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Gibbs energies of activation for reacting systems with multiple reactant-state and transition-state conformations

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Abstract

Three distinct procedures for obtaining the effective Gibbs energies of activation from computed energies for a reaction involving multiple reactant-state (RS) and transition-state (TS) conformers are shown to be equivalent. If Boltzmann-weighted average Gibbs energies for RS and TS are evaluated, then the Gibbs energy contribution from entropy of mixing of both RS and TS conformers must also be included in order to obtain the correct value for the effective Gibbs energy of activation. Application to a solvolytic reaction of 4,4’-dimethoxybenzhydrylpyridinium cation, which is shown to satisfy the Curtin-Hammett principle with rapid interconversion of RS conformers, demonstrates the use of each procedure for evaluation of the effective Gibbs energy of activation.

Keywords

Gibbs energy of activation, conformational flexibility, multiple reaction pathways, Curtin-Hammett, conformer interconversion.

INTRODUCTION

Many chemically reacting systems involve multiple conformers for both the reactant state (RS) and the transition state (TS). Numerous individual transition structures (i.e. distinct geometrical structures each corresponding to a first-order saddle point on the potential-energy surface)[1] may contribute either in series or in parallel to the TS. A consequence of this is that the experimental activation energy cannot be associated with a “pure” TS with a single physical structure but corresponds to a virtual TS.[2] The application of widely available computational codes for electronic-structure calculations allows for location and characterisation of individual energy minima and transition structures for complex reacting systems, but care must be exercised in attempting to make comparison between calculation and experiment. The purpose of this paper is to note some salient points in this regard. A recent computational study on heterolyses of *N*-benzhydryl-pyridinium ions by Matić and Denegri[3] is extended by inclusion of transitions between RS conformers and is used to demonstrate alternative approaches for evaluation of the Gibbs energy of activation.

EFFECTIVE ACTIVATION ENERGIES

For P multiple reaction pathways in parallel, the apparent Gibbs energy of activation $\Delta^{\ddagger}G_{\mathrm{app}}$ derived from experiment is given by Eqn 1, with $s = -1$, and is smaller than any of the values $\Delta^{\ddagger}G_{\mathrm{i}}$ for reaction through each of the individual transition states i = 1 to P relative to one and the same reactant state.

$$\Delta^{\ddagger}G_{app} \;=\; (s)\, RT \ln\{ \textstyle\sum_{i}^{P} exp\,[(s)\;\Delta^{\ddagger}G_{i}/RT\,]\,\} \tag{1}$$

For P multiple reaction steps in series, the apparent Gibbs energy of activation $\Delta^{\ddagger}G_{\mathrm{app}}$ derived from experiment is also given by Eqn 1, but with $s = +1$, and is larger than any of the values $\Delta^{\ddagger}G_{\mathrm{i}}$ for each of single transition states $i = 1$ to P relative to the same reactant state.[2]

In general, parallel reaction pathways may involve both multiple transition structures and multiple reactant structures. Suppose that computed energies for (in general, different numbers of) RS and TS conformers are available, the effective free energies of activation can be calculated by any of three equivalent procedures.

Procedure 1

Since the effective rate constant for a system with multiple TSs in parallel — and for which interconversion of reactant-state conformers is rapid relative to the rate of reaction (Curtin-Hammett conditions) — is the sum of the individual rate constants, the effective free energy of activation may be obtained by extension of Eqn 1 (with $s = -1$), leading to Eqn 2.

$$\exp\left(-\Delta^{\ddagger}G_{eff}/RT\right) = \; x_{0}^{RS}\left[\textstyle\sum_{j}^{TS} \exp\left(-\Delta^{\ddagger}G_{0}^{j}/RT\right)\right] \tag{2}$$

The right-hand-side of Eqn 2 involves a summation of Gibbs energies of activation $-\Delta^{\ddagger}G_{0}^{j}$ for individual transition structures j, each evaluated with respect to the energy of one and the same RS conformer of lowest Gibbs energy. However, since the reactant state is an equilibrium mixture of RS conformers, the summation must by multiplied by the mole fraction x_{0}^{RS} of the lowest-energy conformer RS_0, the for the RS conformer of lowest energy. Moreover, x_{0}^{RS} is (by definition) the reciprocal of the RS partition function Q^{RS} and the summation in square brackets is none other than the TS partition function. Thus,

$$\exp\left(-\Delta^{\ddagger}G_{eff}/RT\right) = \; Q^{TS}/Q^{RS} \tag{3}$$

as required by transition state theory.

Procedure 2

Baldwin *et al.*[4] have formulated a generalised Winstein-Holness equation:

$$k_{eff} = \textstyle\sum_{i}^{RS} x_{i}^{RS} \; \sum_{j}^{TS} k_{i}^{j} \tag{4}$$

where each k_{i}^{j} is the individual rate constant for reaction from the ith RS conformer to the jth TS conformer. This can be expressed in terms of Gibbs energies of activation as follows.

$$\exp\left(-\Delta^{\ddagger}G_{eff}/RT\right) = \; \left[\textstyle\sum_{i}^{RS} x_{i}^{RS} \; \sum_{j}^{TS} \exp\left(-\Delta^{\ddagger}G_{i}^{j}/RT\right)\right]/n^{RS} \tag{5}$$

Here, each individual Gibbs energy of activation $\Delta^{\ddagger}G_{i}^{j}$ is for an individual reaction path from RS_{i} to TS_{j}. The RS summation is necessary because the individual rate constants are from specific RS conformers, but it is necessary to introduce the normalisation factor ($1/n^{RS}$) to correct for multiple counting of passage through the same TS conformer.

