General Discussion

Prof. Shaik opened the discussion of Prof. Schleyer's paper: (1) Is the magnetic susceptibility exaltation limited to cyclic delocalization, or would you see this phenomenon also for cases with linear delocalization?

(2) Is the Li^+ acceleration effect special for aromatic transition states?

(3) Is the acceleration correlated with the polarizability differences between transition states and ground states?

Prof. Schleyer replied: (1) Magnetic susceptibility exaltation does appear to be limited to cyclic delocalization. Dauben *et al.* examined several highly delocalized polymethenium salts of the type $R_2N(CH=CH)_nCH=NR_2^+$ which have essentially equal CC bond lengths. These so-called 'linear aromatics' showed no magnetic susceptibility exaltation. We have examined conjugated polyenyl cations and also find no exaltation. It probably would be useful to restrict the term 'aromaticity' to systems with cyclic delocalization and refer to linear and to Y-conjugation rather than 'linear aromatics' and 'Y-aromatics'.

(2) The Li^+ acceleration effect is not necessarily associated with aromatic transition states. The stereomutation of methane and the degenerate rearrangement of the atoms in acetylene is strongly accelerated by Li^+ complexation. On the other hand, not all aromatic transition states are stabilized preferentially by Li^+. The degenerate cyclic exchange involving three H_2 molecules is not accelerated significantly by Li^+.

(3) We have computed the polarizability differences between ground and transition structures in too few cases to ascertain if there is a correlation with the acceleration. I doubt if polarizability is the only effect involved.

Prof. Francl said: If magnetic susceptibility exaltation is to be used as a signature for aromaticity, what would you recommend as a cut-off value for aromatic compounds? Some of the values presented seem very close to me. For example, cyclopentane has an exaltation of about 3, and is clearly not aromatic, while one of your aromatic examples had an exaltation of around 5.

Prof. Schleyer replied: Ultimately, the answer to your question will depend on the degree of variation in the group susceptibility increments as a function of structure in non-aromatic reference compounds. However, thus far we have not found differences due to strain, conformational changes *etc.* The ring size and number of electrons also are important. A diamagnetic susceptibility exaltation of 5 ppm cgs in a three-membered ring system probably is significant, but not in a ten-membered ring.

Prof. Williams said: In your lecture you mentioned that the transition-state energy for the Cope rearrangement of semibullvalene is lowered relative to that of the reactant molecule when zero-point energy effects are included in the computations of the Li^+ complexation. As described in our paper at this Symposium, this 'inversion' of potential-energy surfaces is actually observed for the radical cation derived from semibullvalene, and this is attributed to the large cationic stabilization energy that results from the reduction in ionization potential (*ca.* 2 eV by calculation) of the neutral molecule in going to the transition state. Given that the b_2 HOMO of the semibullvalene transition state (Fig. 3 of my paper) is essentially a through-space combination of *nonbonding* allylic orbitals, can you indicate the likely extent of radical cation character introduced by Li^+ complexation in this favourable case?

Prof. Schleyer replied: Thank you for pointing out this relationship and, in effect, calling attention, to the large changes often noted in going from hydrocarbon systems to their radical cations. This is another strategy which can be used to reduce or eliminate rearrangement barriers in pericyclic reactions. Nevertheless, I do not think that radical cation character of the hydrocarbon moiety contributes to the acceleration effects we observe upon Li^+ complexation. As the charge on the lithium cation is nearly unity and remains so, no charge transfer is evident. Furthermore, essentially the same acceleration effect is computed when the lithium cation is replaced by a point positive charge.

Prof. Houk said: You have discovered interesting new information about pericyclic transition structures, and the diamagnetic exaltation is a very interesting way to confirm and quantify the aromaticity of these species.

I have related questions about the calculated chemical shifts in the transition structures.

(1) You note the upfield shifts of the hydrogens 'inside' the Diels–Alder and hexatriene electrocyclic transition states. Perhaps coincidentally, we calculate anomalously high secondary deuterium isotope effects for these same hydrogens in these transition structures. This indicates high bending HCC force constants for these hydrogens due to steric crowding. Could this influence their chemical shifts?

(2) In Möbius aromatic transition states, such as cyclobutene openings and octatetraene cyclizations, there is formally no difference between the top and bottom of the π cloud. Will this influence the ring-current effects? Have you calculated chemical shifts for protons in transition states of pericyclic transition structures involving Möbius aromatic systems?

Prof. Schleyer replied: (1) This is an interesting analogy, but I doubt if the same effects which result in anomalously high secondary deuterium isotope effects are responsible for the upfield chemical shifts we compute. Crowding may influence chemical shifts, but to a lesser extent. We find pronounced upfield proton chemical shifts in cases where no crowded environments are involved.

(2) The Möbius transition structures we have investigated had C_2 symmetry (*i.e.* both sides are the same), but the ring-current effects (magnetic susceptibility exaltation and displacement of the hydrogen chemical shifts) are quite pronounced. The existence of a ring current in an electron-delocalized cycle is important, whatever the overall symmetry of the species may be.

Dr. Reynolds said: In the light of your comment that rate acceleration of hydrocarbon reactions by Li^+ is not observed experimentally because of the lack of a suitable medium for Li^+, could you comment on whether you have investigated methods for including the solvent and, if not, could you also predict how you would expect such calculations to affect your results?

Prof. Schleyer replied: The simplest method to investigate solvation effects would be to complex the Li^+ with one or more model solvent molecules. Alternatively, continuum models can be employed (self-consistent reaction field, SCRF) or a combination of the two. Actually, we have been aiming to find large influences, rather than ways to attenuate them!

Since Li^+ binds moderately strongly to unsaturated hydrocarbon substrates, acceleration effects might be observable in the gas phase or in saturated hydrocarbon solvents with a very weakly binding gegenanion. Perhaps the large electrostatic fields in zeolites would function similarly. Our findings are quite new, and practical applications have not yet been explored.

Dr. Mitchell said: The ability of Li^+ to lower the energy of a transition state is of interest in relation to the possible catalytic behaviour of Li^+ and other cations acting as Lewis acids. It was not clear, however, from your presentation whether Li^+ was merely a probe for aromatic character in the transition state or whether Li^+ was inducing aromaticity. It would also be helpful to know if the lowering of the activation energy was due to interaction of the transition state with the Li^+ or to the induction of aromaticity. Do Li^+, and other cations, also lower the energy of non-aromatic transition states?

Prof. Schleyer replied: We have examined the Li^+ accelerating effect with a set of model calculations. If Li^+ is replaced by a point charge, the energy difference between ground and transition state remains essentially the same. This also is true, if the charge plus the lithium orbitals (i.e. the basis set expansion of the Li-less systems) are both employed. However, the lithium orbitals alone have very little effect relative to the parent hydrocarbon systems. The magnetic susceptibility exaltation of the transition structure is nearly the same whether or not Li^+ is present; hence, I do not think Li^+ acts primarily to induce or increase aromaticity, although there is some change in the geometries.

The problem in studying antiaromatic transition structures is that they cannot be located properly computationally. By imposing symmetry, stationary points might be found, but these have a higher order (more than one imaginary frequency) and are not true transition structures. However, we have computed some remarkably large Li^+ accelerations, e.g. for rearrangements in which aromatic transition states are not involved.

Prof. Borden said: You have said that 'aromatic' transition states are polarizable and also have large diamagnetic ring currents. However, polarizabilities increase with the proximity of filled and unfilled orbitals, as do paramagnetic ring currents, provided that the filled and unfilled orbitals can be mixed by a magnetic field. Is the resolution of the apparent paradox that you have presented that in aromatic transition states the proximate filled and unfilled orbitals have the wrong symmetry to be mixed by a magnetic field? I suspect this to be the case. Since they have different numbers of nodes, mixing the filled and empty orbitals in an aromatic system does not give rise to orbital angular momentum and, hence, does not give rise to paramagnetic ring currents.

Prof. Schleyer replied: Although we have carried out polarizability calculations which do indicate transition states to be more polarizable than ground states, we do not know if this effect is sufficiently large to account for the Li^+ electrostatic accelerations. Your thoughtful comment needs further

examination. The IGLO program does provide a break-down of the total magnetic susceptibility into diamagnetic, paramagnetic (as well as non-local) contributions. In the systems we have examined, the paramagnetic contributions generally are small, but there are some exceptions. Prof. Kutzelnigg and his group have considered these contributions in detail in some cases, but we have not carried out a systematic analysis at Erlangen.

Prof. Shaik communicated: I note with much interest that what you so invincibly showed is that the magnetic susceptibility exaltation is a mark of the topology of electronic delocalization: the topology that we call 'aromatic'. At the same time your analysis showed that this property belongs to stable molecules as well as to transition states. Do you observe any dependence of the exaltation on the stability of the 'aromatic' species, namely, whether it is a transition state or a stable ground state?

Prof. Schleyer replied: The diamagnetic susceptibility exaltation is known to depend on the number of delocalized electrons as well as the radius of the 'ring-current' cycle. It should also depend on the 'degree' of delocalization, but it does not seem to matter whether a ground state or a transition state is involved.

