# Remarkable cleavage of molecular hydrogen without the use of metallic catalysts: a theoretical investigation

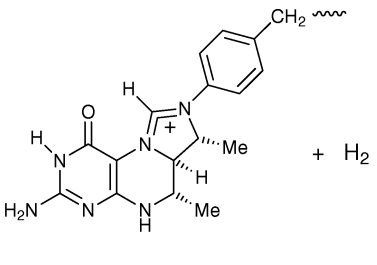
**Anthony P. Scott,[a] Bernard T. Golding[b] and Leo Radom[a]**

[a] *Research School of Chemistry, Australian National University, Canberra, ACT 0200, Australia*
[b] *Department of Chemistry, University of Newcastle upon Tyne, Newcastle upon Tyne, UK NE1 7RU*

NJC Letter

High level *ab initio* molecular orbital calculations show that molecular hydrogen can be cleaved by the 1,3-dimethylimidazolidin-2-yl cation in the presence of a base such as $NH_3$ or $HCOO^-$ with quite a modest barrier, in a reaction that models the non-metallic hydrogenase from methanogenic archaea.

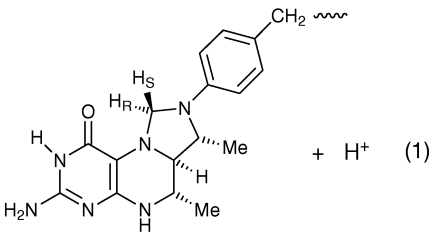
The generation and consumption of hydrogen are environmentally important processes that occur in both oxic and anoxic habitats.[1] These processes are catalysed by enzymes called hydrogenases, which have normally contained an iron–sulfur cluster and usually nickel. The metal centre(s) had been believed to play an indispensable role in the activation of the $H_2$ molecule. However, Thauer and his co-workers have discovered a hydrogenase in methanogenic archaea that is devoid of any metal centre, yet can either generate or consume $H_2$.[1,2] This remarkable enzyme operates with a folate-like cofactor [$N^5$,$N^{10}$-methenyltetrahydromethanopterin, **1a** ($CH{\equiv}H_4MPT^+$)], which in the $H_2$-consuming reaction acts as a sink for the hydride ion delivered by enzyme-mediated deprotonation of $H_2$, yielding $N^5$,$N^{10}$-methylenetetrahydromethanopterin, **1b** ($CH_2{=}H_4MPT$):




$CH{\equiv}H_4MPT^+$

**1a**

hydrogenase



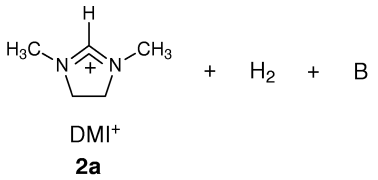

$CH_2{=}H_4MPT$

**1b**

In the production of $H_2$, the pro-*R* hydrogen of the C-14a methylene group of the cofactor **1b** reacts with a proton from the enzyme.

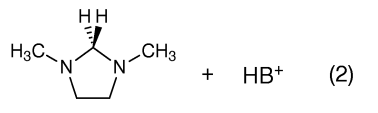
Cioslowski and Boche[3] have recently used *ab initio* molecular orbital calculations on model systems to show that the reaction of **1a** with $H_2$ to give **1b** is thermodynamically feasible provided that a base is present to consume the proton released. They have also considered the effects of geometric distortions, finding that non-planarity in the amidinium moiety of **1a** is likely to be energetically more costly than the corresponding distortion in **1b**. This would lead to an energetically more favourable forward reaction. An additional important theoretical paper on this topic by Berkessel and co-workers[4] has just appeared, after the present calculations were substantially complete. It includes calculations both on the reaction enthalpy for a number of amine bases and of the barrier for a model hydrogen-cleavage reaction. A nearly thermoneutral reaction was predicted when methylamine is the base.

We have examined theoretically the full reaction profile for the interconversion of a number of systems related to **1a** and **1b** and a selection of results is presented in this letter. The 1,3-dimethylimidazolidin-2-yl cation ($DMI^+$, **2a**) and 1,3-dimethylimidazolidine (DMIH, **2b**) were used to model the $CH{\equiv}H_4MPT^+$ cation (**1a**) and neutral $CH_2{=}H_4MPT$ (**1b**), respectively, and the formate anion and ammonia were used to exemplify bases that might be provided by the enzyme or incorporated into model systems. Thus we initially examined energy profiles for the reaction:




$DMI^+$

**2a**




DMIH

**2b**

either in the absence of the base B or with formate anion or ammonia as the base. The conformation chosen throughout

for the imidazolidine ring has both nitrogen lone pairs in an axial orientation because this would facilitate their possible binding to one or more acidic sites on the enzyme.[2e,]† Such a conformation would also provide antiperiplanar stabilization of the transition structure for reaction (2). The most striking finding of the present study is that, consistent with the previous work at a lower level of theory,[4] the cleavage of molecular hydrogen can take place with quite a modest barrier.

