

Supporting Information

**Experimental and computational aspects of molecular
Frustrated Lewis Pairs for CO₂ hydrogenation: en route for
heterogeneous systems?**

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S1. Extended version of Section 3.1 of the main text – H₂ splitting in molecular FLPs: a first required step.

S1.1. Atomistic characterisation of reaction mechanisms.

As mentioned in the main text, the very first example of reversible H₂ splitting by an FLP system was reported by Stephan and co-workers in 2006.^{S1} Specifically, the Mes₂P(C₆F₄)B(C₆F₅)₂ (Mes = C₆H₂(CH₃)₃) compound, containing both a boron LA and a phosphorus LB centres, was found to split H₂ at room temperature to form a zwitterionic phosphonium borate, Mes₂P⁺H(C₆F₄)B⁻H(C₆F₅)₂, the latter being able to release H₂ to regenerate the initial compound when heated at 150 °C. In view of the long P...B distance within this molecule (ca. 6.2 Å), which precludes the direct heterolytic splitting of H₂ on P and B centres simultaneously, the authors proposed two possible multi-step reaction mechanisms, namely the hydride- and the proton-migration pathways, which are schematically represented in Fig. S1. These consist in the addition of H₂ either to the P—C or to the B—C bonds, followed by the migration of the hydride or the proton to the respective Lewis acid/base site through the structure of the molecule.

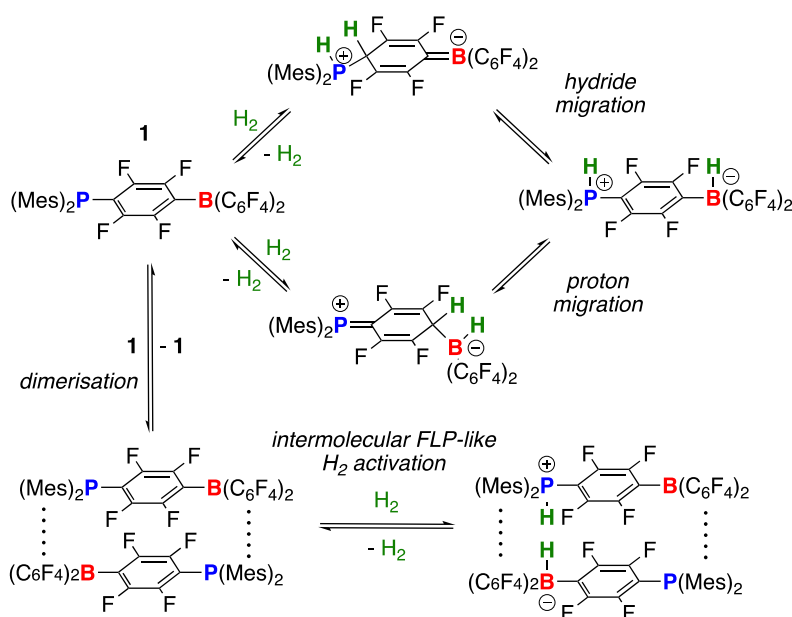


Fig. S1 Proposed reaction mechanisms for heterolytic H₂ splitting promoted by the Mes₂P(C₆F₄)B(C₆F₅)₂ (Mes = C₆H₂(CH₃)₃) compound, labelled as **1** in the Figure.