Several electrocyclic transitions structures we have examined have diamagnetic susceptibility exaltations somewhat greater than those of benzene.

In a collaborative study with Prof. Peter Freeman (who was a sabbatical-year guest at Erlangen), we have analysed the aromaticity/antiaromaticity in five-membered ring carbocycles ($C_5H_5^+$ and $C_5H_5^-$), and a number of heterocyclic analogues. The aromatic stabilization energies were evaluated by using appropriate five-membered ring reference compounds. We find a remarkably linear relationship between these aromatic stabilization energies and the magnetic susceptibility exaltation, both diamagnetic (for the aromatic species) and paramagnetic (for the antiaromatic systems). While it may be premature to generalize these findings, they suggest that it may be possible to develop suceptibility exaltations into a quantitative measure of cyclic delocalization.

Of course, such electron delocalization is only one of the energy contributions. Thus, one cannot expect a correlation between the diamagnetic susceptibility exaltation and e.g. the degree of concert of a pericyclic process when 'strain' and steric factors are important.

Prof. Michl communicated: Qualitatively, I would guess that the extra polarizability in an aromatic transition state appears in the 'aromatic plane', which is not where the Li^+ ion or the extra positive charge was located in most of the calculations you have told us about. This suggests that even larger effects might be predicted at other geometries, with the positive charge in this 'plane'.

I wonder whether the non-uniform nature of a central field is important and whether it would be useful to calculate the polarizability tensor for the transition state, i.e. look at the energy change in a uniform electric field and predict changes in the activation energy from that.

Prof. Schleyer replied: These are interesting suggestions for further investigation. In my lecture, I attributed electrostatic acceleration by Li^+ to the greater polarizability of the transitions state over the ground state. While we have carried out a few polarizability computations which confirm this assumption, we have not yet attempted to assess the magnitude of

the polarizability or other effects or to analyse them in greater detail. The greater binding energies of Li^+ to TSs over GSs may be due to the larger number of contacts or to the greater average effectiveness of the interactions in the TS, when the coordination remains the same.

We have generally employed optimized geometries in our work, but have also carried out model computations along the lines of your question. Moving the Li^+ out, away from the equilibrium position, results in a smaller acceleration. Conversely, moving Li^+ in towards the 'aromatic plane' results in a greater effect. (The shielding effect on the chemical shift also responds similarly and is largest in the centre of the ring.)

Using equilibrium geometries, a greater acceleration results if Li^+ is replaced by Be^{2+}, a small dication.

Dr. Quapp said: My comment concerns the first topic of Prof. Schlegel's paper, the bifurcation of reaction paths. With the steepest-descent path[1] (SDP)

$$\frac{dx}{dt} = -\text{grad } E(x)$$

we cannot describe, in principle, bifurcations outside of stationary points. The system of equation is an autonomous differential equation system, which has outside of stationary points grad $E \neq 0$ definite solutions, thus it cannot admit bifurcations. If a reaction path bifurcates along a slope on the PES, this cannot be described with the mathematical tool of a gradient system. We need the more complicated tool of gradient extremals (GE).[2] Curves running along a valley floor path, or along a ridge, are GE. They cross a level line at that point where the slope of the gradient is extremal. Thus, a GE probes the extremal curvature of the level lines.[3] Surprisingly, the GE differ from SDPs. They are isolated curves, because they are solutions of $(N-1)$ equations between the N independent coordinates. This is also contrary to the definition of SDPs given above.

I will give three examples in analogy to Fig. 1 of Prof. Schlegel's paper; and I will explain the behaviour of the test potentials near a bifurcation point. A surface linear in y and
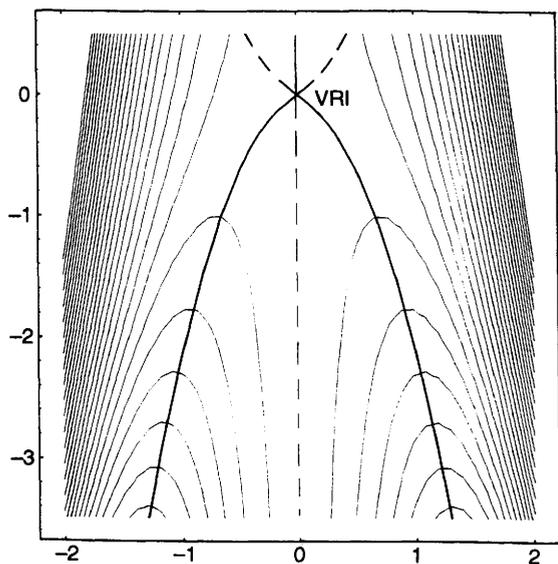
Fig. 1 The test potential $x^4 + x^2y$ represents a special monkey saddle where one valley ground path and the opposite ridge are flat lines (the vertical centre line). Zero point (0, 0) is the valley–ridge inflection point (VRI) where the gradient extremals also meet. The dashed curves are ridges and the bold curves are valley ground lines.

quartic in x is

$$F(x, y) = x^2(x^2 + y)$$

It is a special monkey saddle with a flat valley and a flat ridge in the opposite direction. The 2D gradient extremal condition is:

$$0 = GE(x, y) = F_{xy}(F_x^2 - F_y^2) + (F_{yy} - F_{xx})F_xF_y$$

Thus

$$GE(x, y) = 2x^3(-x^2 - 8x^4 + 2y^2) = 0$$

Its solution is (see Fig. 1)

$$\{y_1(x) = x \sqrt{[(1 + 8x^2)/2]}$$
$$y_2(x) = x \sqrt{[(1 + 8x^2)/2]}$$
$$x \equiv 0, \quad \text{thus } y_3(x) = (y - \text{axis})\}$$

The zero point (0, 0) is the valley–ridge inflection point. It is also the bifurcation point of the three valley grounds (bold curves) and three ridges (dashed curves) of this potential.

A second surface, also linear in y and quartic in x, is the following:

$$F(x, y) = y + x^2(x^2 + y)$$

The 2D gradient extremal condition gives:

$$GE(x, y) = 2x[(1 + 2x^2 + 25x^4 + 8x^6) + 16x^2y$$
$$+ 2(1 - x^2)y^2] = 0$$

Its solution is (with an apparent singularity at $x = \pm 1$),

$$y_1(x) = \frac{8x^2 + (1 + x^2)\sqrt{2}\sqrt{(-1 + x^2 + 8x^4)}}{2(-1 + x)(1 + x)}$$

$$y_2(x) = \frac{8x^2 - (1 + x^2)\sqrt{2}\sqrt{(-1 + x^2 + 8x^4)}}{2(-1 + x)(1 + x)}$$

$$x \equiv 0; \quad \text{thus } y_3(x) = (y - \text{axis})$$

given in Fig. 2. Along the three gradient extremal curves their character is changed: $y_3(x)$ is composed of a valley ground (bold) and a ridge (dashed). The two pieces are divided by the valley–ridge inflection point (cross). The other two branches $y_1(x)$ and $y_2(x)$ are also composed of two different curves:

The bold parts $y_2(x)$ are again the valley grounds of the two side valleys. They end in a turning point; and the curves continue as flank lines $y_1(x)$ (dot-dashed), dividing the corresponding valleys from the ridge.

There is no connection between the three bold curves, which are the reaction paths, if we understand the valley ground as the reaction pathway. All the valley ground curves are continuable, but the continuation is different: one ridge, characterized by passing the valley ridge inflection point, and two flank lines, on the other hand.

I think this figure is similar to the test potential of Fig. 1 of the paper of Prof. Schlegel. If there is no connection between the three valley floor curves, then this connection cannot be found by any special SDP either. Of course, the gradient of the surface is non-zero, outside the zero point (0, 0). Hence, we can go up or go down in the gradient direction starting from any point of the surface. In Fig. 3, a steepest ascent, starting in T, is given by bold arrows about the gradient field. In comparison an SDP is also drawn starting near the zero point. The two paths do not meet. The existence of turning points, and their role for understanding the valley ridge structure of a surface, are discussed in ref. 4, see also a proposal.[5]
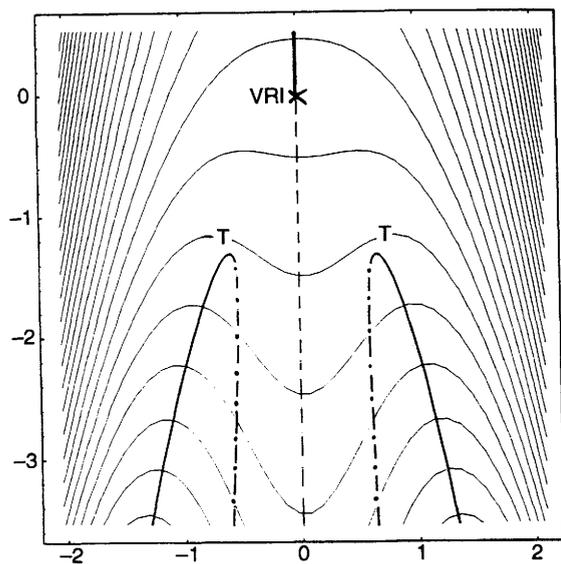
Fig. 2 Test potential $x^4 + x^2y + y$ with gradient extremals without a bifurcation point. The straight centre line, downhill in potential (bold), is a valley ground path which meets the valley–ridge inflection point (VRI) at (0, 0) and continues to the ridge (dashed). Dot-dashed curves are flank lines between the ridge and the two valleys. There is no bifurcation point between the three (bold) floor lines. Flank lines and ground paths meet together in two turning points (T) where the flanks and the grounds end.

