ELSEVIER

Journal of Molecular Structure (Theochem) 587 (2002) 159–169

THEO CHEM

www.elsevier.com/locate/theochem

Theoretical study of the influence of phosphonate substituents on Diels–Alder reactions

R. Robiette[a], J. Marchand-Brynaert[a], D. Peeters[b,*]

[a]*Unité de Chimie organique et médicinale Bâtiment Lavoisier, Université Catholique de Louvain, place Louis Pasteur 1, B-1348 Louvain-la-Neuve, Belgium*

[b]*Laboratoire de Chimie Quantique Bâtiment Lavoisier, Université Catholique de Louvain, place Louis Pasteur 1, B-1348 Louvain-la-Neuve, Belgium*

Received 6 November 2001; received in revised form 7 February 2002; accepted 5 March 2002

Abstract

A theoretical study of the effect of a phoshonate substituent on carbon–carbon double bonds is presented and its influence on the reactivity in Diels–Alder reactions commented. Energetic, structural and electronic effects on displacement reactions between various references and their substituted counterpart are investigated. Both, conventional 6-31G(d,p) Hartree–Fock (RHF) and density functional theory (DFT), within the Becke's three parameter functional calculations are performed. Taking the cycloaddition of the butadiene on ethylene as reference, the influence of substitution at each position of reactants is discussed. For every possible substitution, reactants, transition states and products are obtained and analysed from a structural, energetic and electronic point of view. DFT and RHF results lead to the same conclusions.

Keywords: Cycloaddition reaction; Ab initio calculations; Phosphonate substituents; Transition state; Energy barriers

1. Introduction

Since its discovery in 1928 [1] by Otto Diels and Kurt Alder, the Diels–Alder (D–A) reaction has become one of the most powerful tools in organic synthesis. A tremendous amount of experimental and theoretical work has been devoted to the cycloaddition reaction between *cisoid* conjugated dienes and alkenes. This pericyclic reaction showed remarkable regio- and stereo-selectivities, leading to the formation of two carbon–carbon bonds and the creation of up to four chiral centres [2–14]. Moreover, the possibility of asymmetric induction has been demonstrated [15–18] for more than 30 years. Thanks to those properties, the D–A reaction is nowadays a method of choice for the construction of polysubstituted six-membered rings with high stereochemical control.

Aiming at the development of a new general strategy for the synthesis of β-, γ- and δ-aminophosphonic derivatives [19–24], we are interested in D–A reactions involving phosphorylated partners (dienes or dienophiles). Even though the [4 + 2] cycloadditions of partners substituted by a carbonyl function have been well documented [25,26], those involving phosphonic partners have been scarcely described. The results available show that phosphono-dienes and dienophiles are poorly reactive in D–A reaction [19–24,27–33]. The activation brought by a phosphonate group is dramatically lower compared to the

* Corresponding author. Tel.: +32-1047-2819; fax: +32-1047-2707.

E-mail address: peeters@chim.ucl.ac.be (D. Peeters).

0166-1280/02/$ - see front matter
PII: S0166-1280(02)00113-6

carbonyl group, while the ability of both functions to stabilize a negative charge created in α appears to be almost similar.[1]

The effect of a phosphonic function on the stabilization of a negative charge in α is now well understood owing to significant studies of Denmark [34–37] and Anders [38]. On the other hand, the stabilization of a carbon–carbon double bond by a phosphonic group and its possible effect of activation in pericyclic reactions have never been extensively studied. We are interested in understanding the reasons of the poor reactivity of phosphonic derivatives in [4 + 2] cycloadditions in opposition to their high reactivity in Michael addition. Therefore, we set up an ab initio study that, the first part of this paper analyses the effect of a phosphonate function on carbon–carbon bonds, and the second part comments on its influence on the reactivity in D–A reactions.

2. Methodological approach

The calculations have been performed with the Hartree–Fock and density functional methods using the GAUSSIAN series of programs [39]. The chosen basis set must be well balanced to obtain an adequacy between quality and cost. For a mechanistic approach including elements from the third row, at least double zeta polarised basis sets are required. The 6-31G(d,p) of Pople's group has thus been chosen to perform these calculations. Both conventional Hartree–Fock (RHF) and density functional theory (DFT), within the Becke's three parameter functional (B3LYP) [40], were used in order to check the sensitivity of the calculations on the nature of two electron distributions. The DFT approach should mimic the effect of some electron correlation and the convergence of these two methods towards a single description of the studied systems will comfort us in our interpretation of the results.

A full optimisation of each species has always been performed and the various conformations of the phosphonate group explored by rotating the functional group around the C–P bond. A PO_3H_2 group, where hydrogen atoms are positioned in an orientation avoiding external hydrogen bonds, models the phosphonate. For all studied compounds, such conformation of the group was maintained in order to obtain constancy within the substituent and to allow for a better comparison of the observed effects.

The energy properties of the substituents are studied through the use of isodesmic reactions [41,42] which allow an easy comparison between stabilisation/destabilisation effects due to structural or electronic factors.

The electronic structures have been studied by conventional Mulliken population analysis completed, when pertinent, by the Boys localisation method [43,44] and an NBO analysis [45–47].

