

S_N2 reactions with allylic substrates—Trends in reactivity

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Received 3 November 2006; received in revised form 7 February 2007; accepted 7 February 2007

Available online 13 February 2007

Dedicated to Jean Futrell, gentleman and scientist.

Abstract

The gas-phase identity S_N2 reactions of allylic substrates has been studied by systematic altering of the nucleophile/nucleofuge X, the remote substituent Y, and the number of methyl substituents at the reaction centre: $X^- + YCHCHCZ_2X \rightarrow YCHCHCZ_2X + X^-$ ($X = H, CH_3, NH_2, F, Cl$; $Y = F, OH, H, CHO, BH_2$; $Z = H, CH_3$). Key regions of the potential energy surfaces have been explored by MP2, B3LYP, G3B3 and G3 calculations; the latter two methods providing accurate estimates of the reaction barrier. The calculations show that irrespective of theoretical level, for the second row of the periodic table ($X = CH_3, NH_2, OH, and F$), the tendency is that the barrier height decreases in going from left to right in agreement with the previously observed trend for identity S_N2 reactions at methyl. The barrier height decreases by introduction a π electron withdrawing substituents, Y, remote from the reaction centre. The barrier height increases by introducing methyl groups ($Z = CH_3$) next to the reaction centre, but the effect is less than half of that of changing the remote substituent from $Y = CHO$ to $Y = OH$. The trends cannot be explained by simplified valence bond theory and are discussed in light of a simple electrostatic bonding model of the transition structure.

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Keywords: Ab initio calculations; Basicity; Nucleophilic substitution; Reaction mechanisms; Nucleophilicity

1. Introduction

More than a hundred years after it was recognized [1], the S_N2 reaction continues to fascinate chemists. Despite a vast amount of information from synthetic and mechanistic studies of nucleophilic substitution reactions in solution and despite the quite helpful rule-of-thumb explanations of S_N2 reactivity given in textbooks [2–5], the molecular characteristics that steer the outcome and velocities of nucleophilic substitution reactions are still under investigation and debate, and the underlying electronic structure relationships are rather poorly understood. There exists a very valuable literature on quantum chemical modelling of S_N2 reactions, which was recently critically reviewed [6]. It was concluded in that review and elsewhere [7–9] that accurate energy barriers can only be expected when electron correlation is treated extensively—for example using quadratic configuration interaction with single and double excitations, and triple exci-

tations added perturbatively (QCISD(T))—while at the same time employing large atomic basis set. For this reason the consistency of early calculations of barriers [10–22] by simpler and more approximate methods like HF and MP2 with small and medium sized basis sets should be reconsidered. With the advent of practically useful and accurate methods for routine quantum chemical calculations during the last 10 years, we are now in a much better situation than before in correctly describing the intrinsic molecular factors that determine the rate of S_N2 reactions.

For any nucleophilic substitution of this kind (only the anionic case is illustrated)



there is a number of factors that influence the course and the rate of reaction. The primary factors are associated with the nature of the entering and leaving groups X^- and Y^- (nucleophile and nucleofuge) and the alkyl group R of the substrate. In addition, an important contribution comes from the solvent. In order to unravel the intrinsic molecular factors we take advantage of the great simplification obtained by investigating the reaction in vacuo. This has obvious computational advantages. We simplify

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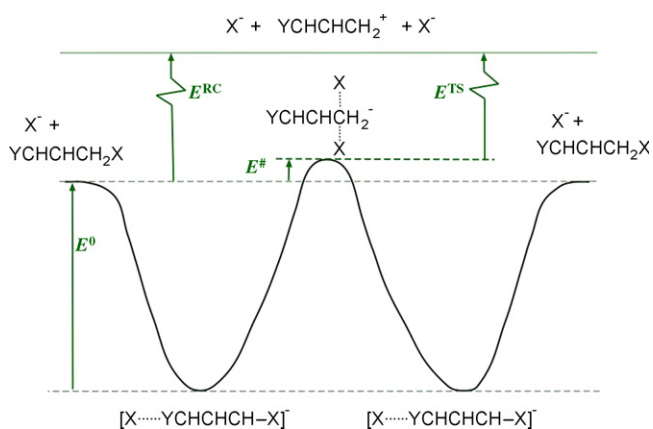