These findings motivated the first computational exploration of the H₂ splitting mechanism by Mes₂P(C₆F₄)B(C₆F₅)₂, which was carried out by Guo and Li in 2008.^{S2} Employing DFT calculations, the authors showed that both the hydride- and proton-migration mechanisms exhibit prohibitively high free-energy barriers of 69.1 and 54.7 kcal mol⁻¹, respectively. They thus proposed an alternative mechanism that involves the initial formation of a non-covalent dimer between two FLP molecules arranged in a head-to-tail fashion (Fig. S1, bottom). The latter gives access to shorter P...B distances of ca. 5.5 Å, enabling the concerted activation of H₂ by the P and B centres of two different molecules through a lower free-energy barrier (33.7 kcal mol⁻¹) when compared to the hydride- and proton-migration pathways. Thus, even though

$\text{Mes}_2\text{P}(\text{C}_6\text{F}_4)\text{B}(\text{C}_6\text{F}_5)_2$ can be classified as an *intramolecular* FLP, DFT calculations strongly suggested that it operates as an *intermolecular* FLP, made of two distinct molecules those conforming a reactive pocket for H_2 dissociation. Even so, the mechanism governing the H_2 -splitting activity of this FLP was reanalysed one year later using a $(\text{CH}_3)_2\text{P}(\text{C}_6\text{F}_4)\text{B}(\text{CF}_3)_2$ model system.^{S3} Complex, multi-step mechanisms that do not require the dimerization of this FLP were characterised and claimed to be operational. However, the reported energy differences from the most stable intermediate to the highest transition state (TS) found later along the path account for overall energy barriers of $>45 \text{ kcal mol}^{-1}$, being thus unable to compete with the intermolecular pathway proposed by Guo and Li.^{S2}

The same principle applies to a family of P/B intramolecular FLPs of formulae: $\text{Mes}_2\text{PCHRCH}_2\text{B}(\text{C}_6\text{F}_5)_2$ (R = H, Me and Ph) and $\text{Mes}_2\text{PCH}_2\text{CH}(\text{SiMe}_3)\text{B}(\text{C}_6\text{F}_5)_2$, whose reactivity towards H_2 was thoroughly investigated by Spies *et al.*^{S4-S6} Interestingly, $\text{Mes}_2\text{PCHRCH}_2\text{B}(\text{C}_6\text{F}_5)_2$ (R = H, Me) were experimentally found to split H_2 heterolytically, but conversely, both $\text{Mes}_2\text{PCH}(\text{Ph})\text{CH}_2\text{B}(\text{C}_6\text{F}_5)_2$ and $\text{Mes}_2\text{PCH}_2\text{CH}(\text{SiMe}_3)\text{B}(\text{C}_6\text{F}_5)_2$, which both bear bulky substituents, were unable to react with H_2 . For the ones splitting H_2 , early computational studies showed that the most stable “closed” conformer displaying a weak P—B bond can be easily open (with an energy cost of only ca. 7 kcal mol^{-1}) allowing for subsequent activation of H_2 .^{S4,S7,S8,S9} However, some years later, the reactivity of these systems towards H_2 was revisited by Vankova and co-workers using DFT calculations.^{S10} These revealed that the assumed mechanistic scenario in which a single FLP molecule activates H_2 in a bimolecular concerted way (intramolecular path in Fig. S2a) is unable to explain the observed differences in reactivity as a function of the bulkiness of the substituents. In contrast, the authors proposed an alternative, intermolecular mechanism (intermolecular path in Fig. S2a) where H_2 is split by a stacked dimer of “open” FLP conformers arranged in a head-to-tail configuration, similar to what Guo and Li proposed for the $\text{Mes}_2\text{P}(\text{C}_6\text{F}_4)\text{B}(\text{C}_6\text{F}_5)_2$ FLP.^{S2} Such mechanism was fully characterized and unlike the intramolecular pathway, served to explain the inertness of sterically demanding FLPs based on the steric clash between substituents that prevents their dimerization required to create a suitable reactive pocket. Still, such an intermolecular mechanistic picture cannot be generalized to all intramolecular or linked FLPs. More recent computational studies have disclosed numerous examples of FLPs being able to split H_2 through an intramolecular pathway with no need for FLP dimerization.^{S11-S14} In these cases, as illustrated in Fig. S2c (intramolecular path), H_2 is heterolytically cleft in between LA and LB centres contained within a single molecule through a concerted transition state, which directly attains the formation of a zwitterionic molecule that supports a hydride and a proton on the LA and LB sites, respectively.