Concerning the mechanistic approach, reactants are allowed to interact on the same potential energy surface (PES) and form a pre-reaction intermolecular complex. The rearrangement of such complex on the (3N-6) dimensions of the PES evolves further through the activated complex to the desired reaction product. Minima and transition structures are fully optimised at the chosen level using the second derivatives of the local PES. The correctness of the curvature and its eigenvector was checked in order to guarantee the quality of the obtained results and the reaction mechanism. For reactivity also, most of the discussion relies on a comparison between the effects induced by the substituent on a reference reaction, which we have chosen to be the simple addition of ethylene to butadiene.

3. Analysis of the properties of a phosphonate substituent

The best way to analyse the effect of a substituent is to compare its incidence on various reference molecules describing each a characteristic structural situation. In this work, a PO_3R_2 (R = H) substituent has been added onto references such as CH_4, C_2H_6, C_2H_4 and C_6H_6. The optimised results are discussed from an electronic, structural and energy point of view. While C_2H_5X (X = PO_3R_2) will furnish information on inductive effects, C_2H_3X and C_6H_5X will provide information on mesomeric effects.

3.1. Does PO_3R_2 induce stabilisation?

In order to answer such a question, we have

[1] The anion stabilization energies calculated by the isodesmic reaction $CH_3^- + CH_3R \rightarrow CH_4 + CH_2^-R$ at B3LYP 6-31G** level are −61.02 kcal mol^{-1} for R = COOH and −59.71 kcal mol^{-1} for R = PO_3H_2.

Table 1
Isodesmic reaction energies involving phosphonate substituents (kcal mol^{-1})

Reaction[a]	ΔE (RHF)	ΔE (DFT)
$CH_3P + C_2H_6 \rightarrow C_2H_5P + CH_4$	0.03	−0.48
$C_2H_5P + C_2H_4 \rightarrow C_2H_3P + C_2H_6$	−1.14	−1.54
$C_2H_5P + C_2H_4 \rightarrow C_2H_3P(a) + C_2H_6$	−0.17	−0.89
$C_2H_5P + C_6H_6 \rightarrow C_6H_5P + C_2H_6$	1.12	0.09
$C_2H_5P + C_6H_6 \rightarrow C_6H_5P(a) + C_2H_6$	–	0.34

[a] P represents systematically the PO_3H_2 functional group.

analysed the energy effect of a displacement reaction between various references and their substituted counterpart. If one admits that the reference molecules are not stabilised and that no peculiar effect should be obtained with methyl phosphonate, then the reaction energy of isodesmic reactions such as reported in Table 1, should bring direct information about (de)stabilisation induced by the substituent. One will notice that RHF and DFT results presented in the table are very close to each other. Further, the inductive effect that should appear in the first reaction is almost non-existent. Under the same conditions, an aldehyde substituent induces a much more impressive stabilising effect of −2.81 kcal mol^{-1} at RHF level and −3.20 at DFT level.

Looking at the effect of the substituent on a double bond, two conformers are obtained. The most stable presents the P=O bond located into the vinyl plane, while the other (denoted (a) in the Table 1) brings the P–OH bond into this molecular plane. This very small stabilisation close to −1.1 and −1.5 kcal mol^{-1} must be compared to the corresponding −4.4 and −5.8 values obtained for HC=O. This stabilisation is even lost when the substituent acts on a phenyl group. A first conclusion stresses that no peculiar effect, neither inductive nor mesomeric, is obtained by the phosphonate substituent, irrespective of the methodology being used.

3.2. The structural properties

The optimised structures obtained may lead to various conformations depending on the value taken by the dihedral rotation angle around the C–P bond. The most stable conformation will be considered. It is usually obtained with P=O and CC bonds lying in the same plane. The rotation along the C–P single bond does not change significantly the interatomic bond distances, as reported in Table 2. Even though the DFT method lengthens systematically the bonds compared to Hartree–Fock results, this table shows almost constancy within a chosen method, of those bonds involved in the phosphonate group. The structure of this substituent appears thus to be independent of the nature of binding carbon atom.

3.3. The electronic properties

We shall mainly focus on the global charges of the

Table 2
Interatomic distances in phosphonate substituent (Å)

Molecule[a]	Method	C–P	P=O	P–O	C–C(P)	Ref. (CC(H))
CH_3P	RHF	1.788	1.458	1.593		
	DFT	1.802	1.486	1.628		
C_2H_5P	RHF	1.795	1.459	1.595	1.532	1.527
	DFT	1.810	1.488	1.630	1.534	1.530
				1.586		
C_2H_3P	RHF	1.781	1.456	1.598	1.320	1.317
				1.619		
	DFT	1.792	1.486	1.633	1.334	1.330
				1.586	1.393	
C_6H_5P	RHF	1.790	1.456	1.598	1.389	1.386
					1.402	
	DFT	1.798	1.486	1.628	1.396	1.396

[a] P represents systematically the PO_3H_2 functional group.