A third test surface, linear in y and quartic in x, is

$$F(x, y) = -y + x^2(x^2 + y)$$

Here, we find two saddle points. The 2D gradient extremal condition gives:

$$GE(x, y) = 2x[(-1 + 2x^2 + 23x^4 - 8x^6) + 16x^2y$$
$$+ 2(1 + x^2)y^2] = 0$$

Its solution is a set of three crossing curves, given in Fig. 4:

$$\{y_1(x) = \frac{-8x^2 + (1 - x^2)\sqrt{2}\sqrt{(1 + x^2 + 8x^4)}}{2(1 + x^2)}$$

$$y_2(x) = \frac{-8x^2 - (1 - x^2)\sqrt{2}\sqrt{(1 + x^2 + 8x^4)}}{2(1 + x^2)}$$

$$x \equiv 0; \quad \text{thus } y_3(x) = (y - \text{axis})\}$$

Again, the zero (0, 0) is the valley–ridge inflection point. However, the bifurcation point (B$_1$) of the three valleys is
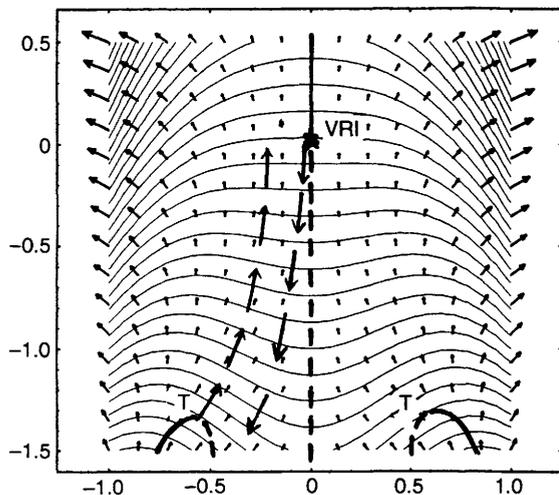

Fig. 3 Enlargement of the region between the turning points (T) and VRI of Fig. 2 with level lines and the gradient field. The bold arrows give a steepest descent and a steepest-ascent path.
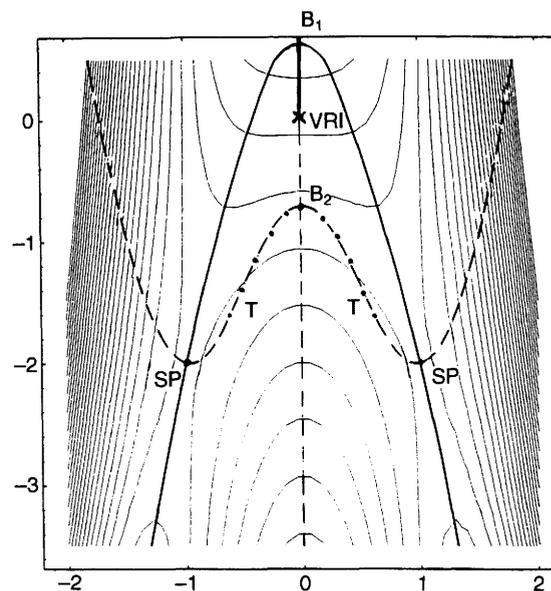

Fig. 4 Test potential $x^4 + x^2y - y$ with gradient extremals of different types Bold curves are valley ground paths. The dashed curves are ridges. The valley–ridge inflection point (VRI) at (0, 0) is not the bifurcation point (B$_1$) of the three ground lines, and it is not the bifurcation point (B$_2$) of the three ridge/flank lines. Ridges and ground paths meet in the two saddle points.

shifted downhill, and the bifurcation point (B$_2$) of the other branches $y_1(x)$ is shifted uphill. Ridges and valleys meet in two saddle points (SP). The behaviour of the three ridges is further disturbed by saddle points which are between the central ridge and the two side ridges. After passing one of the SPs from outside, we find a small piece of a ridge. However, then a very flat turning point (T) emerges, and the curve of the GE continues as a flank line up to B$_2$.

The message of Fig. 1–4 is the following: Bifurcation points can be defined and we can calculate bifurcation points of valley floors (at least on simple test potentials). However, in the theory of GE curves, the valley–ridge inflection point (VRI) and the bifurcation points (B) may be different points.

1 W. Quapp and D. Heidrich, *Theor. Chim. Acta*, 1984, **66**, 245.
2 D. K. Hoffman, R. S. Nord and K. Ruedenberg, *Theor. Chim. Acta*, 1986, **69**, 265.
3 D. Heidrich, W. Kliesch and W. Quapp, *Properties of Chemically Interesting Potential Energy Surfaces*, Lecture Notes in Chemistry, Vol. 56, Springer, Berlin, 1991.
4 W. Quapp, *Theor. Chim. Acta*, 1989, **75**, 447.
5 M. V. Basilevski, *Chem. Phys.*, 1982, **67**, 337.

Prof. Truhlar commented (in part communicated): It was stated in one of the discussion remarks that an imaginary frequency in one of the modes orthogonal to the reaction path signals a reaction-path bifurcation. This is not true. First of all as already stated in Prof. Schlegel's paper and in the remarks by Dr. Quapp, the steepest-descent path, as a mathematical entity, cannot bifurcate. In actual calculations the steepest-descent path would follow the ridge at a valley–ridge inflection (VRI) point,[1] except for the tendency of round-off error to push it to one side or the other. Furthermore, an imaginary frequency orthogonal to the reaction coordinate should not always be considered to be a signal of a physically significant valley–ridge transition. Rather it may often signal a valley–ridge inflection point in non-physical coordinates of a system that is best thought of as residing in a single valley in more physical coordinates. This state of affairs is temporarily disorienting to many researchers because we are all so used to calculating frequencies at

stationary points (equilibrium structures, saddle points, ...) where the frequencies are independent of the choice of coordinates, e.g. they are the same in internal coordinates (bond stretches, bond angles, dihedral angles, ...) as in cartesian coordinates. But this invariance does not hold at non-stationary points along a reaction path because the gradient does not vanish. These issues are discussed in detail in a 1991 paper in the *Journal of Chemical Physics*.[2]

Let me state a related central issue: Every VRI point does not signal a case where there are two products (*i.e.* two local minima), with a ridge between them. Non-physical VRI points may occur even when the reaction path leads straight to a single product.

1 See, e.g. B. C. Garrett, D. G. Truhlar, A. F. Wagner and T. H. Dunning Jr., *J. Chem. Phys.*, 1983, **78**, 4400.
2 G. A. Natanson, B. C. Garrett, T. N. Truong, T. Joseph and D. G. Truhlar, *J. Chem. Phys.*, 1991, **94**, 7875.

Prof. Schlegel replied: The correct terminology was used in the paper. The question of coordinate systems is an important one. Only the stationary points are invariant to a change in coordinate system. The steepest-descent path, and hence the valley–ridge inflection points depend on the choice of coordinate system.

Dr. Stachó said: Let *c* be a smooth curve such that the energy function *E* has a local minimum at any point of *c* on the hyperplane, orthogonal to the tangent vector of *c*. Then the tangent vector must necessarily be parallel to the gradient of *E*. (Thus in this sense minimal energy paths are automatically steepest-descent/ascent paths.) It follows from the Hartman–Grobman theorem that if *c* ends in a stationary point *p* with a non-degenerate Hessian then the tangent vector of *c* at the point *p* is an eigenvector of the Hessian (of *E*). Thus, in most cases, bifurcations of the reaction path are *orthogonal*, similar to our example 3.5 in ref. 1.

Could you treat our function with your method?

1 M. I. Bán, *Theor. Chim. Acta*, 1992, **83**, 433.

Prof. Schlegel replied: Our methods for following reaction paths can in principle be applied to any continuous potential-energy surface. As already stated by a number of authors, true bifurcations of reaction paths occur only at stationary points, and, at stationary points, reaction paths are orthogonal.

Dr. Quapp said: In response to the question of Prof. Schlegel about the Müller–Brown Potential,[1] a gradient extremal (GE) of this potential, see Fig. 5,[2] is a nice example showing the action of the definition of these curves. The bowl of Min 1 is a deep, long and relatively straight valley. In contrast, the SP 1 looks like a 'swallows nest' at its height. The col of SP 1 opens to the main valley, and a steepest-descent path perpendicularly goes downhill to the level lines of the hollow ground. At the floor it joins the floor line. However, nowhere on the floor line can we decide a point of line crossing because this is an asymptotic join.