Fig. 1. Generalized potential energy diagram for an identity S_N2 reaction of an allylic substrate in the gas phase. In addition to the reactant and product states, there are minima corresponding to reactant and product complexes. In between these double-well potential is the local maximum, corresponding to the symmetrical transition structure.

the matter further by eliminating any thermodynamical driving force by putting $X = Y$, assuming validity of the Hammond and Marcus type formulations [7,22–25]. By restricting ourselves to identity S_N2 reactions for a given R, we are in a very comfortable situation realizing that the intrinsic nucleophilicity and nucleofugacity of any X^- is fully described by only one parameter, namely the energy barrier, $E^\ddagger = E^{TS} - E^{RC}$ for the reaction (Fig. 1).

For reactions on methyl substrates, $R = CH_3$, it has been found that intrinsic nucleophilicity is correlated with ionization energy [26]. Interestingly, while F^- is an extremely strong nucleophile in this sense, NH_2^- is a poor one. Intrinsic nucleophilicity has also been associated with electronegativity [17,18,27] and position in the periodic table [28].

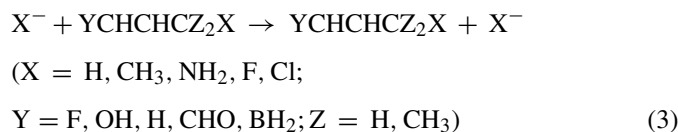
An S_N2 reaction can often be described by a double-well potential energy function of Fig. 1 where the minima represents association complexes between the reactants and product, respectively, while the maximum separating them is due to the well known umbrella inversion transition structure (TS) [29,30]. There are exceptions for very exothermic reactions for which the central barrier may disappear [31]. If $E^\ddagger > 0$ the rate-determining step is passage through the TS. In some cases, and typical for substitution at other elements than carbon – in particular for elements below the second row – the symmetrical $X-R-X$ structure is a minimum rather than a first order saddle point of the potential energy surface, reflecting the ability for pentacoordination around these atoms [32,33].

Although methyl with its attractively simple structure has been the mostly studied, other substrates have also been at the centre of interest. To this end the evidence is unclear in terms of reactivity trends. Higher alkyl groups demonstrate “normal” reactivity (tertiary > secondary > primary > methyl) in cationic identity reactions between ammonia and protonated amines [34], while this reaction trend is reversed for reactions between water and protonated alcohols [35]. This apparently puzzling situation is due to differences in relative stabilization between TS and RC (Fig. 1) due to the influence of increasing number of

methyl substituents at the central carbon atom. Increasing the number of methyl groups results in reduced binding of the X group for both TS and RC, but to a different degree, depending on X. Some authors have claimed a benzylic effect meaning that in S_N2 reactions of benzyl derivatives the π electron system stabilizes the transition structure thereby favouring reaction [13,27,36,37]. In general π electron accepting substituents – also in substrates without $C=C$ double bonds – appear particularly favourable, although some of the experimental and theoretical evidence seems somewhat conflicting and difficult to interpret. One simple and intriguing model system for studying these effects is reactions with allyl ($R=CH_2CHCH_2$) with its relatively small size and built-in possibility of fine-tuning the electronic properties by appropriate substituents. The effect on reactivity of the nucleophile on the reaction



was investigated in great detail 12 years ago by Lee et al. employing HF and MP2 in conjunction with the 6-31G++(d,p) basis set [27,38]. They concluded that the activation process is related to the electronegativity of the R and X groups. Recently, Streitwieser et al. performed HF/6-31 + G(d) calculations in which substituent effects were studied [39]. Both Streitwieser et al. and Lee et al. provide interesting results, but based on rather modest level calculations compared to current standards. The validity of their HF and MP2 calculations – in particular the calculated barrier heights – is unfortunately uncertain, and should be compared to higher level estimates now at hand. The plan of the present work was to redo some of their calculations at a more reliable level of theory, and to significantly broaden the scope by extending calculations to include effects not previously studied. This will be of particular importance in firmly establishing reactivity trends based on the nature of the nucleophile, the structure of the substrate and substituent effects [40,41]. To obtain this we report the results of systematic altering of the nucleophile/nucleofuge X, the remote substituent Y, and the number of methyl substituents at the reaction centre for the reaction