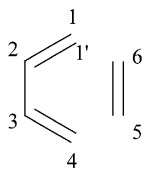
Table 3
Natural population analysis of some phosphonate reference compounds

CH_3P		C_2H_5P		C_2H_3P		C_6H_5P	
PO_3H_2	0.32	PO_3H_2	0.32	PO_3H_2	0.32	PO_3H_2	0.35
P	*2.64*	*P*	*2.64*	*P*	*2.63*	*P*	*2.66*
OH(2*)	*−0.55*	*OH*	*−0.56*	*O*	*−0.55*	*OH*	*−0.55*
O	*−1.21*	*O*	*−1.21*	*O*	*−1.21*	*O*	*−1.21*
CH_3	−0.32	CH_2	−0.36	CH	−0.49	C	−0.53
		CH_3	0.04	CH_2	0.17	CH *o*	−0.01
						CH *m*	0.07
						CH *p*	0.04

substituent obtained by a population analysis. As Mulliken and NBO charges show similar trends, only natural charges of some phosphonate reference compounds are reported in Table 3. The charge carried by the PO_3H_2 group is remarkably constant. The same constancy is found for the various constituents inside the group. All oxygen atoms are negatively charged and this charge is very impressive for the singly bounded oxygen. No dependency on the hybridisation of the bounded carbon group is found. No polarisation is detected, even when aromaticity is present. Nevertheless, the presence of a third row phosphorous element renders the bounded carbon atom very negative and the subsequent carbon skeleton of the chain polarises in a conventional way.

Localisation procedures leading to Boys localised orbitals and to natural localised orbitals [48] have also been applied to the Hartree–Fock wave functions in order to complete our description of the electronic structure of this functional group. Those two electronic structural analyses provide slightly different electronic descriptions depending on the method used but both are coherent with previous work performed on phosphine oxide [49] and lead to a very polar PO bond centred close to the oxygen atom which is surrounded by three lone pair orbitals.

To summarise this first part, one concludes that the functional phosphonate group presents a very constant internal structure that does not interfere significantly with the neighbour groups and can be transferred from one environment to another. No peculiar inductive or mesomeric effects seem to be accounted for, but the phosphorous atom itself appears, in any case, to be a good electron donor to its attached atoms, especially the singly bonded oxygen which is strongly charged. As these conclusions may be extended to any other studied compound, the analysis will not be reported except when new information, pertinent to the discussion, is brought.



Scheme 1. Numbering of the carbon atoms.

4. The phosphonate substituted Diels–Alder reaction

Before discussing the reaction mechanism, it is worthwhile to comment on the various reactants and products of the reaction and try to find out if the conclusions obtained for phosphonate substituents on reference molecules are retrieved. The numbering of the carbon atoms is presented in Scheme 1.

4.1. Global reaction and positioning of the substituent

For substituted butadienes as well as for cyclohexenes, various conformations of the phosphonate group are found. In butadienes, the most stable conformation is obtained when the P=O bond lies in the C=C plane. Energy differences between rotamers are found close to 1 kcal mol^{-1}. It is slightly higher in the $1'$ position, due to the influence of neighbour hydrogen atoms, which will stabilise the obtained conformation. In cyclohexenes, P=O adopts a staggered position versus the CH bond but the other conformers are all very close (within 1 kcal mol^{-1}).

Concerning butadienes, *transoid* conformations are

Table 4
Characteristic data of conformers around the C2–C3 bond (angles in degrees, energies in kcal mol^{-1})

	Ref.		1		$1'$		2	
	RHF	DFT	RHF	DFT	RHF	DFT	RHF	DFT
$\Delta E_R(cis)$	3.01	3.52	3.10	3.41	4.96	5.27	0.70	1.45
θ	39.0	30.4	36.1	26.3	49.2	40.7	42.1	35.1
$\Delta E^{\ddagger}_{Rot}$ (*trans* → *cis*)	6.06	7.55	6.36	7.79	7.24	8.87	3.08	4.52
$\theta^{\ddagger}$	102.0	100.1	100.9	98.9	93.7	94.9	104.6	98.6
$\Delta E^{\ddagger}_{Rot}$ (*cis* → *cis*)	0.87	0.35	0.64	0.21	2.00	2.31	1.20	0.65

the most stable. As the reaction, to take place, requires a rotation around the C2–C3 bond, such an analysis has been performed and Table 4 provides the corresponding relative energies. The butadiene molecule, taken as reference, is also reported in the table. As the *cisoid* conformer is generally not planar, θ dihedral angles are given for this conformation as well as for the rotational transition state. The corresponding energy barriers are also provided. The main information obtained from this analysis is that the substitution of hydrogen by phosphonate has almost no effect on the results at position 1. The situation at position $1'$ is quite different but is coherent with a steric hindrance induced by the substituent. Substitution on carbon 2 presents the lowest rotation barrier and a very small isomerisation energy. Such observation may result either from a stabilisation of the *cisoid* structure or from the destabilisation of the *transoid* structure. Table 5, which gives some isodesmic reaction energies of the various partners of the reaction, attempts to bring some insight into this question. Indeed, the phosphonate exchange with ethane for 2-substituted *trans* butadienes is endothermic by 2.7(1.66) kcal mol^{-1} while it is thermoneutral for *cis* butadienes (0,38; −0,41) and slightly exothermic with ethylene (Table 1). These data show clearly that the 2-substituted *trans* butadiene is destabilised rendering the *cis*/*trans* isomerisation process easier. A 2 kcal mol^{-1} stabilisation is obtained for substitution at position 1, but this stabilisation appears on both conformers, maintaining the barrier at the level of butadiene.