The GE curve, on the other hand, shows totally different behaviour. It also runs along the col of SP 1, but then it shears off and goes on uphill! Very strange? No, this behaviour is a clear consequence of its definition, to mirror the existence of a valley floor curve: the col of SP 1 ends at the slope of the greater valley of Min 1. Thus, the GE of the valley also has to end. Its end point is then a turning point (T). The curve continues as a flank line of the potential.
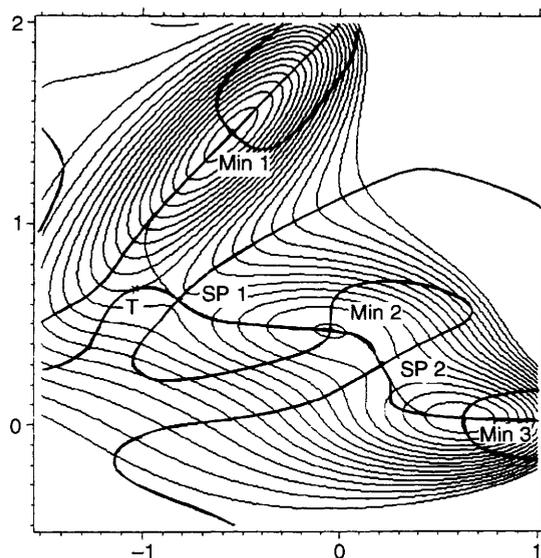
Fig. 5 Solid lines are level lines and the special steepest-descent curves connecting the stationary points, and bold faced curves are gradient extremals on the Müller–Brown test potential, see also ref. 3. T is a turning point of a GE curve. Note: Between the left deep minimum and the next saddle point SP 1 there is no connection by a gradient extremal!

1 K. Müller and L. D. Brown, *Theor. Chim. Acta*, 1979, **53**, 75.
2 O. Imig, Diplomarbeit, Fachbereich Chemie, Universität Leipzig, 1993.
3 J-Q. Sun and K. Ruedenberg, *J. Chem. Phys.*, 1993, **98**, 9707.

Prof. Schlegel commented: Steepest-descent paths and gradient extremals are both useful tools for exploring potential-energy surfaces. The properties of steepest-descent paths are well known. Gradient extremals have some satisfactory properties, They pass through stationary points, they are locally defined and they can handle some types of bifurcation, as discussed by Dr. Quapp. However, gradient extremals show some unsatisfactory behaviour. They do not necessarily connect a saddle point and nearby minima. Gradient extremals can have turning points (they can change direction from downhill to uphill or *vice versa*) and can have discontinuities (see Fig. 5 of Dr. Quapp's comment). If the intent is to model the behaviour of a reaction on the potential-energy surface, it is perhaps better to avoid the idiosyncracies of gradient extremals and tolerate the few limitations of steepest-descent reaction paths.

Prof. Karplus said: My question is for both Prof. Schlegel and Dr. McDouall.

The Elber algorithm was developed to determine relatively crude reaction paths for complex systems with 1000 or more degrees of freedom and we have found it useful in some applications. I was interested to see how well it works for small systems and am curious about the time required relative to that of the more standard approach of Prof. Schlegel. Conversely, I am curious to know whether Prof. Schlegel could indicate whether his approach can be extended to large systems (like proteins). Also, I should like to mention that we have been concerned with finding true saddle points for large systems and have developed a method for doing so in large systems.[1] This has been tested in model systems such as the Müller–Brown potential.

1 S. Fischer and M. Karplus, *Chem. Phys. Lett.*, 1992, **194**, 252.

Prof. Schlegel replied: The methods currently used for small molecules for finding minima, transition states, reaction paths and conical intersections have been reviewed recently.[1] For macromolecules, there can be many minima of similar energy, many comparable transition states and numerous reaction paths. Statistical and dynamical methods are probably the best current approaches for such high-dimensional systems.

1 H. B. Schlegel, *Geometry Optimization as Potential Energy Surfacer*, in *Modern Electronic Structure Theory*, ed. D. R. Yarkony, World Scientific, Singapore, 1994.

Dr. McDouall also replied to Prof. Karplus: We are aware of the conjugate-peak-refinement approach of Prof. Karplus and co-workers. Our intention in the present work was to obtain a method which would give reasonably accurate reaction paths over which we could follow the evolution of various molecular properties. More accurate saddle-point location was not a major concern.

I believe the 'Elber–Karplus-type' approach that we have adapted, and others are looking at, has a major role to play in future studies of reaction paths for large molecular systems, where traditional methods become impracticable.

Dr. Nguyen said: When exploring potential-energy surfaces and/or characterizing transition structures, we often encounter branching points, in particular when the TS has no symmetry and/or the product possesses two distinct conformations.[1] We know that these non-stationary points exist only in a certain formalism; a true steepest-descent path does not bifurcate. Nevertheless, for both practical and educational purposes, it seems to me useful if we could somehow 'define' those points. Some years ago, Baker and Gill[2] attempted to do that and proposed an algorithm to locate branching points. Accordingly, a branching point is a point where the eigenvalue of the Hessians perpendicular to the reaction coordinate vanishes. Would you comment on this view?

1 S. Malone, A. F. Hegarty and M. T. Nguyen, *J. Chem. Soc., Perkin Trans. 2*, 1988, 477.
2 J. Baker and P. M. W. Gill, *J. Comput., Chem.*, 1988, **9**, 465.

Prof. Schlegel replied: As already pointed out by Ruedenberg, and reiterated here by myself and by Prof. Truhlar, the point on a reaction path where the Hessian perpendicular to the path has a zero eigenvalue should be termed a valley–ridge inflection point, not a 'branching point'. Indeed these points have topological significance for the connectivity between various stationary points, but it is incorrect to draw a steepest-descent reaction path as bifurcating at the valley–ridge inflection point.

Prof. Bán asked: (1) What kind of improvement can be expected in the results if we apply your method of higher order in comparison with your lower-order calculations?
(2) What are the convergence criteria of your methods?

Prof. Schlegel replied: I am hoping for an improvement of up to a factor of five in the step size for the explicit fourth-order methods, when compared to other explicit second-order methods. The comparison in cost with our implicit second-order method is difficult to estimate because the latter involves an optimization but no Hessian calculations. We have recently found that the convergence criteria for our second-order implicit method must be tightened considerably

to obtain accurate projected frequencies in the immediate vicinity of the transition state.

Dr. Stone said to Dr. McDouall: It seems to me that a more suitable functional would be obtained by omitting the factor of $1/L$ in eqn. (1). The functional given is the average energy along the path, and can be made arbitrarily close to the minimum energy by choosing a path which follows an arbitrarily long and convoluted trajectory near the minimum. This deficiency in the formal definition is related to, but is not the same as, the problem experienced by the authors in formulating their numerical approximation to the functional.

Dr. McDouall replied: You make a valid comment regarding the term in eqn. (1). Leaving this term out will certainly avoid the possibility of generating an arbitrarily long path. A preferable alternative in my view would be to replace $1/L$ by $1/M$ (where M is the number of grid points). In this case eqn. (1) will still represent the average value of the grid points (though not of the path).

Prof. Tomasi said: This definition of reaction path apparently depends upon the choice of the coordinate. I would like to know if you have any experience of the effect of passing, for example, from cartesian coordinates to mass-weighted coordinates.

Dr. McDouall replied: We have not looked at the use of mass-weighted coordinates. Our main concern was to obtain the minimum-energy path on the surface rather than to obtain the detailed atomic displacements during a reaction. To study the latter we would certainly need to use mass-weighted coordinates.

Prof. Shaik said: I am trying to understand the bifurcation problem in chemical terms. Is it true that the addition of HF (HX in general) to C_2H_4 will have a bifurcation point, supposedly because it leads to two conformers **1** and **2**? If so, then a lot of reactions will possess this bifurcation, *e.g.* when two enantiomers lose their optical activity. How did you resolve, in the past, the bifurcation problem in the case of HF + C_2H_4?

1   **2**
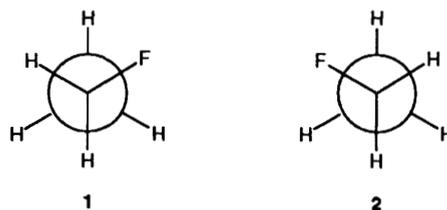
Prof. Schlegel replied: The reaction HF + C_2H_4 has a stationary point with HF hydrogen-bonded to the π system.
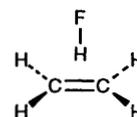
At a stationary point, a reaction path can bifurcate[1] and the paths lead to fluorine adding to either carbon. In the more general case there will be a valley–ridge inflection point before the transition states rather than an intermediate. To a first approximation for these surfaces, the branching ratio for

the formation of the products will be determined by the two transition states rather than by the path bifurcation on the valley–ridge inflection point. The situation where the valley–ridge inflection point lies beyond the transition state is more complicated, and it is the detailed dynamics on the surface that will determine the branching ratio.

1 K. Ruedenberg *et al.*, *Theor. Chim. Acta*, 1986, **69**, 281.

Dr. Stachó said: What can be stated about the numerical stability of your methods? Your paper stated that none of your methods could handle the case with a Fresnel spiral-shaped reaction path. What was the reason? What was the definition of the energy function in this case?