2. Methods

Quantum chemical calculations were carried out using the program system Gaussian 03 [42]. Relevant critical points (reactants, transition structures (TS), and products) of the potential energy surface were characterised by complete optimisation of the molecular geometries using the hybrid density functional scheme B3LYP [43] with the 6-31G(d) basis set, which is abbreviated by B3LYP/6-31G(d) as well as Møller Plesset perturbation theory (MP2) [44] with the same basis set. Relative energies (B3LYP and MP2) were calculated by including unscaled zero-point vibrational energies (ZPVE). When practically possible, i.e., for Z=H, energies were also calculated

Table 1

Geometrical and energetical data for the reaction $X^- + \text{CH}_2\text{CHCH}_2\text{X}$. Energy barriers are in kJ mol^{-1} , while bond distances are in Å. See Fig. 2 for definition of bond distance parameters

X	MP2/6-31G(D)								B3LYP/6-31G(D)								G3	G3B3
	r_1	r_2	r_3	R_1	R_2	R_3	R_4	E^\ddagger	r_1	r_2	r_3	R_1	R_2	R_3	R_4	E^\ddagger	E^\ddagger	E^\ddagger
H	1.34	1.50	1.10	1.34	1.47	1.67	1.67	140.0	1.34	1.50	1.10	1.34	1.47	1.72	1.72	78.9	156.57	156.4
CH ₃	1.34	1.49	1.53	1.35	1.46	2.13	2.13	132.0	1.33	1.50	1.54	1.34	1.46	2.21	2.21	98.8	151.58	147.8
NH ₂	1.34	1.50	1.47	1.35	1.46	2.02	2.02	56.4	1.33	1.51	1.47	1.35	1.46	2.09	2.09	26.0	91.16	89.0
OH	1.34	1.49	1.43	1.35	1.46	1.89	1.89	-19.6	1.33	1.50	1.43	1.35	1.47	1.93	1.93	-48.7	28.81	26.7
F	1.34	1.49	1.40	1.34	1.47	1.78	1.78	-75.3	1.33	1.50	1.40	1.34	1.47	1.81	1.81	-115.8	-12.64	-14.5
Cl	1.33	1.49	1.80	1.34	1.46	2.36	2.36	24.4	1.33	1.49	1.83	1.33	1.46	2.45	2.45	-24.8	5.24	9.5

using G3 and G3B3. G3 [45] is a composite computational scheme which involves initial geometry optimizations at the HF/6-31G(d) level and subsequent calculation of ZPVEs at the same level of theory. Then the geometry is re-optimized at the MP2(full)/6-31G(d) level whereupon a number of single-point MP2, MP4 and QCISD(T) calculations are performed in order to obtain an energy estimate which is effectively QCISD(T)/G3Large. G3B3 [46] uses the same higher levels as G3, except that geometries and frequencies are calculated using B3LYP/6-31G(d). Relative energies obtained by G3 and G3B3 are therefore almost identical provided structures are approximately the same.

3. Results and discussion

3.1. Nucleophile/nucleofuge X

Table 1 provides barrier heights and the most essential geometrical parameters obtained by variation of X keeping $Y = R = \text{H}$. The geometrical parameters are defined in Fig. 2.

Irrespective of theoretical level, we observe that within the second row of the periodic table ($X^- = \text{CH}_3^-$, NH_2^- , OH^- and F^-) the tendency is that the barrier height decreases in going from left to right. We also note that the barrier is somewhat