Concerning substituted cyclohexenes, the most stable isomer is obtained at position 2. The other isomers lie in a range from 3 to 5 kcal mol^{-1}. In ascending order: 6eq (3 kcal mol^{-1}) < 1 (3.5–4.0 kcal mol^{-1}) < 6ax (5 kcal mol^{-1}). Table 5 permits also to comment on the influence of the substituent on cyclohexene. The stabilisation obtained for the phosphonate on the double bond is slightly greater than in ethylene (Table 1) while in position 6, the equatorial substitution is clearly preferred, even though no further stabilisation is obtained. For 1 substituted cyclohexene, the distinction between the axial and equatorial positions is illusory, but a slight destabilisation is observed.

The global reaction energies are given in Table 6. Once more, relative energies show that the obtained results are close to the reference but always unfavourable as the exothermicity decreases slightly except for position 2 that presents a greater exothermic reaction energy. This results from the cumulative effect of an already mentioned destabilisation of the diene, and a stabilisation of the product.

Table 5
Isodesmic reaction energies (kcal mol^{-1}): XP + RH → XH + RP

X	R	RHF	DFT	RHF	DFT	RHF	DFT
		1		$1'$		2	
C_2H_5	tr. C_4H_5	−2.08	−2.53	−0.06	−1.33	2.69	1.66
C_2H_3	tr. C_4H_5	−0.94	−0.99	1.08	0.21	3.83	3.20
		1		6		2	
C_2H_5	C_6H_9 ax	0.93	0.77	3.17	1.88	−2.17	−3.14
C_2H_5	C_6H_9 eq	1.01	0.29	0.70	0.04	–	–

Table 6
Reaction energies (kcal mol^{-1} with respect to the *trans* diene)

Substituted at position	ΔE_R ($\Delta\Delta E_R$)[a]	
	RHF	DFT
Ref.	−41.59(0.00)	−42.18(0.00)
1	−38.58(3.01)	−38.88(3.30)
1′	−40.60(0.99)	−40.08(2.10
2	−46.45(−4.86)	−46.98(−4.80)
6	−39.75(1.84)	−40.59(1.59)

[a] $\Delta\Delta E_R = \Delta E_R$(reaction) − ΔE_R(ref.).

4.2. Transition states

As for reactants, the optimised transition state structures may lead to various conformers depending on the value of the dihedral rotation angle around the C–P bond. Once again, energy differences between rotamers are small and close to 1 kcal mol^{-1} except, as already mentioned for the reactants, at position 1′. The most stable rotamer is systematically obtained when the P=O bond lies in the C=C plane. Only the latter will be considered from now on. In the case of substitution at position 6, both *endo* and *exo* configurations of the transition states will be considered.

4.2.1. The structural properties

Six parameters define the global approach of the two species towards the transition state. The four most pertinent are presented in Fig. 1. R and $\alpha 1$ describe the distances and angular approach between the centres of the two moieties. $\alpha 2$ shows the in plane shift of the dienophile while finally $\alpha 3$ brings information about its orientation. We report in Table 7 the value of these parameters for the reference reaction and their variation in the various reactions. This variation appears to be small.

Table 7
Reaction governing parameters

		R (Å)	$\alpha 1$ (deg)	$\alpha 2$ (deg)	$\alpha 3$ (deg)
TSref.	RHF	2.839	−39.9	90.0	84.2
	DFT	2.898	−40.4	90.0	82.5
		ΔR (Å)	$\Delta\alpha 1$ (deg)	$\Delta\alpha 2$ (deg)	$\Delta\alpha 3$ (deg)
TS1	RHF	0.020	−0.4	1.4	1.2
	DFT	0.004	−0.4	2.0	2.0
TS1′	RHF	0.022	1.35	1.1	0.5
	DFT	0.015	0.84	1.6	1.3
TS2	RHF	−0.001	−0.3	2.7	−2.7
	DFT	0.003	−0.6	2.1	−3.3
TS6 *endo*	RHF	0.008	0.1	2.4	1.1
	DFT	0.013	0.3	2.7	1.8
TS6 *exo*	RHF	−0.018	−0.6	2.7	0.0
	DFT	−0.011	−0.3	3.5	1.3

The results presented in Table 7 reveal quite similar approaches of the two species for every studied reaction. If the presence of a phosphonate function does not influence significantly the global angular approach ($\alpha 1$, $\alpha 2$ and $\alpha 3$) nor the distances (R) of the two reactants, the substitution of one partner gives rise however to an asynchronicity in the concerted mechanism as shown by the variation of C1–C6 and C4–C5 distances (Table 8). The C1–C6 bond is systematically longer while the formation of C4–C5 is more advanced than in the reference (TSref). As

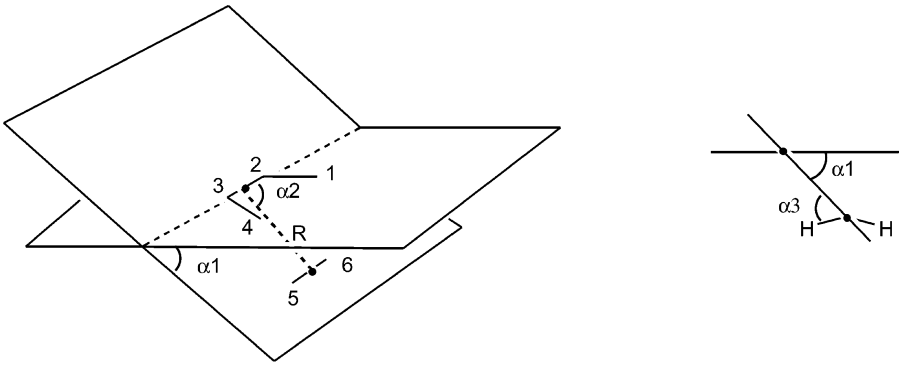


Fig. 1. Parameters of the approach of the two partners for the D–A reaction.