Prof. Schlegel replied: Based on the tests with the logarithmic spiral valley (Fig. 6 of our paper), our fourth-order explicit method 2 has about the same stability as our second-order implicit methods, and both are more stable than the LQA second-order explicit method. A more detailed assessment of the methods will be made once they are incorporated in the electronic structure codes. No single-valued two-dimensional surface was constructed for the Fresnel spiral because the logarithmic spiral incorporates the essential features (curvature changing monotonically with the reaction path). A three-dimensional Fresnel spiral could be constructed in the same fashion as the helical valley, but the mathematical form would be rather complicated because of the nature of the Fresnel integrals.

Dr. Stachó (communicated): In all of the examples given so far, the reaction path is a curve tangential to the gradient field of the energy function and whose tangent vectors are Hessian eigenvectors. The space transformation-invariant Jasien–Shepard reaction path concept is defined in terms of vector field dynamics of slightly more general type than that of gradient fields. With what modifications can your methods be applied to follow reaction paths in dynamical systems defined by general vector fields? How can your explicit methods be used to treat orthogonal bifurcations? In particular, how can they be applied to determine the reaction paths of the model function given in ref. 1.

1 L. L. Stachó and M. I. Bán, *Theor. Chim. Acta*, 1993, **84**, 536.

Prof. Schlegel replied: Most reaction path following methods depend only on the gradient, and thus should be applicable to functions defined only as vector fields. Orthogonal bifurcations occur at stationary points. Any reaction path following method can be used to follow a path from a first-order saddle point down to a stationary point. If this stationary point is also a first-order saddle point, then the reaction path following method can be used to follow the path downhill in both directions. Your surface is an example of the case where the path from one first-order saddle point descends to another first-order saddle point.

Prof. Karplus said: I am curious to know what work, if any, has been done to analyse the dynamics on a bifurcated surface (*e.g.* one that is asymmetric). Near the bifurcation, there is presumably a very low barrier in a direction approximately perpendicular to the reaction coordinate. This could cause rather complex dynamics.

Prof. Schlegel replied: Dynamics on bifurcating surfaces have been discussed by Krauss and De Pristo.[1] There are probably also more recent references.

1 W. A. Krauss and A. E. De Pristo, *Theor. Chim. Acta*, 1986, **69**, 309.

Prof. Truhlar also replied: The dynamical behaviour when a minimum-energy path is a ridge depends strongly on the system and the energy. In the vicinity of a valley–ridge inflection point, the ridge will be only a little higher in energy than the dual valleys it separates, and in such a case the system will typically pass easily between the valleys. Ridges that are higher compared to the available energy can isolate a system on one side or another.

Dr. van Duijnen said: In my experience most continuum SCRF approaches use cavities which are too small, *i.e.* they place source charges too close to the boundary. This is irrespective of the form of the cavity. Changing the size of the cavity, *e.g.* by taking different atomic radii, 'solvation' energies may range from $-\infty$ to 0! Most choices for the cavity's size are 'intuitive' or 'practical' rather than physical. (See, *e.g.* ref. 1, where we put (*ad hoc*) the boundary at least one solvent radius away, and ref. 2, where we gave physical reasons for doing so and why it is necessary to include at least one discrete solvation layer.)

In your example $CO_2 + OH^- \rightarrow HCO_3^-$ the initial and final states are overwhelmingly ionic with a monopole too close to the boundary of the cavity, while the charge distribution of the transition state may be diffuse, probably putting the monopole farther from the boundary. Hence, your barrier heights are too large. In this respect, the simulation with explicit solvent molecules is much better and more trustworthy.

1 J. A. C. Rullmann and P. Th. van Duijnen, *Mol. Phys.*, 1987, **61**, 293.
2 A. H. de Vries, P. Th. van Duijnen and A. H. Juffer, *Int. J. Quantum Chem., Quantum Chem. Symp.*, 1993, **27**, 451.

Prof. Truhlar said: Dr. Van Duijnen has remarked on the inappropriateness of an ellipsoidal cavity for describing the progress of a reacting system along a reaction path and on the difficulty of choosing the ellipsoid boundaries. In this respect, I note that not all continuum solvation models require spherical or ellipsoidal cavities. A much better model in many cases is the assumption of a set of superimposed spheres centred at the atomic nuclei. This model has been used, for example, in SCF calculations by Tomasi and co-workers[1] and Cramer and myself,[2] in molecular mechanics calculations by Still *et al.*,[3] and in Poisson or Poisson–Boltzmann calculations by Honig and Karplus and their co-workers.[4,5] In a poster presented at this Symposium, the Nancy group has also discussed an extension of their formulation to allow such more general cavities.[6]

With such arbitrarily shaped cavities the continuum models can better represent the solute at any point along the reaction path. The difficulty of choosing the boundary between the inside and outside of the cavity remains, but it can be alleviated in two ways, namely (i) choosing the atomic radii semiempirically, and/or (ii) including first-solvation-shell effects explicitly to make up for the inhomogeneity of the dielectric properties of the solvent in the boundary layer. Both approaches are employed in the SMx models developed by Cramer and myself.[2]

1 S. Miertus, E. Scrocco and J. Tomasi, *Chem. Phys.*, 1981, **55**, 117.
2 C. Cramer and D. G. Truhler, *J. Am. Chem. Soc.*, 1991, **113**, 8305; *J. Computer-Aided Molec. Design*, 1992, **6**, 629.
3 W. C. Still, A. Tempczak, R. C. Hawley and T. Henrickson, *J. Am. Chem. Soc.*, 1990, **112**, 6127.

4 K. A. Sharp and B. Honig, *Annu. Rev. Biophys. Biophys., Chem.,* 1990, **19**, 301.
5 D. Bashford and M. Karplus, *Biochemistry,* 1990, **29**, 10219; C. Lim, D. Bashford, and M. Karplus, *J. Phys. Chem.,* 1991, **95**, 5610.
6 V. Dillet and S. Antonczak, poster at this Symposium; see also V. Dillet, D. Rinaldi, J. G. Angyán and J-L. Rivail, *Chem. Phys. Lett.,* 1993, **202**, 18.

Dr. van Duijnen responded: My remark had more to do with the *size* of the cavity than with its form. Most cavities are just too small (in particular in water). Including the discrete first solvation layer has been our standard for many years (see, *e.g.* ref. 1 and 2 in my last comment). This requires some thermodynamical averaging in order to arrive at something like a Gibbs energy. However, the problem of the distance between this first solvation shell and the boundary with the continuum remains the same of course!

Prof. Shaik opened the disscussion on Prof. Butler's paper: Let me see if I understood you correctly. You are saying that the C—Br cleavage is not efficient because it must involve avoided crossing ($n\pi^*-n\sigma^*$ type). But actually the C—Cl cleavage involves precisely the same avoided crossing, so what is the difference? Does the larger avoided crossing for C—Cl cleavage make the two barriers equal?

Prof. Butler replied: While the barriers along the C—Br and C—Cl fission reaction coordinates are both formed from avoided electronic configuration crossings ($n_0 \pi^*_{C-O}-n_x \sigma^*_{C-X}$ (X=Br, Cl) ($a'a''-a''a'$)), and what you or Silver (ref. 9) would call the 'resonance energy stabilization' or 'barrier energy lowering' at the avoided crossing to C—Cl fission is larger than that for C—Br fission, it is not enough of a difference to make the two barriers equal. The barrier to C—Cl fission is still about 10 kcal mol^{-1} higher than the barrier to C—Br fission. [The electronic configuration interaction matrix elements (B_Q in your notation) are only 0–3 kcal and the C—Cl diabatic crossing (ΔE_C in your notation) is more than 10 kcal mol^{-1} higher than the C—Br crossing, so the resulting barrier height, ($E_{barrier} = \Delta E_C - B_Q$) along the C—Cl reaction coordinate is still higher than that along the C—Br reaction coordinate.] The key difference between the C—Br and the C—Cl reaction coordinates in bromopropionyl chloride is that the crossing is so weakly avoided along the C—Br reaction coordinate, with typical splittings ($2B_Q$) between the adiabats of 20 cm^{-1} as compared to 400 cm^{-1} along the C—Cl reaction coordinate, that the rate constant for C—Br fission is dramatically reduced due to the nuclear dynamics non-adiabatically recrossing the C—Br reaction barrier. You may view this recrossing as follows: the electronic configuration interaction matrix elements between the $n_0 \pi^*_{C-O}$ and the $n_{Br} \sigma^*_{C-Br}$ configurations are so weak that the electronic wavefunction cannot change rapidly from $n_0 \pi^*_{C-O}$ to $n_{Br} \sigma^*_{C-Br}$ in character as required if it is to follow the adiabatic reaction coordinate for C—Br fission. Instead, each time the molecule tries to cross the barrier to C—Br fission, the electronic wavefunction retains $n_0 \pi^*_{C-O}$ character and the C—Br bond retains a bonding electronic configuration. The probability of retaining the $n_0 \pi^*_{C-O}$ configuration (which results in a 'hop' to the bonding region of the upper of the two adiabats at the avoided crossing) as the molecule attempts to traverse the avoided crossing can be roughly estimated from a Landau–Zener model, $P_{hop} = \exp[-2\pi(V_{12})^2/(\hbar|\Delta F|v_{rel})] = 1 - 2\pi(V_{12})^2/(\hbar|\Delta F|v_{rel})$ (for small V_{12}). Thus the reduction in the rate of the reaction is

huge when V_{12} (or B_Q in your notation) is small; roughly there is a 99.95% chance that a trajectory trying to undergo C—Br fission will retain bonding character at the avoided crossing rather than adiabatically crossing the barrier and continuing to dissociation. Since V_{12} is much larger at the barrier to C—Cl fission, the nuclear dynamics are much more likely to cross the barrier to C—Cl fission barrier adiabatically with each try. Thus, you get the wrong prediction for the branching ratio if you consider just the relative barrier heights, as the nuclear dynamics can rarely adiabatically cross the barrier to C—Br fission. The reduction in rate constant due to non-adiabatic recrossing is well understood for long-distance electron-transfer reactions (ref. 7); our work here shows that it is critical for predicting the rate constants of Woodward–Hoffmann-forbidden reactions.