However, if there are the same number of RS and TS conformers, i.e. $n^{RS} = \; n^{TS}$, then the equation may be simplified (Eqn 6).

$$\exp\left(-\Delta^{\ddagger}G_{eff}/RT\right) = \textstyle\sum_{i}^{RS} x_{i}^{RS} \exp\left(-\Delta^{\ddagger}G_{i}^{i}/RT\right) \tag{6}$$

This is the method employed by Matić and Denegri[3] (hereinafter denoted as MD). Note that substitution into Eqn 2 of $x_0^{RS} = 1/Q^{RS}$ and $\Delta^{\ddagger}G_0^{j} = \Delta^{\ddagger}G_i^{j} + \Delta G_i^{RS}$, and with the same number of RS and TS conformers, leads to

$$\exp\left(-\Delta^{\ddagger}G_{eff}/RT\right) = \sum_{j=i}^{TS}\exp\left(-\Delta^{\ddagger}G_i^{j=i}/RT\right)\exp\left(-\Delta G_i^{RS}/RT\right)/\,Q^{RS} \tag{7}$$

However, because $x_i^{RS} = \exp\left(-\Delta G_i^{RS}/RT\right)/Q^{RS}$, this simplifies to Eqn 6.

Procedure 3

Alternatively, it may be attractive to consider the effective Gibbs energy of activation as the difference in "average" Gibbs energies G_{eff}^{RS} and G_{eff}^{TS} for RS and TS, respectively.

$$\Delta^{\ddagger}G_{eff}/RT = G_{eff}^{TS}/RT - G_{eff}^{RS}/RT \tag{8}$$

The first term on the right-hand side of Eqn 8 is the sum of the weighted average of the Gibbs energies for the TS conformers, each denoted by a subscript *j*, together with the Gibbs energy contribution from of the entropy mixing of these conformers:

$$G_{eff}^{TS}/RT = \sum_j^{TS} x_j^{TS}G_j^{TS}/RT + \sum_j^{TS} x_j^{TS}\ln x_j^{TS} \tag{9}$$

As before, x_j^{TS} is the mole fraction of TS conformer *j*:

$$x_j^{TS} = \exp\left(-G_j^{TS}/RT\right)/Q^{TS} \tag{10}$$

and Q^{TS} is a partition function:

$$Q^{TS} = \sum_j^{TS}\exp\left(-G_j^{TS}/RT\right) \tag{11}$$

The sum of mole fractions is, of course, equal to 1, and so therefore:

$$\begin{aligned} G_{eff}^{TS}/RT &= \sum_j^{TS} x_j^{TS}\left(\frac{G_j^{TS}}{RT} - \frac{G_j^{TS}}{RT} - \ln Q^{TS}\right) \\ &= -\ln Q^{TS} \end{aligned} \tag{12}$$

Similarly, the effective Gibbs energy for the RS is the sum of the weighted average of the Gibbs energies for the RS conformers, each denoted by a subscript *i*, together with the free energy of mixing of these conformers:

$$\begin{aligned} G_{eff}^{RS}/RT &= \sum_i^{RS}\frac{x_i^{RS}G_i^{RS}}{RT} + \sum_i^{RS} x_i^{RS}\ln x_i^{RS} \\ &= -\ln Q^{RS} \end{aligned} \tag{13}$$

Therefore, the effective Gibbs energy of activation is equivalent to (*RT* times) the natural logarithm of the ratio of partition functions for the RS and TS:

$$\Delta^{\ddagger}G_{eff}/RT = ln(Q^{RS}/Q^{TS}) \tag{14}$$

Procedures 1, 2 and 3 all lead to the same result in the general case where $n^{RS} \neq n^{TS}$, and in the special case where $n^{RS} = n^{TS}$, lends support to their correctness. Importantly, this means that it necessary to include the Gibbs energies of mixing of both RS and TS conformers, along with the Boltzmann-weighted average values of those RS and TS conformers, when following procedure 3: it is not enough to take only the weighted average for the RS and for the TS. Failure to include the mixing term causes a systematic error in the calculated Gibbs energy of activation. The Boltzmann-weighted average of the activation energies for the individual TSs is more than the lowest of the alternative activation energies, but it follows from Eqn 1 that the effective activation energy for a series of alternative reaction pathways in parallel is less than the activation energy of any of the individual pathways; inclusion of the entropy of mixing contribution to the Gibbs energy of activation is an essential requirement to ensure the correct result.

METHODS

Full geometry optimisation was performed for all structures with the M06-2X/6-311+G(2d,p) method using default parameters in the GAUSSIAN 16 (version A.03) program.[5] Transition structures were initially located and characterised using the smaller 6-31G(d) basis with the M06-2X density functional, and their hessians were used to assist TS searches with the larger basis. Frequency calculations provided thermal corrections at 298.15 K as well as confirming each structure as either a minimum or a first-order saddle point. Single-point energies were evaluated with M06-2X/6-311+G(2d,p) using the IEFPCM method for implicit solvation by ethanol treated as a continuum with relative permittivity 24.852. Coordinates of optimized geometries are given in the Supporting Information.