Standard *ab initio* molecular orbital calculations[5] were carried out with the GAUSSIAN 94[6] and MOLPRO[7] programs.‡ Unless otherwise noted, structural parameters in the text are MP2/6-31G(d,p) values and relative energies correspond to MP2/6-311 + G(3df,2p) values (for the systems involving formate anion) or G2(MP2,SVP)[8] values (for all the remaining systems) at 0 K including a zero-point vibrational correction in all cases. The SCIPCM model[9] was used to estimate the effect of solvation.§ The present calculations have been performed at a higher level of theory than the previous studies.[3,4] In addition, we examine, for the first time, the reaction profile with formate anion as the base, and the effect of solvation and zero-point energy on the reaction barriers. The last two effects both make substantial contributions to the calculated relative energies.

We find that, in the absence of base, the gas-phase reaction of the 1,3-dimethylimidazolidin-2-yl cation with $H_2$ to produce 1,3-dimethylimidazolidine plus $H^+$ is highly endothermic (by 975 kJ $mol^{-1}$, Fig. 1), in keeping with previous findings.[3] At the other extreme, use of the $HCOO^-$ anion as a base leads to a highly exothermic (by 457 kJ $mol^{-1}$) reaction with no overall barrier, producing neutral 1,3-dimethylimidazolidine plus formic acid. The intermediate situation involves ammonia as base, producing 2,4-dimethylimidazolidine plus $NH_4^+$ in a reaction that is endothermic by 130 kJ $mol^{-1}$.¶ The striking result in this case is that the barrier for cleavage of the $H_2$ molecule is just 132 kJ $mol^{-1}$.

When we incorporate solvation into our calculations using a continuum model, the two very different gas-phase potential energy profiles for B = $HCOO^-$ and B = $NH_3$ become quite similar (Fig. 1). This arises because of substantial relative stabilization of reactants (by 451 kJ $mol^{-1}$) for B = $HCOO^-$ and a much smaller relative stabilization of products (by 113 kJ $mol^{-1}$) for B = $NH_3$. The barriers for reaction (2) are now 114 ($HCOO^-$) and 140 ($NH_3$) kJ $mol^{-1}$ and the reaction enthalpies are −6 ($HCOO^-$) and +17 ($NH_3$) kJ $mol^{-1}$.

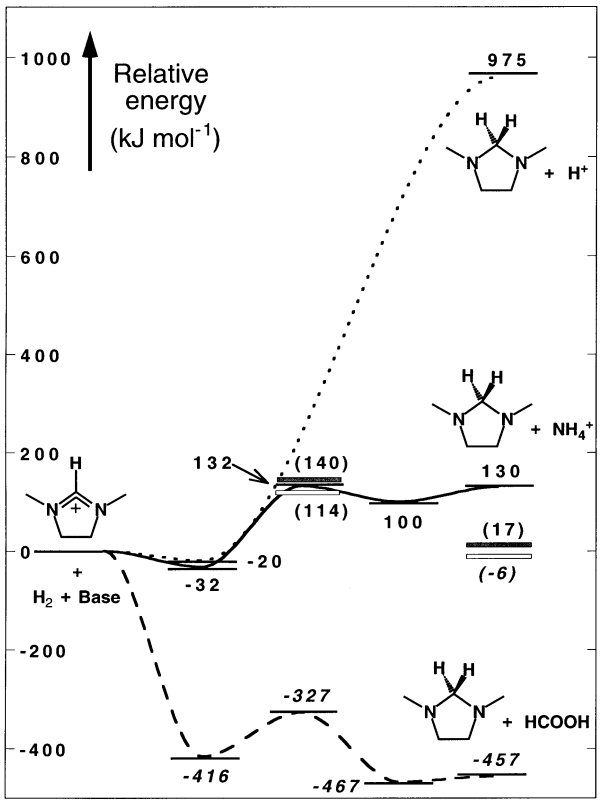



**Fig. 1** Schematic energy profiles [G2(MP2,SVP) (in regular bold type) or MP2/6-311 + G(3df,2p) (in bold italics)] showing the cleavage of molecular hydrogen by the 1,3-dimethylimidazolidin-2-yl cation (**2a**) to form 1,3-dimethylimidazolidine (**2b**), both in the absence of base (·····) or with $HCOO^-$ (– – – –) or $NH_3$ (———) as base. Energies including solvation effects are given in parentheses and indicated by open rectangles ($HCOO^-$ system) or filled rectangles ($NH_3$ system). See text for details

The calculated transition structures (TSs) for reaction (2) with B = $HCOO^-$ and B = $NH_3$ are displayed in Fig. 2. Both transition structures contain an antiperiplanar arrangement of the nitrogen lone pairs of the ring with respect to the forming/