Prof. Karplus said: From the molecular beam experiment, you have some idea of the lifetime of the excited molecule before it dissociates. Does it have many chances to try the reaction so that even if the probability of a single 'try' is small there might nevertheless be a significant probability for dissociation by the forbidden path. I am curious to know the orders of magnitude involved, *i.e.* how often does the molecule try?

Prof. Butler replied: The molecular beam experiments on bromopropionyl chloride and bromoacetone do give us a crude upper limit to the lifetime of the excited molecule before dissociation. Our photofragment angular distributions are highly anisotropic, so molecular rotation has not had time to smear out the anisotropic orientations of excited molecules produced by photoexcitation with linearly polarized light. (The angular distribution can also be smeared by distortion of the molecular frame, but we are talking about an upper limit here so will not further discuss this.) The rotational cooling in our particular supersonic expansion is only moderate. Roughly, the anisotropic angular distributions indicate that dissociation occurs in less than a few picoseconds. A few picoseconds is, however, a long time for nuclear dynamics. The vibrational frequency of a C—Br stretch is of the order of 600 cm^{-1}, so in a classical model a trajectory that has tried and failed to cross the barrier to C—Br fission adiabatically (by hopping to the upper adiabat as the bond is stretching, reaching the outer turning point of the C—Br stretch on the upper adiabat and hopping back down to the lower adiabat as the C—Br bond length decreases) might attempt to cross the barrier again in 50–60 fs in a crude approximation. Of course, the energy can drain from the C—Br reaction coordinate before the next attempt and the molecule may instead sample the region of phase space near the barrier to C—Cl fission and be lost to C—Cl fission before it has a chance to retry crossing the barrier to C—Br fission. An RRKM estimate tells us that statistical trajectories sample the C—Br barrier (with enough energy to surmount the barrier) heading toward products much more often than the C—Cl barrier, so it is non-adiabatic recrossing that is the cause of the rate constant for C—Br fission being smaller.

We do not know the heights of the barriers to C—Br or C—Cl fission relative to the bottom of the A″ potential-energy surface accurately enough to calculate a good RRKM estimate of the rate constant for C—Br and C—Cl fission in the absence of non-adiabatic recrossing. This would let me tell you how many times a picosecond the molecule would attempt to cross the C—Br and C—Cl fission reaction barriers, respectively. The excess energy above the C—Br reaction barrier is at least *ca.* 10 kcal mol^{-1}, so I would guess the

molecules would have multiple tries at adiabatically crossing the barrier to C—Br fission. Of course, the probability of crossing the C—Br fission barrier adiabatically is small at every retry, but especially for bromoacetyl chloride, not negligible. Experimentally, although non-adiabatic recrossing has essentially completely suppressed C—Br fission in bromopropionyl choride where the splitting at the avoided crossing is of the order of 20 cm^{-1}, we do see significant C—Br fission from $n\pi^*$ excitation in bromoacetyl chloride, and not all of these have to be from a first attempt at crossing the barrier adiabatically. Sorry I can't be more specific.

Dr. Olivucci said: The experimental results reported by the authors clearly demonstrate a competition between C—C and C—Cl fission in n–p* chloroacetone. However, the reported *ab initio* computations seem too crude to provide a firm demonstration that this competition is due to reduction in the C—Cl rate constant from non-adiabatic effects. The major source of criticism arises from the way in which the authors define the C—Cl fission pathway and, in turn, evaluate the non-adiabatic recrossing rate for the reaction.

In general, the rigorous determination of a reaction pathway involves the location of the minimum-energy reaction path (MERP) *via* the computation of the intrinsic reaction coordinate (IRC) on the relevant potential-energy surface. In contrast, the reaction coordinates investigated by the authors correspond to cross-sections along the C—Cl and C=O stretchings and therefore do not involve full relaxation of all the internal coordinates of the system along the path. Obviously this leads to a rather arbitrary view of the n–p* reaction pathway and, in turn, to an incorrect evaluation of the magnitude of non-adiabatic recrossing rate for the reaction. Furthermore, one should recognize that, in general, MERP are usually located far from conical intersection (CI) points where one has large non-adiabatic effects. In fact, CI points appear as 'local maxima' on the potential-energy surface. Furthermore, because of the 'double cone' ground and excited state surface topology at a CI, small displacements of the MERP from a CI point usually lead to a large energy gap between ground and excited states and therefore to negligible non-adiabatic effects.

In conclusion, in order to provide reasonable computational evidence that the non-adiabatic effects reduce the reaction rate of the C—Cl fission, the authors should in my opinion demonstrate that the rigorously computed MERP does lie near a conical intersection (or weakly avoided crossing) point.

Prof. Butler replied: The experiment measures how the C—C : C—Cl fission branching ratio changes with molecular conformation, finding that we observe a larger branching to C—C fission when we increase the fraction of *gauche* conformers in the molecular beam. The calculations of cuts along the C—Cl reaction coordinate were undertaken to determine whether the larger branching to C—C fission from the *gauche* conformer was due to a larger rate constant for C—C fission in the *gauche* conformer or a smaller rate constant for C—Cl fission in the *gauche* conformer, or both. (The C—C : C—Cl branching ratio is k_{C-C}/k_{C-Cl} so one must consider how each rate constant changes with molecular conformation.) Indeed, our calculations indicated that non-adiabatic recrossing of the C—Cl reaction coordinate could not explain the observed conformation dependence of the branching, as the recrossing reduces the rate constant for C—Cl fission more in the *anti* than in the *gauche* conformer. The increase in the C—C : C—Cl fission for the *gauche* conformer must thus be driven by a conformation dependence of the C—C fission

rate constant. Your question implies that we were invoking a conical intersection along the C—Cl reaction coordinate. We were not; we invoked the importance of the conical intersection along the C—C reaction coordinate, as shown schematically in Fig. 7 of the paper. For the C—Cl reaction coordinate, the cuts along the C—Cl stretch at different C=O bond lengths were meant to show that the crossing was, if anything, more strongly avoided for the *gauche* conformer for most of a wide range of C=O geometries sampled as the C—Cl bond stretches through the avoided crossing. We do not think the C—Cl dissociative trajectories sample near a conical intersection.

If you would allow me to reword your question, one might say that although by symmetry there must be a conical intersection along the C—C reaction coordinate if the molecule retains a plane of symmetry as it dissociates, it may be that the potential-energy surface offers a lower-energy path to dissociation at non-planar geometries and that few of the trajectories attempt to cross the barrier to C—C fission near the conical intersection even if one excites the *anti* (planar) conformer [by, for instance, the C—(C=O)—C atoms distorting to a pyramidal geometry in the excited state]. We plainly need both a potential-energy surface and a dynamics calculation to address this question theoretically. I hope you will undertake a calculation of the minimum-energy reaction path along the C—C reaction coordinate (not the C—Cl one!). I would also be very interested in cuts that retain the plane of symmetry for the C—(C=O)—C atoms and the angle of the C—Cl bond with respect to the plane for the *anti* and the *gauche* conformers as you stretch the C—C bond. Our experiments on the closely related system of bromoacetone have measured the angular distributions of the C—C and the C—Br fission photofragments; the observed anisotropy of the C—C products suggest that pyramidal distortion is not great during dissociation.

I do not agree with your last comment that because of the 'double cone' shape of a potential-energy surface near a conical intersection, that the splitting between the upper and lower cone with small displacements becomes so great that non-adiabatic effects are negligible. There are countless examples where this is untrue (try the dissociation of ICN or CH$_3$I through a conical intersection, where the branching to both the adiabatic and the diabatic products are both significant). Indeed, the importance of non-adiabatic effects near conical intersections has long been recognized. (There are numerous papers by Truhlar, for example, on this subject.)

Prof. Simons said: One way of establishing the differential photochemical behaviour of *gauche* and *trans* conformers of chloroacetone would be to record the photofragment excitation (PHOFEX) spectra under jet-cooled conditions. Cl atoms are readily detected using a REMPI scheme.

A more general comment relates to the multidimensional nature of the potential-energy surfaces and their conical, or other kinds of intersection. It may be somewhat simplistic to consider surface crossing/recrossings only at low dimensionality.