Table 8
Structural data of the transition states

		C4–C5 (Å)	C1–C6 (Å)	
TSref.	RHF	2.200	2.200	
	DFT	2.269	2.269	
		ΔC4–C5 (Å)	ΔC1–C6 (Å)	ΔC–P (Å)[a]
TS1	RHF	−0070	0.074	0.002
	DFT	−0.098	0.085	0.001
TS1′	RHF	−0.037	0.108	−0.011
	DFT	−0.069	0.133	−0.014
TS2	RHF	0.075	−0.048	−0.011
	DFT	0.108	−0.058	−0.013
TS6 *endo*	RHF	−0.068	0.092	−0.008
	DFT	−0.091	0.126	−0.007
TS6 *exo*	RHF	−0.083	0.115	−0.012
	DFT	−0.122	0.166	−0.014

[a] Difference with the C–P bond in the corresponding phosphorylated reactant.

anticipated by FMO theory, TS2 constitutes an exception as in this case the asynchronicity acts in opposite.

At the transition state, bond lengths and angles of the PO_3H_2 group remain almost constant and close to those of the related molecules, such observation being independent of the chosen method. The phosphonate function does not influence appreciably the internal structure of the two reactive moieties whatever the position adopted (1,1′, 2 or 6). Covalent bond lengths differ by less than 0,01 Å with substitution.

Some variations of the C–P distance are nevertheless observed as reported in Table 8. The bond length for TS1 still shows constancy while it is shorter in TS1′ when compared to the corresponding diene. This shortening of the C–P bond should however be induced by electronic effects or important steric hindrance, or both. At TS2 and TS6, an increase of the electronic interaction between the butadiene or vinyl moiety with the PO_3H_2 group may be considered.

Table 9
Isodesmic reaction energies (kcal mol^{-1}): C_2H_5P + TSref → TSP + C_2H_6

	RHF	DFT
TS1	−1.76	−2.77
TS1′	3.33	1.27
TS2	−1.44	−1.67
TS6 *endo*	−2.73	−2.75
TS6 *exo*	−2.78	−3.21

Table 10
Activation energies (kcal mol^{-1}) of the studied D–A reactions

Substitution at position	$\Delta E^{\ddagger}(\Delta\Delta E^{\ddagger})$[a]	
	RHF	DFT
Ref.	45.27(0.00)	22.43(0.00)
1	45.59(0.32)	22.19(−0.24)
1′	48.68(3.41)	25.03(2.60)
2	41.51(−3.76)	19.10(−3.33)
6 *endo*	43.69(−1.58)	21.22(−1.21)
6 *exo*	43.64(−1.63)	20.76(−1.67)

[a] $\Delta\Delta E^{\ddagger} = \Delta E^{\ddagger}$(reaction) − $\Delta E^{\ddagger}$(ref.).

4.2.2. The energy properties

The relative stabilizations with substitution, at the transition states of the studied D–A reactions are summarized in Tables 9 and 10. The isodesmic reactions presented in Table 9 may be compared to those of Table 1. They show obviously that substitution by a phosphonate group stabilizes systematically transition states except for TS1′ where the important steric hindrance leads to a global destabilization.

The stabilization of the transition state by a phosphonic group in position 1 is quite similar to those obtained for corresponding reactants (Table 5) leading to a calculated activation barrier comparable to those of the reference (Table 10). The results presented in Table 10 show that substitution at positions 2 and 6 leads to a significant decrease of the activation barrier. This is due to a higher stabilization of the respective transition states compared to corresponding reactants. While 1-phosphono-1,3-butadiene seems to be relatively similar to 1,3-butadiene, the substitution of the diene at position 2 or of the ethylene should increase the rate of the D–A reaction.

4.2.3. The electronic properties

Global natural charges deduced from an NBO analysis of each moiety are reported at Hartree–Fock level in the Table 11.

The substitution increases the electron transfer between the two partners at the transition state. The electronic population on the substituted partner is systematically increased compared to the reference

Table 11
Natural population analysis of the transition states

	TSref	TS1	TS1′	TS2	TS6 *exo*	TS6 *endo*
PO_3H_2		0.33	0.33	0.33	0.32	0.32
C_4H_6	0.00	−0.40	−0.38	−0.38	0.11	0.11
C_2H_4	−0.00	0.06	0.05	0.04	−0.43	−0.43

(TSref). The substitution of the dienophile increases the electronic transfer in the way of a normal electronic demand D–A reaction while the substitution of the diene gives rise to an inverse electronic demand. The presence of a phosphonate group also influences greatly the charge distribution within each partner; the carbon substituted by the phosphorus is systematically negatively charged. This electronic distribution of the phosphono-partner induces an opposite and thus complementary polarization of the second partner. This shows obviously the electron withdrawing character of the phosphonic group.