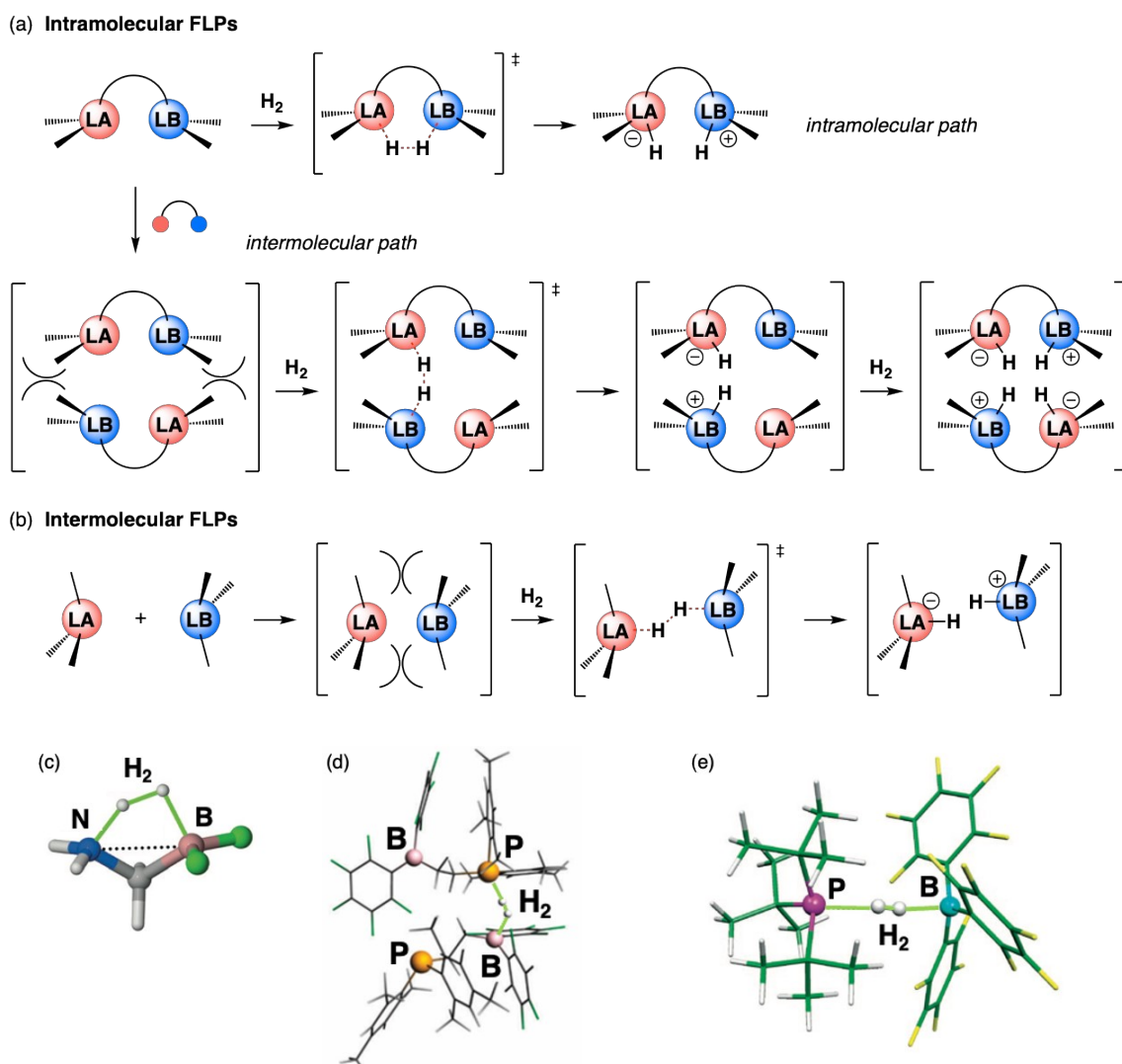


Fig. S2 Overview of the main reaction mechanisms characterised by DFT calculations to govern the H₂ splitting by (a) intramolecular and (b) intermolecular FLPs. 3D-structures on the right show representative transition-state geometries for: (c) H₂ activation by intramolecular FLPs through an intramolecular path. Reprinted with permission from ref. S11. Copyright 2016, Wiley-VCH; (d) an intermolecular path. Adapted from ref. S10 with permission from the PCCP Owner Societies; (e) an intermolecular FLP. Reprinted with permission from ref. S15. Copyright 2008, Wiley-VCH.

Also at the dawn of computational FLP chemistry, Pápai and co-workers applied DFT calculations to analyse the H₂ splitting mechanism promoted by the combination of sterically hindered boranes and phosphines.^{S15} In such *intermolecular* FLPs, the LA and LB partners are separated into two distinct and different molecules (Fig. S2b). To this end, the authors selected the experimentally tested case of B(C₆F₅)₃ and P(^tBu)₃, which was reported in one of the seminal works by Welch and Stephan.^{S16} This study ruled out mechanistic scenarios whereby the H₂ activation initiates by the formation of weakly-bound adducts between H₂ and each of the FLP components, which were previously proposed based on the existence of H₃B...H₂ adducts and by analogy to transition-metal chemistry.^{S15} Instead, the authors characterised a plausible mechanism (represented in Fig. S2e) that starts with the energetically favourable formation of a [P(^tBu)₃...B(C₆F₅)₃] adduct ($\Delta E_{\text{binding}} = -11.5 \text{ kcal mol}^{-1}$) in which the two FLP partners interact via C—H...F hydrogen bonds and dispersion forces. This

association was found to lead to a reactive pocket between the P and the B centres, which are placed 4.2 Å apart. In the latter, H₂ can be heterolytically activated through a concerted TS whereby the H—H bond cleavage occurs concomitantly with the formation of B—H(δ⁻) and P—H(δ⁺) bonds, overcoming a calculated energy barrier from [P(^tBu)₃⋯B(C₆F₅)₃] + H₂ to the TS of only 10.4 kcal mol⁻¹. It is important to note here that more recently, the formation of non-covalent adducts has been further supported for a variety of intermolecular FLP using DFT and more sophisticated coupled-cluster calculations,^{S17–S20} Molecular Dynamics (MD) simulations^{S21,S22} and experimental NMR techniques.