Prof. Butler replied: I would very much like to see a jet-cooled photofragment excitation spectrum of chloroacetone. I hope you have plans to undertake this. There is one worry. We access the A″ potential-energy surface due to Franck–Condon overlap with the inner turning point of the C=O stretch (the equilibrium C=O bond length is longer in the excited state) so the molecule has lots of vibrational energy in it. It may be that the high density of vibrational states and

the short dissociation lifetimes will render the absorption spectrum structureless even under jet-cooled conditions. (Unlike in acetone, where we see very anisotropic photofragment angular distributions from bromoacetone in the $n\pi^*$ absorption band. We assume that photofragmentation in chloroacetone also occurs quickly, and the measurement of $\beta = 0$ for Cl atoms from chloroacetone results from an average over molecular conformers, not from a long timescale for the dissociation.) I would also be interested in the anisotropy and branching in an argon-seeded beam where we could cool the conformer population to primarily *gauche* conformers, but one must be very careful of dimer formation in these expansions.

On your second point, I agree that showing a schematic reaction coordinate for C—C fission with just two degrees of freedom is simplistic. However, because we saw a marked difference in the C—Br : C—C branching for the bromoacetone conformers (C—Br fission dominated in the *anti* conformer but could not compete with C—C fission in the *gauche* conformer) we focussed, in both bromo- and chloro-acetone, on the main geometry difference between conformers, the torsion out of the molecular plane. Where more detailed calculations on the C—C fission reaction coordinate have been possible (ref. 24) they indicate that the dissociation could sample geometries at the barrier where the C—(C=O)—C atoms are somewhat pyramidal, providing a way for both conformers to sneak around the conical intersection. Our anisotropy for the C—C fission products in bromoacetone put an upper limit on how pyramidal the structure becomes *en route* to dissociation; a β of 0.7 for the C—C reaction products suggests the C—C bond direction, along which the recoil occurs, is not on average more than nine degrees from the planar geometry in the ground state when it dissociates. We have tried to focus here on the dominant difference that could cause the branching ratio to depend on molecular conformer, and have admittedly swept much of the richness of the multidimensionality of the problem aside to bring the primary message through as clearly as possible. I should note that many textbooks reduce the problem to only one degree of freedom and describe C—C fission as symmetry forbidden, where we know that it is symmetry forbidden only at a singularity on the potential-energy surface.

Prof. Truhlar commented: In many cases the saddle point of a reaction is actually a local minimum on a ridge that forms a shoulder to a conical intersection. This is the case, for example, even for the very simple $H + H_2$ reaction. Thus one cannot always make a clean distinction between nonadiabatic behaviour at a conical intersection and nonadiabatic behaviour at a saddle point.

Prof. Borden said: (A) What is the difference in the C—Cl and C—Br barriers that you calculate?

(B) If you don't trust the difference between your calculated barriers quantitatively, why do you trust them qualitatively?

Prof. Butler replied: (A) With a single reference CI calculation using an STO-3G* basis, the barrier to C—Cl fission in bromopropionyl chloride is just over 4000 cm^{-1} higher than the barrier to C—Br fission. (We have only investigated the avoided-crossing seam by varying the C=O bond length and stretching the C—Cl or C—Br bonds, respectively, freezing all other internuclear geometries at that of the equilibrium geometry in the ground electronic state. The number given is for the conformer with a plane of symmetry.)

(B) Although the absolute barrier heights are difficult to estimate quantitatively, the relative barrier heights are much

more easily estimated. In particular, before we undertook the calculations (which we undertook primarily to get a feel for the configuration interaction splittings at the avoided crossing near the two barriers) we knew that the barrier to C—Cl fission had to be of the order of 10 kcal mol^{-1} higher than that for C—Br fission (see discussion in ref. 10b). The barrier along the reaction coordinate for C—Cl fission results from an avoided electronic crossing, at stretched C—Cl geometries, between the $n\pi^*_{C-O}(a'a'')$ configuration and the $n_{pCl}\sigma^*_{C-Cl}(a''a')$ repulsive electronic configuration. Likewise, the barrier along the adiabatic reaction coordinate for C—Br fission results from an avoided electronic crossing between the $n\pi^*_{C-O}$ configuration and the $n_{pBr}\sigma^*_{C-Br}(a''a')$ repulsive electronic configuration at stretched C—Br geometries. We can estimate the relative barrier heights to C—Cl and C—Br bond fission on the resulting A'' potential-energy surface by considering the energies at which two $n_{pX}\sigma^*$ (X=Cl, Br) configurations cross the $n\pi^*_{C-O}$ configuration. Absorption spectra of bromoalkanes and chloroalkanes show that the $n_{pBr}\sigma^*_{C-Br}$ repulsive electronic state is much lower in energy than the $n_{pCl}\sigma^*_{C-Cl}$ repulsive electronic state in the Franck–Condon region (200 *vs.* 179 nm) and the repulsive configuration along the C—Br reaction coordinate correlates to a lower asymptotic limit (the C—Br bond is weaker), so the $n_{pBr}\sigma^*_{C-Br}$ repulsive electronic configuration crosses the $n\pi^*_{C-O}$ configuration at lower energies (*ca.* 10 kcal or more lower) than the repulsive $n_{pCl}\sigma^*_{C-Cl}$ configuration does. (The diabatic potential is also a bit softer in the C—Br bond, further reducing the energy at which the repulsive C—Br diabat crosses the bound diabat.) Configuration interaction lowers the two adiabatic barrier heights from the energies at which the two repulsive surfaces cross the bound diabatic surface, but as long as the configuration interaction lowering of the C—Cl barrier is not 10 kcal mol^{-1} more than that for the C—Br barrier, the barrier to C—Cl fission will be higher than the barrier to C—Br fission. The barrier energy lowering ranges from a fraction of a kcal to 3 kcal, so it does not reverse the relative barrier heights.

Prof. Borden began the discussion of Prof. Houk's paper: Do you think that calculations on butadiene dimerization, beyond the CASSCF/3-21G* level, will find that a concerted transition state is lower than that leading to a diradical? Have you performed such calculations?

Prof. Houk replied: The trend observed with CASSCF/3-21G, CASSCF/6-31G* and QCI calculations on butadiene plus ethene does suggest that higher-level calculations on the butadiene dimerization will cause the concerted transition structure and lead to very close diradical energies. This is what experiments on related systems also suggest. The CASSCF calculations without corrections for dynamical electron correlation seems to overestimate the stabilities of diradicals as compared to concerted transition states.

Prof. Nakamura said: There have been allusions to the intervention of single-electron transfer (SET) in the Diels–Alder reaction (Kochi). Since the difference between a concerted reaction and a reaction involving SET followed by rapid in-cage coupling of the resulting radical-ion pair is difficult to decipher experimentally, it would be useful to address this SET issue theoretically. In addition, the SET process has recently been shown to be involved in the [3 + 2] cycloaddition of a dipolar trimethylenemethane.[1] Have you considered, or are you going to explore, this possibility?

1   E. Nakamura, *J. Am. Chem. Soc.*, 1993, **115**, 5344.

Prof. Houk replied: We have not explicitly explored the SET process for the reactions discussed here, although the use of CASSCF calculations would allow such intermediates to be minima if they were favoured. The SET mechanism, to give a radical anion–radical cation pair, has been invoked in cases of strong donor diene or 1,3-dipoles reacting with electron-deficient alkenes. The E_i (donor)–E_{ea} (acceptor) needs to be of the order of 5 eV or less in order to make SET feasible.

Prof. Shaik addressed Prof. Nakamura: The experimental results I am aware of are those of Kochi who examined cycloadditions of tetracyanoethylene to 9,10-disubstituted anthracenes, and found a correlation between the Gibbs energy barriers and the charge-transfer transitions of the corresponding reactants' charge-transfer complexes. In these cases the ionization potentials and electron affinity allow, in principle, an electron-transfer process. Nevertheless, even in these cases one does not observe electron-transfer products, but rather cycloaddition products. We have discussed these kind of problems in the past in terms of curve crossings of the type discussed in my present paper on the ACS paradigm [*e.g.* Fig. 4(*b*) and (*c*) there]. What happens is a curve crossing which involves a significant mixing of the charge-transfer (CT) configuration into the curves of reactants and products.[1] Thus, despite the dominance of the CT configuration in the TS region, the strong VB mixing binds the two reactants strongly and leads to cycloaddition rather than to electron transfer. The fact that Kochi observes correlations of reactivity with charge transfer excitations is reflecting therefore the role of the CT configuration in the avoided crossing and has little to do with an actual electron-transfer reaction.

1   For a description of the reactants' and product curves for allowed cycloadditions, see for example ref. 1(*a*)–(*e*) and 40 cited in my paper in this Symposium, as well as A. Ioffe and S. Shaik, *J. Chem. Soc., Perkin Trans. 2*, 1992, 2101.

Prof. Bally said: (A) You say in your paper that on dimerization of cyclobutadiene (CB) the transition state of the Cope rearrangement of the *syn* dimer is reached. However, as pointed out correctly by you, the Cope rearrangement of the *syn* dimer is not observed due to formation of cyclooctatetraene (COT) by a lower-energy path. So why is COT not observed upon CB dimerization, more than enough energy being available for this process?