5. Discussion

The energetic pathways of the studied D–A reactions, calculated at the B3LYP 6-31G(d,p) level, are represented in Fig. 2. The relative energies were

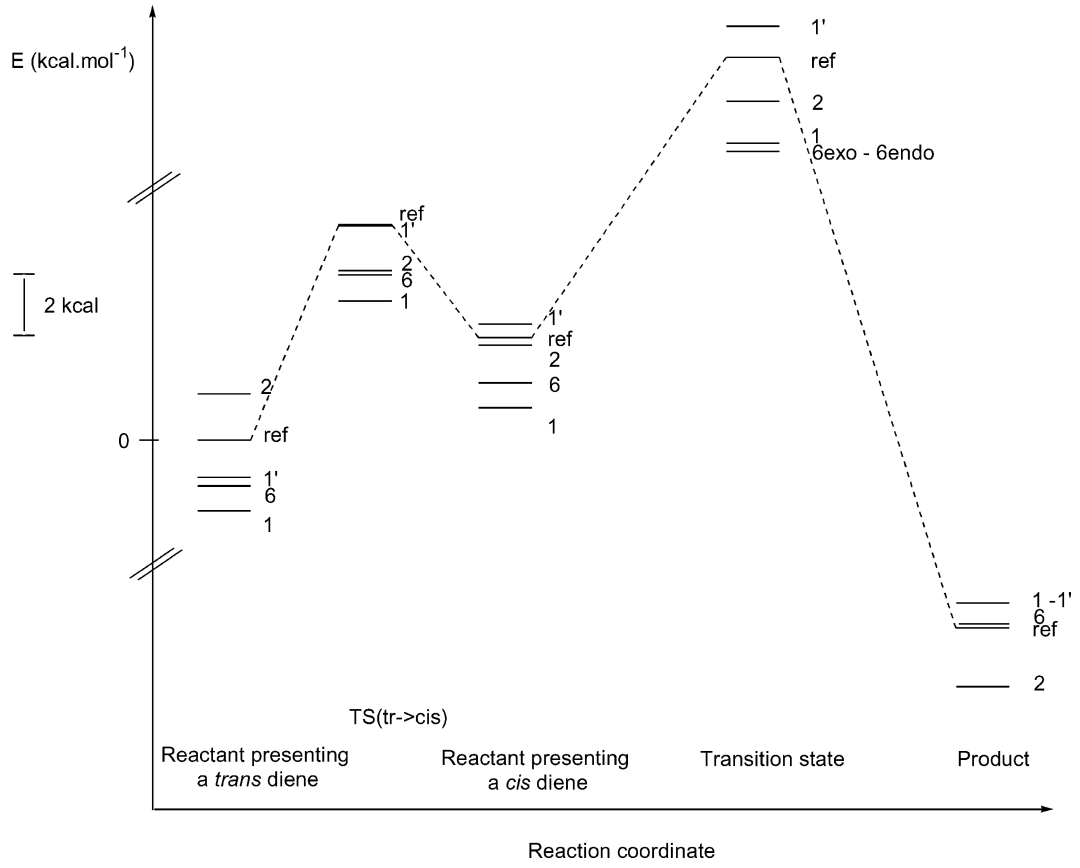


Fig. 2. Energetic pathways of the studied D–A reactions.

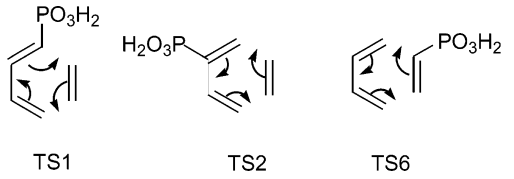


Fig. 3. Schematic electron pair migrations during the D–A reaction.

calculated by the following isodesmic reactions.

$$C_2H_5PO_3H_2 + R\text{–}H \rightarrow C_2H_6 + R\text{–}PO_3H_2$$

where R stands for any reactant, product or transition state.

Those energetic pathways show obviously that the substitution by a phosphonate function stabilizes systematically each structure (except when important steric hindrance overcome the electronic stabilization). The (de)stabilizations of the transition states TS1 and TS1′ are quite similar to those of the *trans* conformer of the corresponding dienes. The substitution at positions 2 or 6 gives rise, on the other hand, to a higher stabilization of the transition state compared to the *transoid* reactants. This higher stabilization of the transition state TS6 compared to the reactants explains fully the lowering of the activation barrier of the D–A reaction by substitution of the ethylene with a phosphonate group. In the case of the diene 2, the substitution increases the relative energy of the *trans* conformer of the diene, presumably by steric interactions which furthermore decreases the activation barrier. In this case the acceleration of the reaction is then due to the stabilization of the transition state combined to a destabilization of the ground state of the reactants.