^{S23,S24} These allowed determining slightly endergonic binding free energies in solution, typically ranging between 0 and 5 kcal mol⁻¹. Of note, these studies stressed that besides including solvent effects employing an implicit solvation model, it is also essential to incorporate thermal effects to electronic binding energies as well as entropic contributions, which account for the energy penalty associated with the reduction of degrees of freedom along an associative, bimolecular process.

Overall, the above findings constituted a well-established mechanistic picture for the activation of H₂ by FLPs that is illustrated in Fig. S2 and can be summarized as follows: On the one hand, *intermolecular* FLPs proceed via the formation of a non-covalent adduct between the LA and LB partners that is usually referred to as “encounter complex”, followed by the insertion of H₂ into the reactive pocket and its subsequent splitting to form a hydrogenated [LB-H]⁺⋯[LA-H]⁻ ion pair. On the other hand, molecules that contain both LA and LB sites and can thus be classified as *intramolecular* FLPs may either activate H₂ by themselves or dimerize to operate as an intermolecular FLP. Although the competition between intra- and intermolecular pathways in intramolecular FLPs has not been systematically investigated for a whole range of systems to set clear conclusions, we can envisage that the prevalence of each of these paths might depend on the equilibrium LA⋯LB distance within the intramolecular FLP structure and on the ability of FLPs to dimerize into stable non-covalent adducts. Up to now, this mechanistic knowledge has been successfully applied to rationalize the H₂ splitting activity of a wide variety of FLPs, including mostly P/B and N/B pairs,^{S25–S27} and less often carbene/B^{S28} and N/TM (TM = Ni, Pt) pairs,^{S29} or even that of heterogeneous systems such as hydroxylated indium oxide surfaces.^{S30–S32}