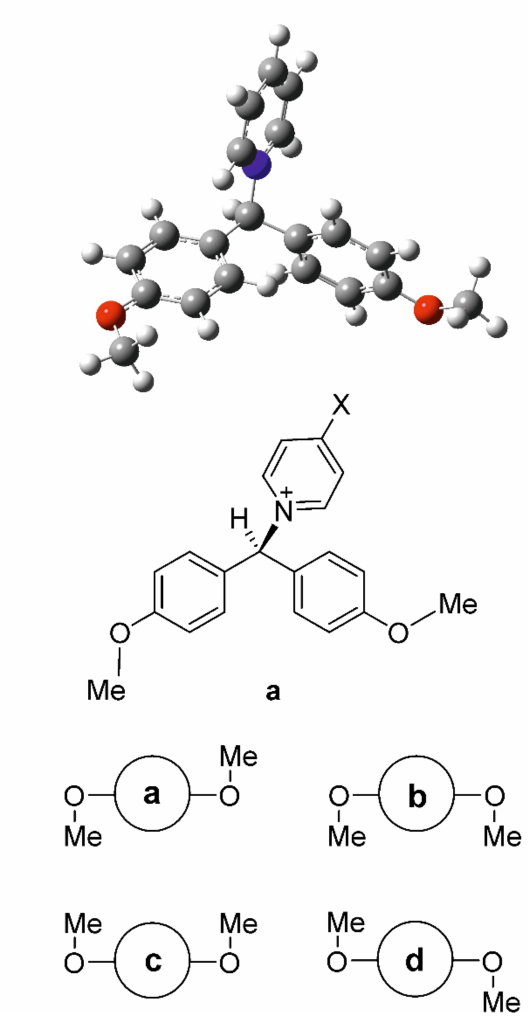

Figure 1. Top: energy-minimised structure for RS conformer **a**. Middle: structural formula for conformer **a**. Bottom: cartoon representations for RS conformers **a**, **b**, **c** and **d** to illustrate methoxy-group orientations.

COMPUTED ACTIVATION ENERGIES

A recent computational study (MD[3])of solvolyses of *N*-benzhydryl-*X*-pyridinium cations used density functional theory calculations with the PCM method for continuum solvation. 21 pyridine nucleofuges (*X*-substituted in the 3- or 4-position) were considered with five solvents for two 4,4'-disubstituted benzhydryl groups. In particular, the M06-2X/6-311+G(2d,p)/IEFPCM method was employed to locate and characterise four RS and TS conformers of 4,4'-dimethoxybenzhydryl-*X*-pyridinium (*X* = 4Me, H and 4-Cl, Scheme 1) in implicit ethanol in order to generate correlations between calculated and experimental Gibbs energies of activation. The very good linear correlations obtained were further extended to estimate reactivities for another 18 *X*-substituted pyridines at 25 °C, thereby enabling the prediction of nucleofugality parameters in five protic solvents.[3] As noted above, MD employed Eqn 6 to calculate the effective Gibbs energy of activation, with $i = 1,4$ for both RS and TS.

In this work transition structures for interconversion of the same four RS conformers (**a**, **b**, **c** and **d**, Figure 1) as determined by MD for 4,4'-dimethoxybenzhydryl-*X*-pyridinium (*X* = H) have been located and characterised using essentially the same computational method. (The only difference was that a single-point IEFPCM energy was obtained for each structure optimised in a vacuum, instead of in the implicit solvent. This approximation has a negligible effect on the energies and is of no consequence for the validity of the conclusion drawn from the results.) Scheme 1 shows the full structural formula for conformer **a**, whose optimised geometry is depicted in Figure 1. This structure is chiral by virtue not only of the methoxy group conformations but also of the propeller-like orientations of the three aryl rings about the quasi-threefold symmetry axis collinear with the central CH bond. This latter feature is the reason why conformers **a** and **d** are not a pair of enantiomers, despite the superficial appearance of their cartoon representations in the lower section of Figure 1. The RS energies of the four conformers are the same as those reported by MD and the Gibbs energies of activation for the conformational interconversions are shown in Figure 2. Each interconversion proceeds by a 180° rotation of one methoxy group relative to the aryl ring to which it is attached. However, since this may occur in either a clockwise or anticlockwise sense (as viewed along the MeO–C_{aryl} bond), there are two transition structures for each interconversion; these are distinguished by a plus or minus sign, respectively, leading to eight processes (viz. **a+b**, **a-b**, **a+c**, **a-c**, **b+d**, **b-d**, **c+d**, and **c-d**) each with its own activation energy. The dihedral angle $C_{Me}O–C_{aryl}C$ in each of these transition structures is therefore approximately either +90° or -90°. In Figure 2, energy-minimum equilibrium RS structures are denoted by black circles, and first-order saddle point TS structures are denoted by squares: blue squares represent the four transition structures for heterolysis (as determined by MD) and green or red squares represent transition structures, respectively, for positive or negative directions of rotation for RS interconversion. Arrows denote downhill-energy directions from saddle points. All Gibbs energies (kJ mol^{-1}, 298.15 K, 1 atm) are relative to that of the lowest RS conformer **a**. Total energies, Gibbs energies of activation, and transition frequencies are given in Table 1; Cartesian coordinates for optimised transition structures are presented in the Supporting Information.