(B) Given the substantial differences between the (CASSCF) predictions with the 3-21G and 6-31G* basis set (for absolute and relative energies, especially in the CB dimerizations), what confidence do you have in the capability of your model to predict the reaction path for CB dimerization correctly? Do you think inclusion of dynamic correlation could alter the picture significantly?

Prof. Houk answered: (A) Perhaps because the reactions in general are studied in solution or in low-temperature matrices, where the energy can be readily dissipated.

(B) I do think that dynamic correlation corrections are necessary in order to obtain reasonable energies. It is possible that a concerted mechanism for the *syn* dimerization could materialize upon inclusion of dynamical electron correlation.

Dr. Walsh said: On the question of cyclobutadiene chemistry, I would like to comment that we have carried out

extensive kinetic studies of hydrocarbons in the C_8H_8 manifold[1] (*viz.* measurements of activation energies and of energy release). We would anticipate that in the gas phase, while the initial products of cyclobutadiene dimerization would be *syn-* and *anti*-tricyclo[4.2.0.0$^{2.5}$] octa-3,7-diene, the energy release would be sufficient to cause isomerization to cyclooctatetraene and its breakdown products. The gas pressure would determine the extent of stabilization of specific C_8H_8 products. To our knowledge such studies as have been carried out have not addressed the issues of energy release and product-yield pressure dependences.

1   K. Hasserück, H-D. Martin and R. Walsh, *Chem. Rev.*, 1989, **89**, 1125.

Dr. Walsh continued: I would like to ask you, and indeed other theoreticians, a question about the accuracy of your calculations. As an experimentalist who has more experience of measuring activation energies, I am used to quoting uncertainties (precision). Depending on the experiment in question these may vary; however, a typical kinetic study of hydrocarbon thermolysis (or cycloaddition) would probably give ± 4 kJ mol^{-1}, if reasonably carefully carried out.

Theoreticians however, often do not assess the accuracy of their (*ab initio*) calculations but rather cite 'a certain level of calculation' with 'a certain basis set' and argue as you, Prof. Houk, have done in your paper that this gives results in agreement with experiment. But we know that improving the basis set and level of calculation can often change the answer, particularly when alternative mechanisms are being compared. How do you judge that the calculation is reliable and that further refinements will not change the outcome?

Prof. Houk replied: The precision is high: the uncertainty in calculations is essentially zero; that is, they may be reproduced exactly to many decimal places. However, the accuracy may not be very good. We have documented in our *Angewandte Chemie* article in 1993, and to a lesser extent in this Symposium, how we can gradually converge on the experimental activation energy by better calculations. Many times, for reactions of the size that organic chemists like to study, it is not possible to perform calculations at a high enough level to be certain they have converged to a final answer. This is why comparisons with experiment are often done. For sufficiently small systems, there are methods, such as Pople's G1 and G2 methods, which are prescriptions for obtaining energies to within ± 2 kcal mol^{-1} of the exact experimental result.

Dr. Williams said: Activation energies are not the only quantity of interest for comparison of theory with experiment, for example, kinetic isotope effects are extremely important experimental probes for transition-state structure. Could you please comment upon the accuracy of your computed isotope effects, particularly in regard to the choice of basis set and the effect of electron correlation? It would be interesting to know how the value of the imaginary reaction-coordinate frequency depends upon the method employed.

Prof. Houk replied: The predicted isotope effects do vary as a function of computational level. Some examples for the butadiene–ethene reactions are shown in Table 1. The forming bond lengths are also shown, to indicate how the position of the transition state is changing.

The isotope effects do vary over a rather large range. The RHF results, which give later transition states, give larger

Table 1   Predicted isotope effects for the butadiene–ethene reaction

computational level	forming bond length/Å	k_{H_2}/k_{D_2}	
		1,1-diene	1,1-dienophile
RHF/3-21G	2.210	0.91	0.91
RHF/6-31G*	2.202	0.92	0.92
MP2/6-31G*	2.286	0.94	0.94
MCSCF/6-31G*	2.223	0.94	0.96

inverse isotope effects than the correlated wavefunctions, which give earlier transition states. Nevertheless, the mechanistic implications are clear when concerted and stepwise mechanisms are compared.[1]

1   J. Storer, L. Raimondi and K. N. Houk, J. Am. Chem. Soc., in the press.

Dr. Nguyen said: My question is related to the results presented in Fig. 2 of your paper. Accordingly, the closed-shell quadratic configuration interaction, RQCISD(T), method gives the best energy barrier compared with the experimental result. The CASSCF method tends to overestimate this quantity. This shows the importance of dynamical electron correlation. There is, however, a difference of ca. 4 kcal mol^{-1} between the results obtained by UQCISD(T) and RQISD(T) methods. Such a large difference is alarming! How would you explain these results? I wonder whether the UHF references are heavily contaminated. On the other hand, are closed-shell single-reference wavefunctions adequate for treating concerted cycloadditions?

Prof. Houk replied: Indeed, dynamical electron correlation is needed to obtain good energies. Yes, the UHF results are highly spin–spin-contaminated, ca. 50% triplet for the diradical, but mostly singlet for the concerted pathway. RHF calculations are quite good for concerted pathway geometries: we know that now by ample experience on many allowed reactions.

Prof. Tomasi addressed Dr. Walsh: I would like to add my comments to the question you raised. The primary goal of theoretical chemistry is that of giving a picture, an interpretation, and not that of checking the numerical outcome of experiments within their error range.

Anyway, the theoretical foundations and the technical methodologies (in perspective) to reach the accuracy typical of good level experiments are available if the material system under scrutiny is of 'limited' size (as, for example, the molecular systems considered in the Houk paper and in many other papers presented in this Symposium). This level of accuracy has not yet been reached, but it is within the limits of the present approaches and surely will represent, in the not too distant future, an interesting alternative to experiments, especially in cases for which experimental measurements are difficult to perform.

The situation is not so clear, in my opinion, for systems of 'large' size. The computational methods theoreticians employ for the study of phenomena occurring in solution or in complex biomolecules are inherently approximate and also their theoretical layout is far from being satisfactory (let me quote, as example, the status of temperature in the molecular quantum-mechanical formalism). Much work must be done

in this field: 'interpretations' are currently proposed, with remarkable success, but the formal connection with a complete and exhaustive theory does not exist.

Prof. Borden added: While I agree that the goal of theory is qualitative description, it is also true that calculations have become capable of quantitative accuracy. There are now many instances where theory has been able to correct experimental results or, more precisely, their interpretation. Relevant to Prof. Houk's talk, his QCISD(T)/6-31G* results show that at this level of theory the activation energy for ethene and butadiene → cyclohexene is calculated with quantitative accuracy (i.e. within 1 kcal mol^{-1} of experiment). We have obtained results of similar quality with CASPT2N and QCISD(T)/6-31G* calculations on the Cope rearrangement and cyclobutene ring opening. However, different reactions may require different levels of theory. For example, calculations of relative C—H and O—H bond strengths at this level are in error by ca. 10 kcal mol^{-1}.

Dr. Walsh said: If Prof. Tomasi is right, then because we have quantum theory and because we have the Woodward–Hoffman rules to give us the picture, we do not need anything else. Theoreticians would soon be out of business if the only goal is pictures. I believe, like Prof. Schleyer, that quantitative prediction is at least equally important. As to whether it can correct experiments, i.e. point out when they are wrong, I accept Prof. Borden's point that it certainly can, and in cases known to me, it certainly has done. Thus I do not wish to imply that experimental results are 'holy', and do not need repeating (as Prof. Schleyer implied). There are good and bad experimental studies just as there are good and bad theories. Experimentalists argue amongst themselves just as much as theoreticians. Experimentalists need theoreticians to guide their vision, but theory will quickly become anaemic if it does not direct its goal to predicting the outcome of experiments.

Dr. S. Wilson communicated: Basis-set truncation effects are widely recognized as the main source of error in contemporary molecular electronic structure calculations,[1] a fact which is well illustrated by the results presented in this paper. Huzinaga[2] has suggested that calculations in which the basis-set truncation error is not controlled should be termed quasi-empirical. Recently, we have developed basis sets which are capable of delivering energies to within a few μE_h of the exact values.[3,4] To date, our work has been limited to the Hartree–Fock model for diatomic systems but with the availability of increasingly powerful parallel processing computing machines able to carry out matrix operations with high efficiency[5] we envisage the emergence of applications of a comparable accuracy to polyatomic systems, to calculations taking account of correlation effects[6] and perhaps even relativistic effects[7] over the next year or so.

1   S. Wilson, Adv. Chem. Phys., 1987, 67, 439.
2   S. Huzinaga, Comput. Phys. Rep., 1985, 2, 279.
3   D. Moncrieff and S. Wilson, J. Phys. B, 1993, 26, 1605.
4   D. Moncrieff and S. Wilson, Chem. Phys. Lett., 1993, 209, 423.
5   D. Moncrieff, V. R. Saunders and S. Wilson, Supercomputer, 1992, 50, 4.
6   B. H. Wells and S. Wilson, J. Phys. B, 1986, 19, 2411.
7   H. M. Quiney, I. P. Grant and S. Wilson, J. Phys. B, 1990, 23, L271.