Atomistic MD simulations of H₂ splitting also conceded unprecedented insights into the topology of the free-energy landscape along the reaction path. Early DFT-based MD simulations of the H₂ splitting by the ^tBu₃P/B(C₆F₅)₃ FLP by Pu *et al.* first validated the overall mechanistic picture inferred from static calculations.^{S33–S36} Nevertheless, the distances relevant to the TS geometry in the presence of explicit (and dynamic) solvent environment, were found to be significantly longer than in the gas phase.^{S34} Interestingly, these simulations revealed as well that reactive trajectories get “trapped” in the TS region of the phase space for sub-picosecond time periods (typically, a few hundred femtoseconds), indicating the presence of what was named a “quasi-bound transient state”. An in-depth analysis of the potential-energy surface (PES) along the reaction path showed that the region around the TS is remarkably flat (see Fig. S3) and that, roughly, the H₂ elongation is followed by the slower closing of

the pocket comprised between P and B centres for them to capture the resulting proton and hydride, respectively.

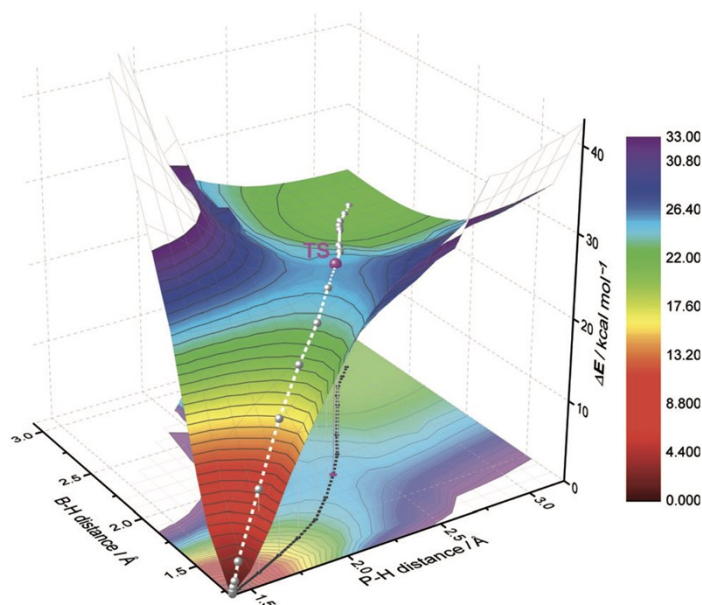


Fig. S3 Potential energy landscape of the $\{t\text{Bu}_3\text{P} + \text{H}_2 + \text{B}(\text{C}_6\text{F}_5)_3\}$ system. The minimum energy path for H_2 splitting obtained from climbing-image nudged-elastic-band calculations (CI-NEB), which connects the $\{t\text{Bu}_3\text{P} + \text{H}_2 + \text{B}(\text{C}_6\text{F}_5)_3\}$ van der Waals adduct and the ionic products, is represented on the two-dimensional space of $\text{P}\cdots\text{H}/\text{B}\cdots\text{H}$ distances. Reprinted with permission from ref. S35. Copyright 2014, Wiley-VCH.