The most important result to note from Figure 2 is that all eight transition structures for RS conformational interconversion lie < 20 kJ mol^{-1} above the lowest RS conformer, whereas all four transition structures for heterolysis (**a**$_{\mathbf{het}}$, **b**$_{\mathbf{het}}$, **c**$_{\mathbf{het}}$, **d**$_{\mathbf{het}}$) lie > 90 kJ mol^{-1} above that RS conformer. This implies that RS conformational interconversion is at least 10^{12} times faster than ethanolysis, and therefore indicates that the Curtin-Hammett principle[6] is applicable to this system. Under these conditions, and since product formation in the solvolytic reaction is a first-order process, the product conformer ratio depends only on the relative Gibbs energies of the TS conformers, and it is in no way related to the Gibbs energies of the RS conformers. In other words, product formation via any of the accessible TS conformers can occur from any of the RS conformers.

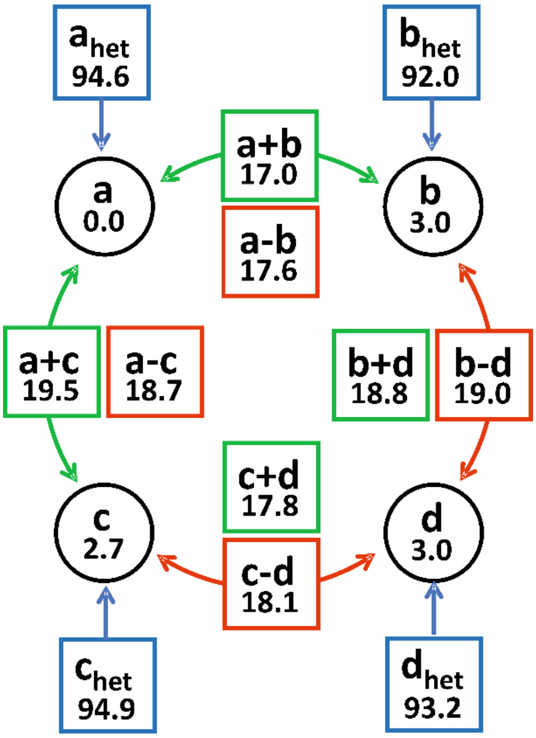

Figure 2. RS conformers (black circles), heterolysis TS conformers (blue squares) and transition structures for interconversion of RS conformers (green squares for positive MeO–C_{aryl} rotation, red squares for negative MeO–C_{aryl} rotation. All M06-2X/6-311+G(2d,p)/PCM(EtOH)//M06-2X/6-311+G(2d,p) Gibbs energies (kJ mol^{-1}, 298.15 K, 1 atm) are relative to RS conformer **a**.

Table 1. M06-2X/6-311+G(2d,p)/PCM(EtOH) total electronic energies E_{tot} , M06-2X/6-311+G(2d,p) thermal Gibbs energy corrections ΔG_{corr} (298.15 K, 1 atm), sum $G°$ of electronic and thermal Gibbs energies, Gibbs energies of activation relative to the reactant-state conformer **a** of lowest Gibbs energy, and transition frequencies $\nu^{\ddagger}$ for optimised transition structures for interconversion of reactant-state conformers of 4,4'-dimethoxybenzhydrylpyridinium cation in ethanol.

TS conformer	E_{tot}/hartree	ΔG_{corr}/hartree	$G°$/hartree	$\Delta^{\ddagger}G$/kJ mol^{-1}	$\nu^{\ddagger}$/cm^{-1}
a-b	-979.062773	0.309458	-978.753315	17.59	52.2*i*
a+b	-979.062829	0.309298	-978.753531	17.02	52.6*i*
a-c	-979.062421	0.309510	-978.752911	18.65	51.0*i*
a+c	-979.061523	0.308928	-978.752595	19.48	65.9*i*
b-d	-979.062316	0.309537	-978.752779	18.99	51.8i
b+d	-979.062224	0.309355	-978.752869	18.76	58.4*i*
c-d	-979.062658	0.309531	-978.753127	18.08	53.3*i*
c+d	-979.062686	0.309466	-978.753220	17.84	51.9*i*

Table 2 presents total energies from MD's Supporting Information[3] for heterolysis of conformers of 4,4'-dimethoxybenzhydrylpyridinium cation in ethanol along with data required for the evaluation of the effective Gibbs energy of activation by means of procedures 1 and 2; corresponding data for procedure 3 are presented in Table 3. Procedure 1 involves multiplying the sum of exponential terms for TS conformers by the mole fraction of the RS conformer of lowest Gibbs energy: this leads to $\exp\left(-\Delta^{\ddagger}G_{eff}/RT\right) = 1.725 \times 10^{-16} \times 0.5196$, thereby yielding $\Delta^{\ddagger}G_{eff} = 91.59$ kJ mol^{-1}. Procedure 2 takes the sum of RS-weighted exponential terms involving individual Gibbs energy differences $\Delta^{\ddagger}G_i^i$ from each RS conformers to its corresponding TS conformer: this leads directly to $\exp\left(-\Delta^{\ddagger}G_{eff}/RT\right) = 8.962 \times 10^{-17}$ and the same value for $\Delta^{\ddagger}G_{eff}$ as obtained by procedure 1. Procedure 3 involves evaluation of average Gibbs energies for RS and TS, respectively 1.40 and 93.14 kJ mol^{-1}, the difference of which is 91.74 kJ mol^{-1}. This value differs from the correct effective Gibbs energy of activation by virtue of the small difference in the entropy of mixing contributions $RT\, x_i \ln x_i$, which are, respectively, -3.02 and -3.17 kJ mol^{-1} for RS and TS. Inclusion of the mixing contribution reduces the effective Gibbs energy of activation by 0.15 kJ mol^{-1}, thereby yielding the same result as procedures 1 and 2. Note that $\Delta^{\ddagger}G_{eff}$ has a smaller value than any of the individual barriers $\Delta^{\ddagger}G_0^j$, as required for multiple reaction pathways in parallel, but that one of the values of $\Delta^{\ddagger}G_i^i$ is smaller still; this suggests that taking activation energies for TS conformers relative to the RS conformer of lowest Gibbs energy may provide a safer method that allows a check to ensure that the resulting value of $\Delta^{\ddagger}G_{eff}$ is indeed lower than that of the individual activation energies.

