl	IV-II	10.85	III(TS)-II	31.99

Table 8: B3LYP Energy of the reactions (AHr) and the activation energy (Ea) in Kcal/mol. for IV –II and III(TS) – II systems for each species. (sub set-C)

Sl.No	R1	System	AHr	System	Ea
1	H	IV-II	9.66	III(TS)-II	25.46
2	Me	IV-II	23.49	III(TS)-II	28.63
3	Et	IV-II	10.72	III(TS)-II	26.08
4	i-Pro	IV-II	5.26	III(TS)-II	20.00
5	t-But	IV-II	-62.27	III(TS)-II	16.05
6	Phenyl	IV-II	4.32	III(TS)-II	21.19

Reaction Pathways of migration of the substituents

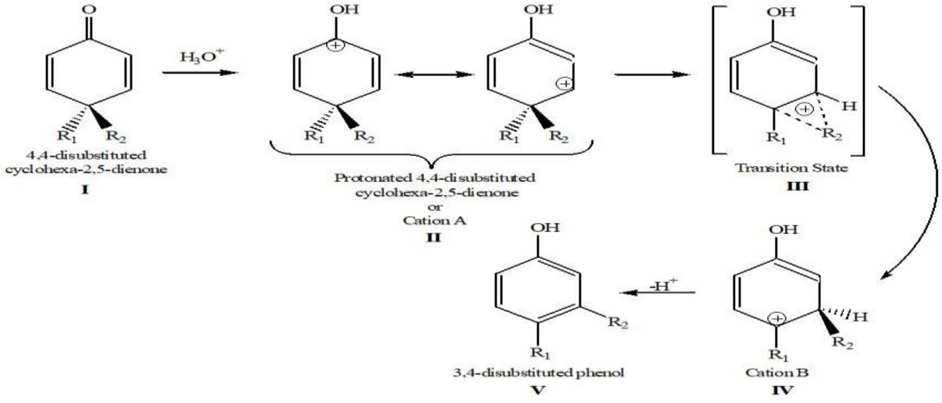


Fig 1: Diagram showing successive steps for a dienone-phenol rearrangement in cyclohexa-2,5-dienones (**R2** is the migrating group)

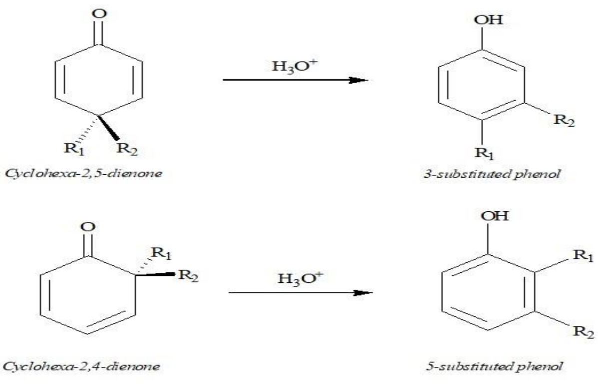
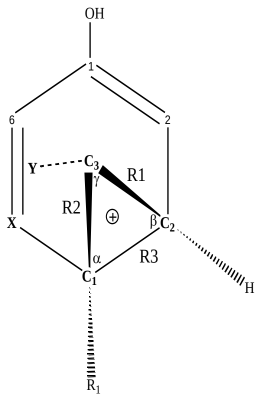


Fig. Dienone-phenol rearrangement of cyclohexa-2,5-dienone .



ϕ_1=[C3-C2-C1-X]
ϕ_2=[C1-C2-C3-Y]
C_1=migration origin
C_2=migration terminal
C_3=migrating group
R2(C1-C3)=Bond breaking
R1(C2-C3)=Bond making

Fig 2: Transition state showing geometrical parameters of the transition state .