In 2017, Liu *et al.* revisited the splitting of H_2 by $t\text{Bu}_3\text{P}/\text{B}(\text{C}_6\text{F}_5)_3$ employing DFT-based metadynamics simulations,^{S37} which allowed for a reconstruction of the free-energy landscape along the reaction coordinate, that is, explicitly incorporating thermal and entropic contributions to the PES. The reaction coordinate was described using three collective variables: the H-H distance and the coordination numbers of B and P by H atoms. The shape of the reconstructed free-energy surface revealed interesting features of the reaction path that are somewhat in contrast with the common beliefs established by static DFT calculations. While the latter consistently predict a concerted process involving a single TS (one-step mechanism), DFT-MD simulations showcase, instead, the presence of a shallow minimum in the TS along a step-wise reaction path (see Fig. S4).^{S37}

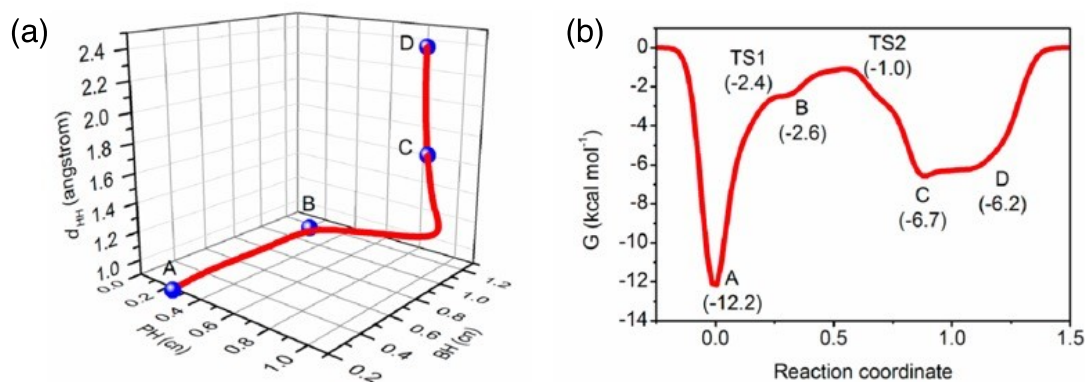


Fig. S4 Path-metadynamics analysis of the H₂ splitting by ^tBu₃P/B(C₆F₅)₃. (a) Minimum energy path projected on a three-dimensional CV space (H-H distance and coordination numbers of B and P by H atoms), where located minima are highlighted with blue circles. (b) Reconstructed free-energy profile along the H₂ splitting process, which indicates a step-wise reaction mechanism. Reprinted with permission from ref. S37. Copyright 2017, American Chemical Society.

After the polarisation of H₂ by the FLP, the H—H bond cleavage was found to initiate a hydride transfer to the LA site followed by the capture of the proton by the LB. As the former step was identified to be rate-limiting, these results suggested that the acidity of the LA partner has a stronger impact on H₂ splitting kinetics than the basicity of the LB. Such a shallow minimum was also observed in simulations of H₂ liberation by the (*o*-C₆H₄Me)₃P-H⁺⋯(*p*-C₆F₄H)₃B-H]⁻ ion pair.^{S38} Although static calculations cannot capture the stepwise nature of this process that manifests in metadynamics simulations, they have been claimed to be somewhat consistent with a two-step mechanism, as the vibrational normal mode connecting reactants and products through a concerted TS has a stronger component from the LA-H(δ⁻) bond formation than from the LB-H(δ⁺) one.^{S26}

This discussion was then implicitly reopened in more recent DFT-MD studies, in which the splitting of H₂ by several types of B/N and P/N intramolecular FLPs was found to involve a single, concerted TS through metadynamics and umbrella-sampling methods, as exemplified in Fig. S5.^{S39,S40} Albeit the actual nature (concerted or stepwise) of the H₂ mechanism remains somewhat controversial, it is widely accepted that relevant features of the free-energy profile, such as kinetic and thermodynamic parameters can be safely retrieved from static DFT calculations. In particular, dispersion-corrected hybrid GGA or meta-GGA functionals such as ωB97X-D, TPSS-D3, B3LYP-D3, M05-2X or M06-2X in combination with implicit solvation models and triple-ζ quality basis sets supplemented by polarisation and diffuse functions have proven to provide accurate geometries, reaction free energies and free-energy barriers when benchmarked either against experimental data or higher-level computational results.^{S25,S41,S42}