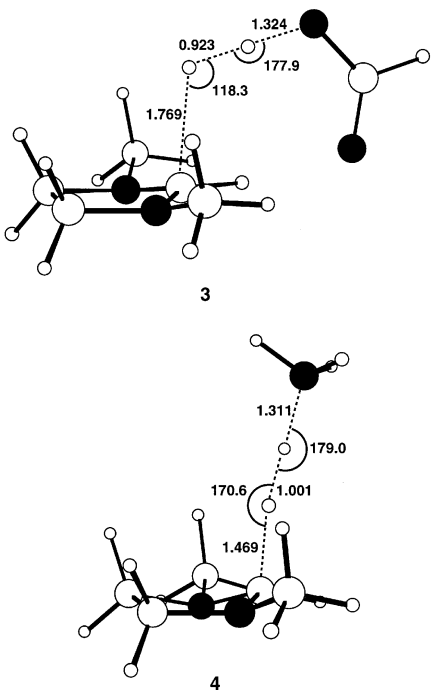



**Fig. 2** Optimized MP2/6-31G(d,p) transition structures for the cleavage of molecular hydrogen with $HCOO^-$ (**3**) or $NH_3$ (**4**) as base. Bond lengths are in Å, bond angles in degrees

† This is in fact the energetically preferred conformation for **2a** (which is actually planar) and for the transition structures **3** or **4** for the reaction. On the other hand, a twist conformation is slightly preferred (by 1.6 kJ $mol^{-1}$) for **2b** and strongly preferred (by 52 kJ $mol^{-1}$) for the complex of **2b** with HCOOH. A pair of products that is lower in energy (by 116 kJ $mol^{-1}$) than **2b** + $NH_4^+$ is $NH_3$ plus the N-protonated form of the twist conformation of **2b** but this is not considered to be relevant to the biological system.

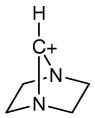
‡ Geometries were obtained at the MP2/6-31G(d,p) level of theory and zero-point vibrational energies (ZPVEs) derived from scaled (by 0.8929) HF/6-31G(d) frequencies. Improved energies were obtained through single-point calculations at the MP2/6-311 + G(3df,2p) and (except for the systems involving formate anion) QCISD(T)/6-31G(d) levels. This leads to G2(MP2,SVP) [effectively QCISD(T)/6-311 + G(3df,2p) + ZPVE] relative energies[8] but with the refinement that MP2/6-31G(d,p) rather than MP2/6-31G(d) geometries are used.

§ Solvent effects were evaluated at the MP2/6-31G(d,p) level using the self-consistent isodensity polarizable continuum model (SCIPCM)[9] through calculations on the optimized gas-phase structures (*i.e.* structures optimized in the absence of solvent) and assuming a dielectric constant of 80.

¶ Differences between the present results and those of references 3 and 4 are associated with the use of the higher level G2(MP2,SVP) procedure, the incorporation of zero-point vibrational corrections (which contribute, for example, 38 kJ $mol^{-1}$ to the endothermicity of reaction 2 with B = $NH_3$), and the inclusion of solvation energies (which, as is evident from Fig. 1, are substantial; these are treated in reference 3 but not reference 4).

breaking C···H bond in their lowest energy conformations. With $HCOO^-$ as the base, the TS (**3**) is quite early, the H···H bond having stretched from 0.734 Å (in molecular hydrogen) to 0.923 Å. The O···H (1.324 Å) and C···H (1.769 Å) bonds are beginning to form. The O···H···H bond angle is close to linearity (177.9°) whereas the C···H···H bond angle is strongly bent (118.3°). This would be consistent with electron donation from $O^-$ to the σ* orbital of $H_2$ and electron donation from the σ orbital of $H_2$ to $C^+$. For $B = NH_3$, the TS (**4**) occurs later on the reaction path, as reflected in a longer H···H distance (1.001 Å) and a shorter C···H distance (1.469 Å). In this case, both the N···H···H bond angle (179.0°) and the C···H···H bond angle (170.6°) are close to linearity. These stereochemical findings are likely to be important both with respect to the enzyme-mediated reaction and potential models. The enzymic base has not yet been identified although lysine ε-amino and carboxylate (*e.g.* glutamate) are obvious candidates. Berkessel and co-workers[4] suggested lys-$NH_2$ on the basis of their calculations but they did not explore the alternative possibility of carboxylate.[1]

There is no evidence in any of our calculated structures of tight three-centre–two-electron bonding.[1] The interaction of $DMI^+$ (**2a**) with $H_2$ occurs *via* a complex in which $H_2$ is bound to the H rather than the C of the C—H bond of **2a** with a binding energy of just 20 kJ $mol^{-1}$. This result could be attributed to the fact that delocalization of the nitrogen lone pairs in **2a** leads to a strongly stabilized carbocation that cannot effectively bind to $H_2$. However, even in the model bicyclic amidinium ion **5** in which the lone pairs are orthogonal to the formally vacant orbital at $C^+$ and therefore cannot participate in such a stabilizing interaction, the C···H bonds are long (2.597 Å) and the binding energy is small (5.9 kJ $mol^{-1}$). Nevertheless, we are investigating further the possible involvement of such structures in the various observed exchange reactions.[1]




**5**

The striking conclusion to emerge from the present calculations is that the barriers for the cleavage of molecular hydrogen by the 1,3-dimethylimidazolidin-2-yl cation and a suitable base can be quite modest. These results agree with those obtained by Berkessel and co-workers.[4] The full relevance of these results to the biological system will be explored in more detail in a forthcoming paper. We are also using the results of the present study for the design of non-enzymic hydrogen-generating/consuming systems.

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