CONCLUSIONS

Three apparently different procedures for obtaining the effective Gibbs energy of activation from computed energies for reactions involving multiple conformers of both the RS and the TS are shown to yield identical results. If Boltzmann-weighted average Gibbs energies for RS and TS are evaluated, then contribution from entropy of mixing of both RS and TS conformers must also be included to obtain a result ensuring that $\Delta^{\ddagger}G_{eff}$ is equal to $RT\ln(Q^{RS}/Q^{TS})$ as required by transition state theory. Failure to observe this would introduce systematic error into computed estimates of Gibbs energies of activation for reactions involving conformational flexibility.

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Table 2. M06-2X/6-311+G(2d,p)/PCM(EtOH) data for reactant-state (RS) and heterolysis transition-state (TS) conformers of 4,4'-dimethoxybenzhydrylpyridinium cation as required for evauation of effective Gibbs energies of activation by means of procedures 1 and 2. Total energies *G*° including Gibbs energy correction (289.15 K, 1 atm), mole fractions x_i^{state} (state = RS or TS), relative Gibbs energies $\Delta^{\ddagger}G_0^j$ and $\Delta^{\ddagger}G_i^i$ and weighted contributions $x_i^{RS}\Delta^{\ddagger}G_i$ for individual conformers,). All relative energies are in units of kJ mol^{-1}.

			procedure 1		procedure 2		
state	conformer	*G*°/Hartree	$\Delta^{\ddagger}G_0^j$	$\exp(-\Delta^{\ddagger}G_0^j/RT)$	x_i^{state}	$\Delta^{\ddagger}G_i^i$	$x_i^{\mathrm{RS}}\exp(-\Delta^{\ddagger}G_i^i/RT)$
RS	**a**	-978.760013			0.5196		
	b	-978.758859			0.1531		
	c	-978.758977			0.1734		
	d	-978.758864			0.1539		
TS	**a**$_{\mathbf{het}}$	-978.760013	94.55	2.718×10^{-17}	0.1576	94.55	1.412×10^{-17}
	b$_{\mathbf{het}}$	-978.758859	92.04	7.498×10^{-17}	0.4347	89.01	3.896×10^{-17}
	c$_{\mathbf{het}}$	-978.758977	94.90	2.361×10^{-17}	0.1369	92.18	1.227×10^{-17}
	d$_{\mathbf{het}}$	-978.758864	93.21	4.670×10^{-17}	0.2708	90.19	2.427×10^{-17}
sum				1.725×10^{-16}			8.962×10^{-17}

Table 3. M06-2X/6-311+G(2d,p)/PCM(EtOH) data for reactant-state (RS) and heterolysis transition-state (TS) conformers of 4,4’-dimethoxybenzhydrylpyridinium cation as required for evauation of effective Gibbs energies of activation by means of procedure 3. Total energies G° including Gibbs energy correction (289.15 K, 1 atm), mole fractions x_i^{RS} and x_i^{TS}, relative Gibbs energies ΔG_0^i and $\Delta^\ddagger G_0^j$, Boltzmann-weighted contributions to average Gibbs energies for RS and TS, and contribution $RT\,x_i \ln x_i$ from entropy of mixing. All relative energies are in units of kJ mol^{-1}.

procedure 3										
			RS				TS			
state	conformer	G°/Hartree	ΔG_0^i	x_i^{RS}	$x_i^{\mathrm{RS}}\Delta G_0^i/RT$	$RT\,x_i \ln x_i$	$\Delta^\ddagger G_0^j$	x_j^{TS}	$x_j^{\mathrm{TS}}\Delta^\ddagger G_0^j/RT$	$RT\,x_i \ln x_i$
RS	**a**	-978.760013	0.000	0.5196	0.0000	-0.8432				
	b	-978.758859	3.030	0.1531	0.4637	-0.7121				
	c	-978.758977	2.720	0.1734	0.4718	-0.7532				
	d	-978.758864	3.017	0.1539	0.4642	-0.7139				
TS	$\mathbf{a}_{\mathbf{het}}$	-978.760013					94.55	0.1576	14.90	-0.7218
	$\mathbf{b}_{\mathbf{het}}$	-978.758859					92.04	0.4347	40.01	-0.8977
	$\mathbf{c}_{\mathbf{het}}$	-978.758977					94.90	0.1369	12.99	-0.6748
	$\mathbf{d}_{\mathbf{het}}$	-978.758864					93.21	0.2708	25.24	-0.8769
sum					1.40	-3.02			93.14	-3.17

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SUPPORTING INFORMATION

Optimised Cartesian coordinates for all transition structures for RS conformer interconversion may be found online in the Supporting Information section at the end of this article.