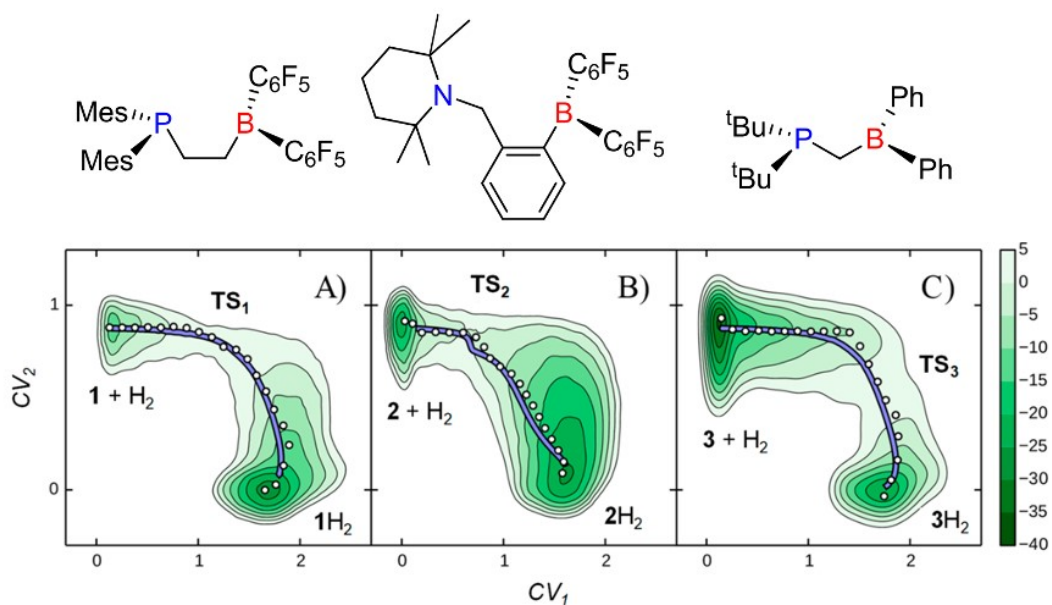


Fig. S5 Free-energy surfaces (kcal mol⁻¹) obtained from metadynamics simulations for the H₂ splitting by three distinct intramolecular B/N FLPs, projected on a two-dimensional CV space, where CV₁ is the sum of two coordination numbers accounting for B-H and N-H bond formations; and CV₂ is a coordination number describing the presence or absence of H-H bond. The minimum free energy path is represented by a blue line and the dotted path derives from IRC calculations. They both support concerted H₂ splitting mechanisms. Reprinted from ref. S40. Copyright 2019 American Chemical Society. This publication is licensed under CC-BY.

S1.2. Origin of H₂ polarisation and cleavage.

To rationalize the physicochemical foundations for the H₂ splitting promoted by FLPs, two computationally derived reactivity models have been proposed, namely the Electron Transfer (ET) model^{S15,S43} and the Electric Field (EF) model,^{S8} which are schematically illustrated in Fig. S6. Although both assume a concerted mechanism, they pose significant conceptual differences. The ET model (Fig. S6a), originally proposed by Pápai and co-workers, postulates that H₂ is activated via simultaneous electron transfers (i) from the non-bonding molecular orbital of the LB hosting a lone pair to the σ^* orbital of H₂, and (ii) from the bonding σ orbital of H₂ to the empty (usually p-type) orbital of the LA, resulting in a progressive cleavage of the H—H bond through a push-pull mechanism. Alternatively, the EF model proposed by Grimme and co-workers, implies that the H—H bond of H₂ is polarised by the electric field generated in the region of the space between the LA and LB centres of the FLP (Fig. S6b). The electron density of H₂ is thus displaced towards the LA partner inducing the formation of a hydride. Also, within the frame of this model, the energy barrier of the process is mainly associated with the introduction of H₂ into the FLP pocket, while the cost of the H—H bond cleavage is inversely proportional to the strength of the EF, becoming even barrierless when the EF is strong enough.