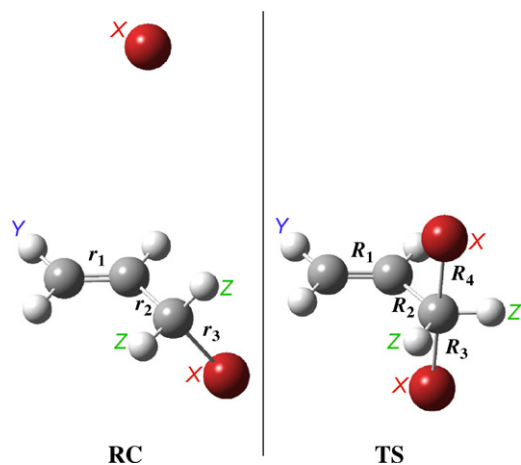


Fig. 2. Optimized structures of reactants and transition structure showing the most essential geometrical parameters obtained by variation of X keeping $Y = R = \text{H}$.

higher for Cl^- than for F^- . This is the same trend that has been noticed previously for identity $\text{S}_{\text{N}}2$ reactions at methyl [7,26,28]. In the case of substitution on allyl substrates, Lee et al. reported that for HF/6-31 + G(d) the barrier for Cl^- is lower than for F^- , while their corresponding MP2 values show the same trends as ours [27]. They did not report any value for $X^- = \text{CH}_3^-$. One should note that relative to the other nucleophiles the barrier for Cl^- is lower with B3LYP and MP2 than with G3.

The periodic trend $\text{CH}_3^- > \text{NH}_2^- > \text{OH}^- > \text{F}^-$ correlates with the corresponding trends in both basicity and electronegativity within the row. In the previously studied case with $R = \text{CH}_3$, the best over-all fit for all nucleophiles – independent of row – was obtained by correlating the barrier heights with the ionization energies [26]. It was concluded that the different measures for electron-donating power (ionization energy, proton affinity, electronegativity, polarizability volume) are interrelated and also related to size. In effect, they all express chemical hardness/softness in different ways [47–49]. A consistent picture emerged from these observations, namely that a nucleophile with a high IE (e.g., F^-) will give rise to strong polar C–X bonds in the TS, whereby little electron density is donated from the attacking nucleophile to the methyl cation [26]. This is supported by Joubert et al. who analysed the electron transfer process during the reaction $\text{Cl}^- + \text{CH}_3\text{Cl} \rightarrow \text{CH}_3\text{Cl} + \text{Cl}^-$ applying Bader's atoms-in-molecules theory on relatively accurate electron densities [50]. They found that a majority of the charge is transferred directly from the incoming chloride to the outgoing, having its maximum at the TS. We note that these results are at odds with the qualitative valence bond picture of Shaik who suggested that a high ionization energy of the nucleophile would lead to a high barrier [37].

As already stated, the qualitative reactivity trends we obtain using MP2/6-31G(d) are in good agreement with the trends found by Lee et al. using MP2/6-31G + (d,p) but the absolute MP2/6-31G(d) barriers are systematically lower. On the other hand, the geometrical features of reactants and transition structures are not much affected by which of the two basis set is used in conjunction with MP2. The same qualitative periodic reactivity trend is reproduced with B3LYP/6-31G(d) but the barrier heights are even lower than with MP2/6-31G(d). There is, however, one noticeable difference between the MP2 and B3LYP results, namely a tendency for longer C–X bonds (R_3) at the TS with the latter, despite C–X bonds in the substrates (r_3) are similar with the two methods. The B3LYP values for R_3 are

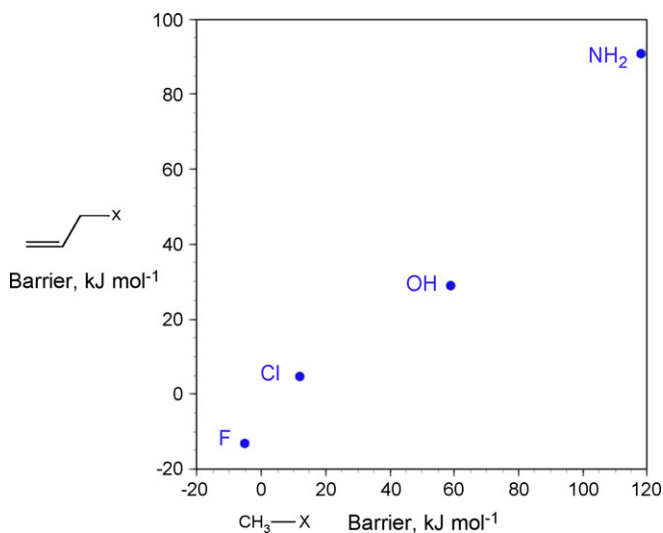


Fig. 3. Relationship between barrier height (E^\ddagger) between allyl and methyl substrates.

invariably longer for B3LYP than MP2, although the difference never exceeds 5%.