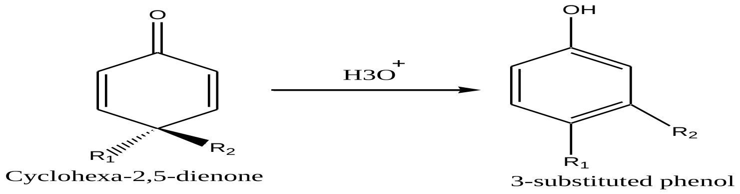


Fig 1: Dienone-phenol rearrangement of cyclohexa-2,5-dienone giving 3-substituted phenol, respectively

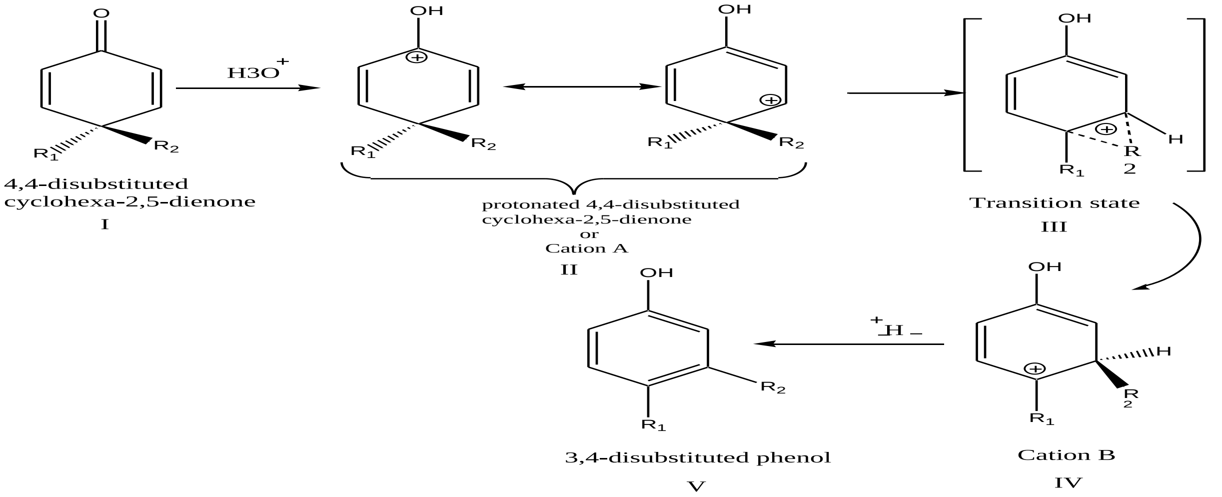


Fig 2: successive steps for a dienone-phenol rearrangement in cyclohexa-2,5-dienones (R2 is the migrating group) showing migration from the C4 to the C3 position

1.1 Relative Migratory Aptitudes

The relative migratory aptitude is rationalized from the kinetic and the thermodynamic points of view. The final outcome is expected to depend primarily on the kinetic factor owing to the instability of the cationic reactive intermediates involved. The various migrating group R were compared with regard to kinetic facility of the 1,2-migration step on the basis of the calculated value of the Ea for the conversion of species III(TS) from II to give IV for each case. The thermodynamic facility of the migration was estimated for each case by enthalpy term AHr, which are the enthalpy change accompanying the rearrangement step as calculated from the AM1 heat of formation of the cation II and the cation IV. It is also known that the capacity of the migrating group R to retain charge in the transition state is a factor that determines facility of migration in carbocation system. Migratory aptitude of the migrating group is compared by using the Ea for the rearrangement step which transform cation II to cation IV via transition state. The AM1 values of (Ea) for sub-set A ranges from 7.27 to 42.75 Kcal/mol, and HF value of Ea for sub-set B ranges from 27.16 to 88.24 Kcal/mol and B3LYP value of Ea for sub-set C ranges from 16.05 to 28.63 Kcal/mol .