Gibbs energies of activation for reacting systems with multiple reactant-state and transition-state conformations

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Supporting Information

Optimised Cartesian coordinates for transition structures for RS conformer interconversion
Full M06-2X/6-311+G(2d,p) geometry optimisation was performed for transition structures for interconversion of RS conformers (**a**, **b**, **c** and **d**) of 4,4’-dimethoxybenzhydrylpyridinium cation. As described in the main text, there are two transition structures for each interconversion; these are distinguished by a plus or minus sign, leading to eight processes (viz. **a+b**, **a-b**, **a+c**, **a-c**, **b+d**, **b-d**, **c+d**, and **c-d**).

a+b

C	2.683548	-1.598564	-0.612427
C	3.810131	-1.173603	0.089784
C	3.681281	-0.182515	1.072403
C	2.447825	0.366790	1.337608
C	1.310712	-0.043494	0.630993
C	-1.838370	-0.020725	-0.725672
C	-2.909521	-0.824783	-1.088168
C	-3.379477	-1.789452	-0.204952
C	-2.784959	-1.942163	1.043360
C	-1.717889	-1.134715	1.400676
C	-1.234980	-0.171134	0.519285
C	-0.009920	0.616724	0.928778
C	1.444659	-1.031065	-0.334973
N	-0.088895	2.006775	0.310969
C	0.725314	2.389013	-0.681772
C	0.591222	3.637856	-1.258035
C	-0.392143	4.496639	-0.795619
C	-1.227692	4.080824	0.235522
C	-1.056217	2.824294	0.765839
O	-4.396102	-2.616488	-0.576026
O	5.048586	-1.654066	-0.093272
C	-5.695302	-2.096383	-0.303545
C	5.235730	-2.681870	-1.054551
H	2.754239	-2.373354	-1.361787
H	4.565627	0.119778	1.617708
H	2.360169	1.124538	2.110042
H	-1.474248	0.717241	-1.432934
H	-3.378768	-0.727740	-2.059069
H	-3.161465	-2.703607	1.714519
H	-1.244405	-1.266598	2.367535
H	-0.059721	0.816033	2.001789
H	0.574108	-1.383386	-0.875181
H	1.475861	1.673466	-0.987507
H	1.260604	3.921160	-2.057829
H	-0.509287	5.480910	-1.230582
H	-2.007330	4.719140	0.626316
H	-1.680291	2.424461	1.554333
H	-6.405672	-2.843518	-0.646316
H	-5.823324	-1.928580	0.768756
H	-5.855496	-1.159332	-0.842789
H	6.294220	-2.921398	-1.030938
H	4.653228	-3.567610	-0.792921
H	4.960617	-2.334634	-2.052750

a-b

C	2.505207	-1.711644	-0.561337
C	3.667366	-1.340601	0.112986
C	3.617614	-0.313623	1.065242
C	2.426878	0.324436	1.327023
C	1.255121	-0.030262	0.647084
C	-1.871674	0.101532	-0.679020
C	-3.030099	-0.601294	-0.973864
C	-3.624677	-1.394012	0.001795
C	-3.057583	-1.486100	1.267923
C	-1.90158300	-0.778827	1.557392
C	-1.299902	0.017805	0.587776
C	-0.012232	0.729039	0.938272
C	1.310481	-1.054699	-0.287473
N	-0.011045	2.096567	0.261379
C	0.837267	2.399179	-0.730137
C	0.777617	3.630929	-1.353895
C	-0.166479	4.556045	-0.940517
C	-1.038242	4.222771	0.090668
C	-0.941022	2.979863	0.669479
O	-4.793178	-2.040549	-0.265911
O	4.869021	-1.906809	-0.070490
C	-4.619611	-3.337076	-0.834134
C	4.975387	-2.971572	-1.003247
H	2.514386	-2.512362	-1.286337
H	4.527362	-0.053531	1.590147
H	2.400353	1.110382	2.075390
H	-1.422288	0.721620	-1.448065
H	-3.495431	-0.530960	-1.948927
H	-3.544194	-2.096394	2.018071
H	-1.463001	-0.848906	2.546808
H	-0.025974	0.977207	2.001938
H	0.411318	-1.365033	-0.805696
H	1.554064	1.635413	-0.997323
H	1.472828	3.848905	-2.152114
H	-0.225850	5.527780	-1.413680
H	-1.790125	4.914135	0.443816
H	-1.598462	2.642151	1.460014
H	-5.615798	-3.737866	-0.999288
H	-4.085107	-3.271586	-1.785165
H	-4.068638	-3.985050	-0.148044
H	6.016446	-3.278533	-0.986170
H	4.340972	-3.809898	-0.708192
H	4.708697	-2.635918	-2.007716

a+c

C	2.431941	-1.906607	-0.615493
C	3.610378	-1.606538	0.063211
C	3.624553	-0.610180	1.040074
C	2.457079	0.078545	1.331463
C	1.270622	-0.210358	0.650624
C	-1.912655	0.059705	-0.576857
C	-3.085380	-0.630089	-0.877555
C	-3.638927	-1.492141	0.071101
C	-3.010812	-1.648306	1.314452
C	-1.851646	-0.955699	1.598279
C	-1.285852	-0.092044	0.653849
C	0.027113	0.578580	0.990688
C	1.264555	-1.212551	-0.319377
N	0.053053	1.958810	0.343711
C	0.873121	2.253845	-0.676944
C	0.828520	3.500689	-1.276765
C	-0.069294	4.448994	-0.807781
C	-0.911868	4.123265	0.252890
C	-0.832844	2.864233	0.805376
O	-4.763018	-2.204432	-0.109636
O	4.737319	-2.327939	-0.182224
C	-5.437390	-2.099883	-1.353409
C	5.570798	-1.786161	-1.204293
H	2.437339	-2.705319	-1.347557
H	4.544198	-0.413847	1.578164
H	2.464538	0.838717	2.107352
H	-1.497034	0.720270	-1.332492
H	-3.551787	-0.488056	-1.842521
H	-3.459906	-2.318581	2.036458
H	-1.371306	-1.092685	2.561870
H	0.048547	0.799739	2.061268
H	0.342479	-1.472033	-0.826674
H	1.553445	1.472179	-0.987142
H	1.498589	3.711909	-2.098910
H	-0.115300	5.431902	-1.260600
H	-1.626012	4.831971	0.649510
H	-1.470523	2.530335	1.614461
H	-6.298969	-2.757589	-1.280618
H	-5.774131	-1.074551	-1.529598
H	-4.794256	-2.428920	-2.174222
H	6.423540	-2.454383	-1.294332
H	5.033789	-1.743211	-2.156614
H	5.914905	-0.784331	-0.930093