From Table 1 we see that the very similar and assumingly more reliable G3 and G3B3 barriers are considerably higher than the corresponding figures obtained using MP2 and B3LYP. The trend $G3 > MP2/6-31G(d) > B3LYP/6-31G(d)$ has been seen previously for S_N2 reactions on methyl [34,51]. In fact, the absolute barrier heights obtained by the latter two methods are so much lower than the high level estimate that it is questionable whether they are of any real value. We would, however, expect that this deficiency could be overcome to some degree by extending the basis set used with MP2. There is some evidence in the literature for this [17,18,27], although a systematic study has not been yet done to verify the assumption. In the case of DFT methods, the underestimated barrier has been inferred to the self-interaction error in both in the exchange and correlation parts of the energy expression leading to an artificial large delocalization of the electron density. This has been discussed at some length by several authors [50,52,53]. Despite the shortcomings of B3LYP and MP2, we have seen that some of the periodic reactivity trends ($CH_3^- > NH_2^- > OH^- > F^-$) are quite well reproduced, while others (Cl^-) are not.

One of the predictions to be made from the present data is that an identity S_N2 reaction on allyl substrates in vacuo in all cases is expected to be faster than on methyl substrates for any nucleophile/nucleofuge X. This can be loosely associated with a benzyl effect. The barriers for the corresponding reaction on methyl substrates are on an average 25 kJ mol^{-1} higher. This number was obtained by comparing the present G3 data on the allyl reactions with literature G2 data on the corresponding methyl reaction [26,34]. The G2 data are within a few kJ mol^{-1} identical to the corresponding values obtained by the very accurate focal-point method [9]. The relationship between allyl and methyl is illustrated in Fig. 3, which also shows that – to the limit of the quite sparse amount of data available – the relationship is linear.

Both G3 and G3B3 are expected to provide accurate values for barrier heights. Since the two methods use exactly the same wave functions and basis sets for obtaining the high level estimates, any deviation is due to differences in geometries and zero point vibrational energies. Typically, the values agree very well – although we detect that in the few cases when the B3LYP and MP2 bond lengths disagree by up to 5% the difference becomes noticeable – never exceeding 4 kJ mol^{-1} . Both zero point vibrational energy differences and the geometry differences contribute approximately equally to the observed differences.

3.2. Substituent Y

At this point we introduced substituents Y to investigate the effect of regulating the electron density at the reacting carbon centre. The naïve idea is that an electron donating or electron withdrawing substituent will influence the transition and reactant structures in different ways, and thereby affect reactivity. It was important to find a way to fine tune the electronic properties of the allyl group without interfering with the steric bulk around the reaction centre. For this reason the substituent Y was positioned as remotely from the reaction centre as possible, in line with the arrangement of Streitwieser et al. [39]. At the onset of the study our hypothesis was that – compared to $Y = H$ – substituents F and OH would act as electron donors to the π electron system of the allyl moiety while BH_2 and CHO would be electron accepting.

The G3B3 barrier heights for the series with $Y = H, F, OH, BH_2$ and CHO are plotted against the corresponding value for $Y = H$ in Fig. 4. The plot was constructed to display the susceptibility of the barrier height to any particular substituent Y as a function of the nucleophile. The trends are very clear, since the barrier heights (with one minor exception) vary with the