Because the steric hindrance created by the phosphonic function must be similar (or lower) in the *cis* conformer of the diene and at the transition state for each reaction, the difference in stabilization energy observed with substitution at positions 2 and 6 suggests the appearance of an electronic effect due to the phosphonate function at the transition state (Fig. 2). The shortening of the C–P bond length at the TS2 and TS6 compared to those observed in the corresponding reactant confirms such an interaction between the PO_3H_2 group and the reactive moieties. The variation of charges within the carbon skeleton at transition state supports this interpretation. However, no specific electronic interaction can be identified from the analysis of the structure and charges within the PO_3H_2 group (Table 11). Furthermore the NBO analysis reveals no significant delocalisation of the carbon–carbon π bond towards the σ^*(P–OH) nor an increase of the P–OH bond distance as it should be the case for the stabilization of a negative charge as described by Anders [38]. Finally, the similitude of the results (from an energetic, structural and electronic point of view) shown by both, Hartree–Fock and DFT methods reinforces our interpretation.

To complete this discussion, a Boys localisation of the molecular orbitals along the reaction coordinate has been performed. The analysis of the migration of the centroïds of charges gives us a clear picture of the electronic displacements near the transition state. It reveals that the presence and position (1,1′, 2 or 6) of a phosphonate group influences significantly the electronic reorganisation in the activated complex. As expected, the exothermic character of the reactions gives complexes, which resemble closely to the reactants. After crossing the transition state, the migration of the centroïds towards the products intervene. These are symbolically represented by the arrows of Fig. 3. Results obtained show obviously that the effect of the phosphonate group is sufficient to inverse the direction of the electronic displacements in the case of substitution at position 1 compared to substitution at positions 2 or 6. This would be predicted by simple resonance theory assuming an electronic withdrawing mesomeric effect of the phosphonic substituent. The absence of specific interaction (see above) and of electronic transfer between PO_3H_2 and the carbon skeleton leads us nevertheless to conclude that a phosphonate function has no mesomeric effect. The PO_3H_2 group acts conversely through an inductive (Coulombic) and polarisation effect helping the electronic transfer between the two reactive moieties. Hence, the shortening of the C–P bond length might be explained by the fact that electrostatic energy and then stabilisation by polarisation have a high distance dependence; effective stabilisation requiring then a short C–P distance.

6. Conclusion

In this paper we have studied the effect of a phosphonate substituent on carbon–carbon bonds and

commented on its influence on the reactivity of D–A reaction.

The analysis of the energetic, structural and electronic effect of displacement reaction between various references and their substituted counterpart has revealed a very constant internal structure of the phosphonate function, which does not interfere significantly with the neighbour groups. A small stabilisation (1.1 and 1.5 kcal mol^{-1}) is however observed when a carbon–carbon double bound is substituted by a phosphonate group.

No decrease of the activation barrier of the D–A reaction is observed when the butadiene is substituted with a phosphonate group at position 1 or $1'$. The presence of a phosphonate substituent on the ethylene or at position 2 on the diene should induce conversely an acceleration of the D–A reaction.

If the acceleration of the D–A reaction by substitution on the ethylene and not by substitution at position 1 of the diene could be explained by the previous work of Fujimoto [50], the decrease of the activation barrier in the case of the substitution of the diene in position 2 compared to the substitution in position 1 is opposite to the expected result. Previous work has indeed shown that substitution at position 1 increases more efficiently the reactivity than the corresponding substitution at position 2 [10,12] Until now, the study of the influence of the substitution position on the reactivity has however only been realized for substituents with predominant mesomeric effect. The substituents having a predominant inductive effect, such as PO_3H_2, seems to have unlike influence.[2]

Aiming to complete the study of the influence of a phosphonate substituent on the reactivity in D–A reaction we examine currently the cycloaddition of a phosphonic reactant (diene or dienophile) with partners substituted by electronic donor or withdrawing groups looking to a possible synergic effect.

Acknowledgements

The authors are indebted to the Belgian National Fund for Scientific Research (FNRS) and the Fonds pour la Reherche dans l'Industrie et l'Agriculture (FRIA; grant to RR) for their financial support to this research. They would like also to thank the FNRS for its support to access computational facilities (FRFC project No. 2.4556.99 'Simulations numériques et traitement des données').

[2] To be published.