a-c

C	2.578575	-1.497716	-0.953235
C	3.760178	-1.101665	-0.337108
C	3.732424	-0.176396	0.703334
C	2.521952	0.356967	1.110851
C	1.332297	-0.021914	0.487950
C	-1.948267	-0.000979	-0.530516
C	-3.062952	-0.792145	-0.789950
C	-3.449840	-1.758758	0.135953
C	-2.714743	-1.917331	1.316335
C	-1.615582	-1.124133	1.559790
C	-1.215968	-0.154532	0.636887
C	0.042975	0.629833	0.925795
C	1.368077	-0.960055	-0.540177
N	-0.097236	2.025019	0.335259
C	0.626408	2.430115	-0.717088
C	0.433973	3.686407	-1.259869
C	-0.512448	4.529290	-0.701571
C	-1.253438	4.090302	0.390554
C	-1.028733	2.827244	0.883834
O	-4.506726	-2.574712	-0.009602
O	4.951673	-1.593173	-0.773322
C	-5.281883	-2.463029	-1.191891
C	5.362596	-2.788777	-0.110010
H	2.623780	-2.222669	-1.756131
H	4.663228	0.114167	1.173792
H	2.501581	1.078377	1.921664
H	-1.662982	0.741706	-1.268858
H	-3.614857	-0.646071	-1.706939
H	-3.034871	-2.669804	2.024910
H	-1.051207	-1.262333	2.475686
H	0.105156	0.814922	2.000692
H	0.448407	-1.280163	-1.014738
H	1.354319	1.728187	-1.098991
H	1.030325	3.987182	-2.109527
H	-0.673737	5.519043	-1.109115
H	-2.001291	4.715690	0.857026
H	-1.581427	2.409060	1.714844
H	-6.066946	-3.207772	-1.104841
H	-5.728082	-1.469211	-1.271983
H	-4.675199	-2.672507	-2.075726
H	6.315401	-3.072071	-0.548091
H	5.485298	-2.609646	0.960825
H	4.630583	-3.584494	-0.267135

b+d

C	2.379170	-1.961919	-0.662136
C	3.514485	-1.771470	0.116753
C	3.507864	-0.836445	1.148798
C	2.362097	-0.100205	1.395609
C	1.218352	-0.280062	0.616346
C	-1.811080	0.210532	-0.843207
C	-2.989644	-0.374672	-1.255115
C	-3.709674	-1.197940	-0.382513
C	-3.230360	-1.417828	0.907873
C	-2.043700	-0.817139	1.308770
C	-1.321320	-0.005270	0.447051
C	-0.000786	0.559770	0.913304
C	1.233347	-1.220911	-0.409810
N	0.148378	1.970290	0.355278
C	1.065089	2.278188	-0.571653
C	1.134451	3.555781	-1.093967
C	0.249164	4.521527	-0.645162
C	-0.695195	4.182181	0.317860
C	-0.727040	2.893493	0.794762
O	-4.844228	-1.721096	-0.874792
O	4.616434	-2.543265	-0.088961
C	-5.609989	-2.570196	-0.034190
C	5.550855	-1.989541	-1.012057
H	2.398314	-2.713647	-1.441051
H	4.393189	-0.723377	1.761610
H	2.351977	0.613548	2.213388
H	-1.269618	0.841078	-1.541455
H	-3.381518	-0.213798	-2.250777
H	-3.768393	-2.044691	1.603823
H	-1.675933	-0.999779	2.312773
H	-0.045998	0.718704	1.992916
H	0.342047	-1.396970	-0.999353
H	1.730352	1.480975	-0.871911
H	1.881785	3.776579	-1.842770
H	0.290601	5.528983	-1.038852
H	-1.405204	4.904260	0.695324
H	-1.448231	2.549797	1.524668
H	-6.465482	-2.881337	-0.625607
H	-5.031203	-3.447519	0.262444
H	-5.953697	-2.032167	0.851904
H	6.371540	-2.697778	-1.083341
H	5.088938	-1.859484	-1.994058
H	5.923731	-1.027744	-0.650497