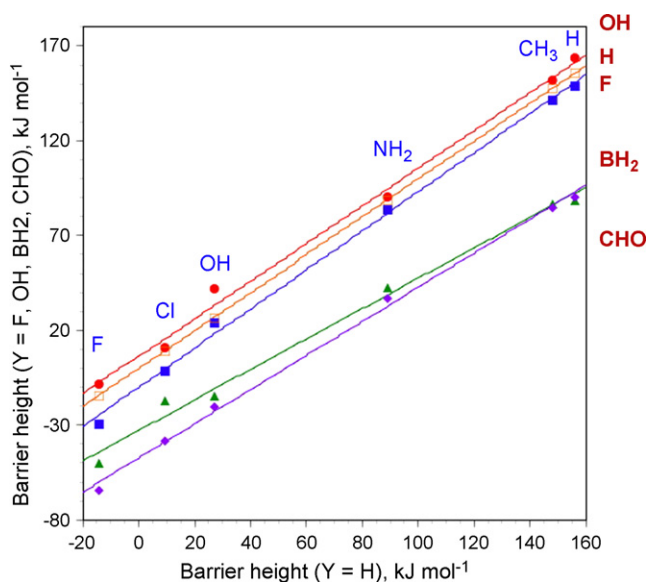


Fig. 4. Variation of the barrier height (E^\ddagger) by introducing the substituents Y (indicated in the column at the far right) barrier heights relative to $Y = H$. One line has been fitted to the data for each substituent. The nucleophiles X^- are indicated within the plot.

substituent according to $\text{CHO} < \text{BH}_2 < \text{H} < \text{F} < \text{OH}$. Before we discuss the significance of this finding in more detail, a commentary on accuracy is required. From the data presented in Fig. 4, it is clear that the anticipated π electron donating substituent OH decreases reactivity. This is contrary to the finding of Streitwieser et al. using HF/6-31 + G(d) [39] but in agreement with expectation. Therefore, we must not only conclude that HF, MP2 and B3LYP to varying degree are inadequate for the purpose of calculating barrier heights with high confidence, but HF is also unreliable in predicting reactivity trends.

The plots of Fig. 4 indicate good linear behaviour with respect to variation of the substituents Y relative to the standard situation with Y = H. This is remarkable, since it shows a stringent pattern for all nucleophiles studied with no apparent synergy, perhaps with a slight exception for X = Cl. Furthermore, with the exception of BH_2 giving a slightly less steep line, the susceptibility of the reaction barrier to all substituents is the same. We want to mention that also the corresponding MP2 and B3LYP plots are linear, showing essentially the same dependence on the substituent, except that the order is $\text{CHO} < \text{BH}_2 < \text{F} < \text{H} < \text{OH}$ in both cases. In addition – compared to G3B3 which predicts X = Cl to lie between OH and NH_2 – MP2 and B3LYP predicts it to lie between F and OH.

The average difference in barrier heights for the extreme substituents OH and CHO is 60 kJ mol^{-1} . The corresponding variation in geometrical parameters is surprisingly small. As a matter of fact, we do not observe any clear pattern in how the geometries of neither reactant nor transition structure change depending on the substituent. The only obvious conclusion we may draw is therefore that there is a purely electronic effect in operation in which electron-donating substituents destabilize the TS more than the RC without effecting bond lengths or angles to any significant degree. We realize that the electronic property of a given substituent is not uniquely defined, but is an empirical factor, which has been inferred from different physicochemical experiments. The consensus seems to be that CHO and BH_2 are both π and σ electron acceptors compared to H, while OH and F are π donors but σ acceptors. To analyze our data we also applied Hammett correlations, using the sigma(+) and sigma(p) sets (we found no value for BH_2 in the literature). A qualitative correlation was found supporting the statements given above on the electronic properties of the substituents. We noted, however, some quantitative discrepancy for Y = F. In this connection we would like to mention that the complicated topic of substituent effect has been comprehensively and critically reviewed very recently [40,41]. In this picture it is clear that it is the π electron properties that influence the reactivity—a notion that is reasonable judging from a simple TS model with a carbocation symmetrically sandwiched between the incoming and outgoing nucleophiles—an “exploded” TS [13,27,36,39]. In this simplified electrostatic picture it seems logical that any substituent capable of removing electron density away from the central carbon will accelerate reaction by attracting the two nucleophiles X even stronger. This effect is illustrated by the fact that twisting the BH_2 group 90° relative to the allylic plane and performing geometry optimization gives a second TS that is 97 kJ mol^{-1} higher in energy compared to the one in which BH_2 is in the