Kinetic facility order for the rearrangement with respect to the migrating R group, as given by the activation energy (Ea) is predicted as follows; t-but > i-pro > H > Et> Phenyl > Me for sub-set A. ; i-Pro > H >

Phenyl > Et > i-But > Me for sub set B, t-but > i-pro > Phenyl > H > Et > Me for sub set C.Among these groups t-But is the most feasible and Methyl group is least feasible due to the activation energy (Ea) and heat of formation. Steric bulk of the migrating group apparently does not play a major role here in stabilizing or destabilizing the transition state III, as seen from the maximum migratory aptitude of the bulky t-butyl group as compare with the low migratory aptitude of the very small hydride group the actual effect operating here is that, the transition state appear to be stabilized by migrating group which have greater capacity to carry +ve charge

Thus, from the data as Ea value is high the relative migratory aptitudes decreases, the reaction will be slow i,e. least feasible. The consensus appear to be the RMA which is affected chiefly by the kinetic factor which is linked to the activation energy barrier Ea. RMA depend upon the participation of the migrating group in the 1, 2-migration step so as to stabilize the electron deficient carbon in the transition state.

1.2 Enthalpy

The enthalpy indices here are as defined earlier in sub section and correspond to the step of (a) o-protonation of I (b) 1,2 migration in II leading to formation of IV via transition state III (c) deprotonation of IV to give V and (d) the net dienone-phenol rearrangement. The second step of the dienone-phenol rearrangement in 1, 2 migration of the group R2 in the resonance-stabilized intermediate II to give rearranged intermediate IV (also resonance-stabilized) via the TS III. This step is marked generally by a significant endothermicity, as seen from the calculated value of AHr, the enthalpy of rearrangement from II to IV. The enthalpy of rearrangement of AHr ranges from **-2.88** to **14.93 Kcal/mol** in AM1, and **6.08** to **67.23 Kcal/mol** in HF , and **-62,27 to 23.49 Kcal/mol** in B3LYP (Shown in table 6, 7 , 8). The mostly positive value for AHr indicates that the rearranged cation IV is usually less stable than the cation II . One thus predict that the old bond between the migrating group R2 and the migration terminus C-1in cation II would be stronger than the new one formed between the R2 and the migration origin C-2 in cation IV. The activation energy barrier Ea is related to the relative migratory facility of the migrating groups.

1.3 Kinetic and thermodynamic factor

Thermodynamically, the order for rearrangement facility is given by the enthalpy index. For the sub-set IA, the thermodynamic facility of rearrangement as represented by AHr in the following order with respect to the migrating group**. i-Bu > H > Et > i-Pro > Me > Penyl**. For sub set IB **is i-Pro > H > Phenyl > Et** > t-**But > Me.** For sub set IC ist-**Bu> Phenyl > i-Pro > H > Et > Me**. It is clear that the kinetic and thermodynamic factor do not furnish the same trends for any of these sub-sets. The consensus appear to be that RMA is affected chiefly by the kinetic factor which is linked to the activation energy barrier Ea.

1.4 Transition State Geometry

This sub-section describes the silent features of the geometries of the transition states involved in the concerted rearrangement of cation II to cation IV via the transition state III. These geometry determinants include the bond lengths (R1, R2, R3), bond angles (α, β, γ) and dihedral angles (ϕ1= (C3-C2-C1-X), ϕ2= (C1-C2-C3-Y)) as shown in the table 4.The hydride cases have the migrating C-3 atom, C1-H and C2-H bond length ranges from 1.246 to 1.446 A, which indicate a roughly equilateral shape. For the C1-C2 bonds, the range agrees with accepted value from normal C-C single bonds in sp^2 hybrid cationic species. The ranges for the C1-C3 and C1-C3 bond generally indicate C-C bonds is in a state of breaking and forming, and so are longer as a result. The different between the C1-C3 and C2-C3 bond length are not very large, and the triangular moiety generally ranges from isosceles in shape to a right angled triangle. While the short and normal C1-C2 (R_3) bond show non-participation of the C1-C2 bond in the migration. These values of the bond length and bond angles (see from Figure) indicate that the transition states geometries are from a right-angled to an isosceles triangle in shape

The bond angles α, β and γ indicate an almost equilateral triangular moiety for the hydride migration cases, but roughly isosceles or scalene triangles for the other cases as shown in Table 5. The C1-C3-C2 angles γ is markedly acute, ranging from 31.73 to 65.42A, where γ values for the alkyl group cases are smaller than those for the aryl/hetaryl group cases. The dihedrals φ1and φ2 indicate non-planar structures for the transition states, where the triangular moiety and the carbocyclic hexagonal moiety are not in the same plane. If one approximates the hexagonal carbo-cyclic moiety as a planer ring, then the dihedral angle between the triangular moiety and the hexagonal ring is given by φ1which ranges from 90.32 to 126.41A, where most cases indicate that these two planes are roughly perpendicular to each other.