b-d

C	0.000000	0.000000	0.000000
C	0.000000	0.000000	1.389894
C	1.203632	0.000000	2.090658
C	2.399340	-0.014387	1.393871
C	2.410064	-0.032001	-0.001546
C	3.414557	-0.453077	-3.214869
C	3.379717	0.037865	-4.502702
C	3.680972	1.381325	-4.752514
C	4.021206	2.218433	-3.691209
C	4.056230	1.706818	-2.399950
C	3.752685	0.377984	-2.144054
C	3.738811	-0.106438	-0.713974
C	1.202056	-0.014492	-0.693281
N	4.303820	-1.522420	-0.675887
C	3.546058	-2.586702	-0.379088
C	4.081673	-3.860424	-0.408106
C	5.415156	-4.028617	-0.741542
C	6.185274	-2.911216	-1.046241
C	5.598860	-1.668690	-1.012833
O	3.621235	1.764655	-6.038171
O	-1.178355	-0.034304	2.069623
C	3.911606	3.118813	-6.347327
C	-1.706834	1.255629	2.377440
H	-0.947348	0.006150	-0.524150
H	1.182264	0.006011	3.173099
H	3.336661	-0.015535	1.941420
H	3.172547	-1.497973	-3.047748
H	3.122248	-0.595667	-5.341242
H	4.263623	3.258084	-3.856033
H	4.317674	2.367738	-1.580511
H	4.465021	0.471102	-0.137817
H	1.195348	-0.002098	-1.776213
H	2.516132	-2.386890	-0.118913
H	3.447116	-4.701294	-0.166615
H	5.853973	-5.017841	-0.765274
H	7.229232	-2.997193	-1.312186
H	6.127129	-0.757716	-1.261844
H	3.799146	3.208996	-7.423288
H	3.209576	3.790129	-5.848095
H	4.935717	3.371052	-6.063833
H	-2.636014	1.087794	2.914555
H	-1.010328	1.814572	3.006992
H	-1.904105	1.816800	1.460977

c+d

C	2.520724	-1.648053	-1.007992
C	3.692837	-1.400242	-0.284927
C	3.653249	-0.553698	0.824552
C	2.449880	0.033934	1.188036
C	1.282880	-0.199611	0.469407
C	-1.930859	0.054476	-0.703921
C	-3.055563	-0.677374	-1.056859
C	-3.518605	-1.681635	-0.215071
C	-2.862406	-1.946590	0.982447
C	-1.741334	-1.211346	1.330386
C	-1.265937	-0.208134	0.490128
C	0.014005	0.499625	0.880378
C	1.332032	-1.058909	-0.632030
N	-0.034891	1.928539	0.353219
C	0.763592	2.348701	-0.636777
C	0.654488	3.635743	-1.128395
C	-0.286309	4.493278	-0.582858
C	-1.104558	4.038563	0.445812
C	-0.960328	2.745548	0.889350
O	-4.590893	-2.437722	-0.580528
O	4.795133	-2.024479	-0.724894
C	-5.847948	-1.883847	-0.199169
C	6.006972	-1.835100	-0.010532
H	2.571639	-2.322686	-1.852457
H	4.539444	-0.359808	1.410990
H	2.427441	0.684597	2.056646
H	-1.574125	0.824885	-1.379749
H	-3.572755	-0.493345	-1.990078
H	-3.234584	-2.737598	1.621029
H	-1.220858	-1.431071	2.256237
H	0.029906	0.631643	1.964514
H	0.429748	-1.281203	-1.189094
H	1.481106	1.631700	-1.010646
H	1.309180	3.948443	-1.929406
H	-0.383987	5.506319	-0.951539
H	-1.850615	4.674719	0.900447
H	-1.575078	2.315358	1.669111
H	-6.609446	-2.575445	-0.548656
H	-5.908807	-1.784699	0.887518
H	-5.995070	-0.906174	-0.665049
H	6.752920	-2.430198	-0.528004
H	6.304586	-0.784333	-0.021865
H	5.908807	-2.185233	1.019114

c-d

C	2.335755	-1.749024	-0.961808
C	3.533781	-1.560659	-0.263444
C	3.569207	-0.681922	0.820572
C	2.414132	-0.003567	1.183268
C	1.222096	-0.177838	0.489219
C	-1.971802	0.184831	-0.635272
C	-3.172429	-0.454501	-0.904904
C	-3.733242	-1.300875	0.045265
C	-3.090778	-1.509128	1.260655
C	-1.892514	-0.865494	1.525204
C	-1.323751	-0.016369	0.580550
C	0.012051	0.619150	0.897932
C	1.195761	-1.070256	-0.586351
N	0.036869	2.024481	0.303124
C	0.865050	2.362301	-0.693852
C	0.827219	3.632033	-1.238440
C	-0.072430	4.558564	-0.738536
C	-0.922280	4.189144	0.298650
C	-0.849582	2.909743	0.795726
O	-4.939303	-1.887258	-0.192151
O	4.584117	-2.270437	-0.700879
C	-4.850356	-3.135353	-0.876977
C	5.818342	-2.141109	-0.011713
H	2.327936	-2.449010	-1.786928
H	4.475895	-0.531429	1.388128
H	2.449911	0.672332	2.031865
H	-1.549685	0.848187	-1.383448
H	-3.695146	-0.293698	-1.839330
H	-3.551329	-2.159929	1.992983
H	-1.394433	-1.027462	2.474903
H	0.069108	0.801148	1.973186
H	0.271830	-1.246771	-1.123641
H	1.548105	1.595341	-1.030978
H	1.504240	3.877263	-2.044351
H	-0.114228	5.559195	-1.149276
H	-1.638872	4.880523	0.718795
H	-1.493614	2.543945	1.584778
H	-5.869072	-3.490084	-1.005990
H	-4.377550	-3.005450	-1.853641
H	-4.279037	-3.855760	-0.286475
H	6.513940	-2.799966	-0.521990
H	6.184610	-1.113369	-0.060414
H	5.715417	-2.452834	1.029734