Table 2

C–C bond lengths of the allylic cations and zero Kelvin bond dissociation energy, E^{RC} , for the processes $\text{YCHHCCH}_2\text{OH} \rightarrow \text{YCHHCCH}_2^+ + \text{OH}^-$ obtained by G3B3

Y	ρ_1	ρ_2	$E^{\text{RC}} (\text{kJ mol}^{-1})$
H	1.38	1.38	937.1
F	1.39	1.37	916.5
OH	1.41	1.36	820.6
BH_2	$1.38^* (1.40)$	$1.45^* (1.37)$	$922.3 (908.0)^a$
CHO	1.39	1.38	979.3

^a The indicated values refer to a planar allylic structure (C_s) that corresponds to a TS, while the values in brackets refer to the more stable minimum structure in which the BH_2 unit is perpendicular to the allylic plane. The ρ values correspond to the C–C bond length in analogy to the definitions given in Fig. 2.

allylic plane. In reality, the situation is more complicated than this, since not only the amount of stabilization of the TS but also the amount of stabilization of the substrate must be considered. The latter can be analyzed by comparing the heterolytic bond dissociation energies



The data for X = OH are presented in Table 2 and shows that the electron accepting substituents CHO and BH_2 stabilizes the reactant configuration compared to Y = H, while Y = OH has a destabilizing effect. An equivalent dissociation reaction giving the same reference state ($\text{YCHCHCH}_2^+ + 2\text{OH}^-$) can be defined for the TS (Fig. 1). The corresponding E^{TS} values show the same trend as the E^{RC} data, but are more strongly dependent on the influence of the substituent. The resulting barriers, $E^\ddagger = E^{\text{TS}} - E^{\text{RC}}$ reflect this in the $\text{CHO} < \text{BH}_2 < \text{H} < \text{F} < \text{OH}$ trend. Also in this case we are surprised by the small variation in the geometrical parameters. The two equivalent C–OH bonds in the TS vary by only 0.03 \AA , being largest for Y = OH and smallest for Y = CHO, which, nevertheless, seems to be in harmony with the trend in barrier heights.

3.3. Effect of methyl substitution, $Z = \text{CH}_3$

By substituting the hydrogens at the reaction centre by methyl groups we wanted to examine to which degree the size and the electronic properties of this substitution may affect reactivity. Separation of the two effects can be achieved by varying this substitution ($Z = \text{H}$ or CH_3) while at the same time systematically varying the Y groups. The remote substitution is expected to primarily affect the electronic structure. By including the effect of the nucleophile as well, the problem is therefore essentially equivalent to determining a three dimensional functional mapping, $E^\ddagger(X, Y, Z)$. The sheer size of the task dictates some modesty in the choice of methods, and this part of the study was conducted using only MP2 and B3LYP. As we have already discussed, we will be careful to draw too much out of MP2 and B3LYP data in terms of absolute values of observables, although most qualitative trends appear qualitatively right with these methods.

Fig. 5 shows the general trend in reactivity by substituting $Z = \text{H}$ by $Z = \text{CH}_3$. As we see from the plots, both B3LYP and

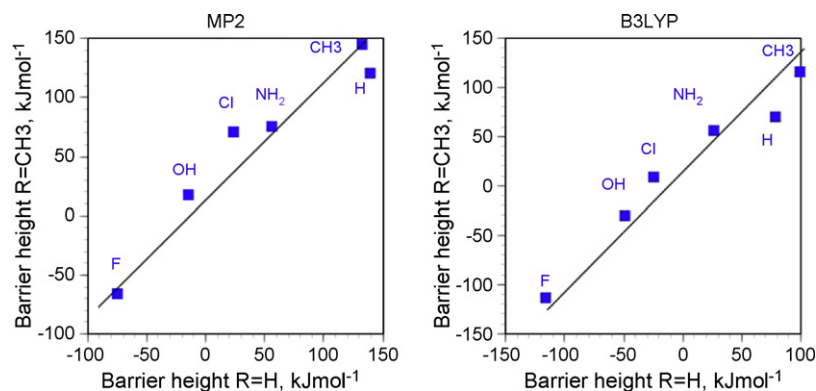


Fig. 5. Trend in reactivity in terms of barrier height (E^\ddagger), substituting $Z=H$ by $Z=CH_3$ with MP2/6-31G(d) and B3LYP/6-31G(d), respectively.