The transition state geometry may also give clues to the relative position of the trasition state along the reaction pathway. One proposes here the ratio R_2/R_1 of the length of the breaking C1-C3 bond to that of the forming C2-C3 bond as an index to help indicate this position along the reaction coordinates. Smaller values of this ratio would indicate the transition state as relatively “early”, while larger values would indicate it as relatively “late”.

These assign-ments of “early” or “late” may then be compared with the degree of exothermicity or endotherm city of the reaction to validate Hammond’s postulate.

CONCLUSION:

Dienone –Phenol re-arrangement was studied in respect of relative migratory aptitude (RMA) for various substituents. It was found that different substituents have different abilities to migrate from one carbon to the adjacent carbon. RMA can be influenced by many factors. Kinetic factor is one of the key influencing factors to be pronounced. Among various groups it was found that t-butyl- is the most feasible while methyl group is the least. The reason of this is the ability of t-butyl group to retain charge through resonance stabilization compared to methyl group, this further lower the activation energy and thus facilitate 1,2 migration. Steric hindrance does not play a major role in relative migration aptitude for various migrating groups. Instead, bulky groups are greater stabilizer to electron deficient carbon than that of smaller groups.

Enthalpy also plays an important role in RMA. The more positive value of AHr (Endothermocity) is because of the fact that, Structure IV is less resonance stabilized than that of Structure II. Protonation and deprotonation steps also play an important role. The rearrangement involves protonation as its initial step which is stabilized by two resonating structures (II). Otherwise, protonation step will have high activation energy and will not be easily attained. Deprotonation takes place in structure IV to form structure V. We know that, in the formation of IV from III (TS). The positive charge formed at C-2 is resonance stabilized after migrating R from C-2 to C-1 thus making the migration easy. Since the positive charge formed at C-2 is stabilized by resonance, deprotonation from C-1 is facilitated. IN the course of migration, C-1 and C-2 bond does not change. This indicates that C-1 and C-2 do not take part during 1, 2 migration. While, The increase in bond length of C1-C3 and C2-C3 and forming isosceles triangle indicates that C1-C3 and C2-C3 are in a state forming and breaking and thus taking part in the migration. In structure III (TS) formation of dihedrals φ1and φ2 indicates the non-planar structure of the transition state.

Reference:

[1] Arnold R, Buckley J, Ritcher J. (1947).The dienone – Phenol rearrangement .Journal of American chemical society. 69 (10). 2322- 2325.

[2] Burnell R, Taylor W, (1954) Ring expansion. Part I. The Dienone – Phenol rearrangement of Spiro [5:5] undeca-1:4- Dinene-3-one. Journal of chemical Society (Resumed).3486-3488.

[3]Hanson J, Raines D, Knights S (1980). The preparation and dienone phenol rearrangement of androsta-2, 5-diene-4, 17-Dione. Journal of chemical society, Perkin Transaction 1.0.1311-1313.

[4] Miller B.(1965) Dienone-Phenol Rearrangements of 6- ALLycyclohexa-2,4-dienones and 4-allycyclohexa-2,5-dienones. Acid Catalysis of Cope Rearrangements. Journal of American Chemical Society.86 (22). 5115-5120.

[5] Joshua A.P,Dannenberg J(2011) A comparison of the Behaviour of Functional / Basis Set Combinations for Hydrogen-Bonding in the water Dimer with Emphasis on Basis Set Superposition Error. Journal of Computational Chemistry 32**:** 1519–1527.