References

[1] O. Diels, K. Alder, Justus Liebigs Ann. Chem. 460 (1928) 98.
[2] W. Carruthers, Cycloaddition Reactions in Organic Synthesis, Tetrahedron Organic Chemistry Series, vol. 8, Pergamon Press, Elmsford, NY, 1990.
[3] K.N. Houk, Acc. Chem. Res. 8 (1975) 361–369.
[4] B.R. Beno, K.N. Houk, D.A. Singleton, J. Am. Chem. Soc. 118 (1996) 9984–9985 and references therein.
[5] J. Sauer, R. Sustmann, Angew. Chem. Int. Ed. Engl. 19 (1980) 779–807.
[6] R.E. Townshend, G. Ramunni, G. Segal, W.J. Hehre, L. Salem, J. Am. Chem. Soc. (1976) 2190–2198.
[7] N.T. Anh, E. Canadell, O. Eisenstein, Tetrahedron 34 (1978) 2283–2288.
[8] S.D. Kahn, C.F. Pau, L.E. Overman, W.J. Hehre, J. Am. Chem. Soc. 108 (1986) 7381–7396.
[9] J.M. Coxon, R.D.J. Froese, B. Ganguly, A.P. Marchand, K. Morokuma, Synlett 11 (1999) 1681–1703.
[10] K.N. Houk, J. Am. Chem. Soc. (1973) 4092–4094.
[11] O. Eisenstein, J.M. Lefour, N.T. Anh, R.F. Hudson, Tetrahedron 33 (1977) 523–531.
[12] R. Sustmann, Tetrahedron Lett. 29 (1971) 2721–2724.
[13] S.L. Craig, A.J. Stone, J. Chem. Soc., Faraday Trans. 90 (1994) 1663–1668.
[14] S. Damoun, G. Van de Woude, F. Méndez, P. Geerlings, J. Phys. Chem. A 101 (1997) 886–893.
[15] H.B. Kagan, O. Riant, Chem. Rev. 92 (1992) 1007–1019.
[16] J.D. Morrison, H.S. Mosher, Asymmetric Organic Reactions, Prentice Hall, Englewood Cliffs, NJ, 1971 p. 252.
[17] L.A. Paquette, in: J.D. Morrison (Ed.), Asymmetric Synthesis, vol. 3B, Academic Press, New York, 1984, p. 455.
[18] W. Oppolzer, Angew. Chem. Int. Ed. Engl. 23 (1984) 876.
[19] N. Defacqz, R. Touillaux, B. Tinant, J.-P. Declercq, D. Peeters, J. Marchand-Brynaert, J. Chem. Soc., Perkin Trans. 2 (1997) 1965.
[20] N. Defacqz, R. Touillaux, J. Marchand-Brynaert, J. Chem. Res. (S) (1998) 512.
[21] N. Defacqz, R. Touillaux, J. Marchand-Brynaert, J. Chem. Res. (M) (1998) 2286.
[22] J. Marchand-Brynaert, N. Defacqz, R. Robiette, in: S.G. Pandalai (Ed.), Recent Research and Development in Organic Chemistry, Transworld Research Network, Trivandrum, India, vol. 5 2001 pp. 2632–2637.
[23] R. Robiette, J. Marchand-Brynaert, J. Chem. Soc., Perkin Trans. 2 (2001) 2155–2158.
[24] N. Defacqz, R. Touillaux, A. Cordi, J. Marchand-Brynaert, J. Chem. Soc., Perkin Trans. 1 (2002) 2632–2637.
[25] R.J. Loncharich, F.K. Brown, K.N. Houk, J. Org. Chem. 54 (1989) 1129–1134.

[26] D.A. Evans, S.J. Miller, T. Lectka, P. von Matter, J. Am. Chem. Soc. 121 (1999) 7559–7573.
[27] W.M. Daniewski, C.E. Griffin, J. Org. Chem. 31 (1966) 3236.
[28] M. Majjei, G. Buono, New J. Chem. 12 (1988) 923.
[29] S.D. Darling, N. Subramanian, Tetrahedron Lett. 38 (1975) 3279.
[30] C.K. McClure, K.B. Hansen, Tetrahedron Lett. 37 (1996) 2149.
[31] E. Ohler, E. Haslinger, E. Zbiral, Chem. Ber. 115 (1982) 1028.
[32] C.E. Grifin, W.M. Daniewski, J. Org. Chem. 35 (1970) 1691.
[33] S.D. Darling, N. Subramanian, J. Org. Chem. 40 (1975) 2851.
[34] S.E. Denmark, C.J. Cramer, J. Org. Chem. 55 (1990) 1806–1813.
[35] C.J. Cramer, S.E. Denmark, P.C. Miller, R.L. Dorow, K.A. Swiss, S.R. Wilson, J. Am.Chem. Soc. 116 (1994) 2437–2447.
[36] M.K. S, E. Denmark, J. Org. Chem. 60 (1995) 5867–5877.
[37] M. Kranz, S.E. Denmark, K.A. Swiss, S.R. Wilson, J. Org. Chem. 61 (1996) 8551–8563.
[38] R. Koch, E. Anders, J. Org. Chem. 60 (1995) 5861–5866.
[39] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery, Jr., R.E. Stratmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, A.G. Baboul, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, J.L. Andres, C. Gonzalez, M. Head-Gordon, E.S. Replogle, J.A. Pople, GAUSSIAN 98, Revision A.7, Gaussian, Inc., Pittsburgh PA, 1998.
[40] A.D. Becke, J. Chem. Phys. 98 (1993) 5648–5652.
[41] W.S. Hehre, R. Ditchfield, L. Radom, J.A. Pople, J. Am. Chem. Soc. 92 (1970) 4796.
[42] P. George, M. Trachmann, C.W. Bock, Tetrahedron 32 (1976) 317.
[43] S.F. Boys, Rev. Mod. Phys. 32 (1960) 296.
[44] S.F. Boys, in: P.O. Löwdin (Ed.), Quantum Theory of Atoms, Molecules and the Solid State, Academic Press, New York, 1966, p. 253.
[45] J.P. Foster, F. Weinhold, J. Am. Chem. Soc. 102 (1980) 7211.
[46] A.E. Reed, F. Weinhold, J. Chem. Phys. 78 (1983) 4066.
[47] A.E. Reed, R.B. Weinstock, F. Weinhold, J. Chem. Phys. 83 (1985) 735.
[48] A.E. Reed, F. Weinhold, J. Chem. Phys. 83 (1985) 1736.
[49] D.G. Gilheany, Chem. Rev. 94 (1994) 1339–1375.
[50] H. Fujimoto, S. Inagaki, K. Fukui, J. Am. Chem. Soc. (1976) 2670–2671.