MP2 predict the barriers for allyl and the corresponding dimethyl substituted substrate to be 25 kJ mol^{-1} higher, putting the bulky $\text{CH}_2=\text{CHC}(\text{CH}_3)_2$ at the same reactivity level as the plain CH_3 . We would like to underline the fact that this number should be regarded to be of much better quality than the MP2 or B3LYP data themselves since it is derived on the basis of systematic trends. The correctness of the estimate is further supported by consideration of the reactivity trends found by variation of Y . Although absolute barrier heights appear too low, both MP2 and B3LYP give essentially the same linear relationships as that illustrated for G3B3 in Fig. 4 in the case of $Z=H$ (for actual plots see Supplementary material). It is furthermore relieving to find the same trends also for $Z=CH_3$ (also Supplementary material), safeguarding our analysis. In other words, the susceptibility for the reaction upon changing the Y s is exactly the same for $Z=H$ as for $Z=CH_3$. The significance of this lies in the fact that the variation in barrier height by going from $Y=\text{CHO}$ to OH is more than two times that of changing the two hydrogen atoms to two methyl groups. The TS geometries are more “exploded” for $Z=CH_3$ than for $Z=H$, but not much so. For the second row nucleophiles the values of R_3 and R_4 (the C–X distances) increase by on an average 0.04 \AA upon dimethylation for both MP2 and B3LYP, by itself not much of a steric effect. In addition to this general trend it is noticeable, in particular for MP2 – as one reviewer has suggested – that size also may have some additional effect, since we note that the small nucleophiles (H and to some extent F) tend to lie below the trend line, while the large (Cl) is above.

4. Conclusion

Based on the findings reported here and in previous papers, the electronic reasons behind identity $\text{S}_{\text{N}}2$ reactivity now appear clearer, and a consistent picture emerges. An electronegative nucleophile (high ionization energy) will give rise to a TS having highly polar C–X bonds, thereby promoting strong bonding. A substrate with a strongly electropositive central carbon in its corresponding carbocation will give rise to a likewise polarized TS, resulting in strong bonding E^{TS} . To obtain an estimate of the reaction barrier, this amount of binding must be compared with the corresponding stabilization of the substrate bond being broken, E^{RC} . Normally, the difference $E^\ddagger = E^{\text{TS}} - E^{\text{RC}}$

results in low barriers for the combination of an allylic substrate and an electronegative nucleophile. The barrier height decreases by introduction a π electron withdrawing substituents, Y , at the most remote position relative to the reaction centre and increases by electron donating substituents. Increased methyl substitution at the central carbon lowers binding at the TS mainly due to electron donation to the carbon, and less to a steric effect—in any instance a term which is difficult to define precisely. Typically, this will give rise to decreasing reactivity with increasing substitution (text book behaviour), although in a few previously studied cases of particularly weak C–X binding in the substrate, the trend may be reversed from that of the text book [35,51,54]. These principles may be extended to more general systems. For example, it explains well the observations that the symmetric $[\text{X}-\text{CH}_3-\text{X}]^+$ structures for $\text{X}=\text{He}$ and Ne are energy minima, rather than saddle points [55]. For other central elements than carbon, below and left in the periodic table, the detailed binding situation is of course different and will require separate analysis of the contributions to $E^\ddagger = E^{\text{TS}} - E^{\text{RC}}$. It is, however, well known that $\text{S}_{\text{N}}2$ at the electropositive sulphur and phosphorus atoms gives rise to low energy symmetric minimum energy structures rather than transition structures [33,56,57], a finding in harmony with our simple electrostatic model. In conclusion, we note that the reactivity trends cannot be explained by a simplified valence bond theory model, as previously suggested [37], since this predicts the opposite trend for nucleophile reactivity as obtained from high level electron structure calculation.

Acknowledgement

The authors are grateful to VISTA – a research cooperation between the Norwegian Academy of Science and Letters and Statoil – for providing R.A.O. with a postdoctoral scholarship.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijms.2007.02.005.

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