For years, the confronting aspects of the EF and ET models have been a matter of intense debate in the community,^{S9,S44–S46} although the latest computational studies indicate that they are complementary.^{S26,S37,S47} Using DFT-based MD simulations in combination with the Metadynamics enhanced-sampling technique, Liu *et al.* reinvestigated the splitting of H₂ by the archetypal ^tBu₃P/B(C₆F₅)₃ FLP.^{S37}

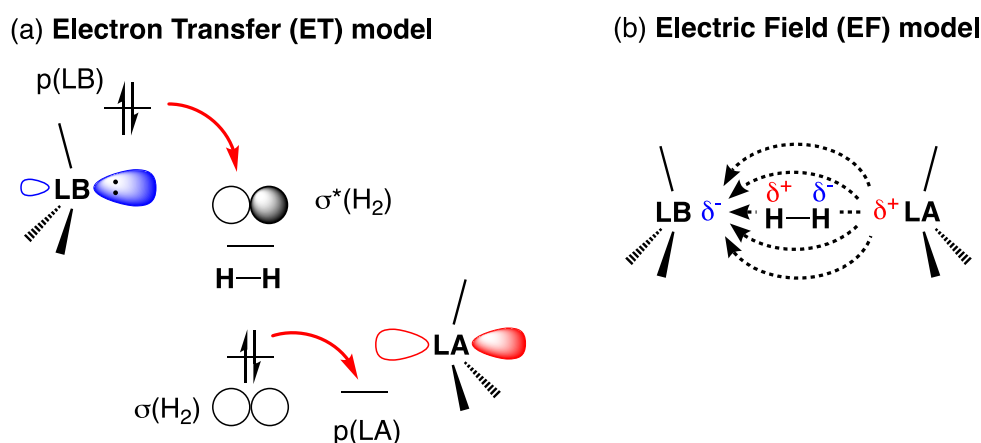


Fig. S6. Schematic representation of the ET (a) and the EF (b) models proposed to explain the physicochemical foundations for H₂ splitting by FLPs.

In addition to providing a comprehensive characterisation of the reaction mechanism in the presence of dynamic effects, these simulations revealed interesting features regarding the origin of the H—H bond polarisation along the reaction coordinate. Specifically, the simulations showed that when H₂ is placed at a distance larger than 2.5 Å from the reactive centres, the H—H bond is indeed polarised by the EF existing between LA and LB partners. As such, the H₂ molecule was found to display an average H—H distance of 0.80 Å that is slightly elongated with regard to the equilibrium distance

of 0.74 Å. Furthermore, clear evidence for charge density transfer from the LB to H₂ and from H₂ to the LA was found at shorter distances, supporting that the ET model governs at short FLP...H₂ distances, although the EF model can also contribute to ease the H₂ splitting. In line with these findings, an earlier computational study on simple NH₃/BX₃ (X = H, F, and Cl) Lewis pairs carried out by Camaioni *et al.* also concluded that the EF has a role in polarising H₂, although the overlap between p(N), σ(H₂), σ*(H₂), and p(B) orbitals at the transition-state structure has a greater impact on the height of the H₂ splitting barriers.^{S45}

By the time that these insights from DFT-MD simulations came out, in 2017, Skara *et al.* scrutinized the reactivity of six Lewis pairs towards H₂ employing DFT calculations.^{S46} These include three classical Lewis pairs: Me₃P–BF₃, Me₃P–B(C₆F₅)₃ and lut–B(C₆F₅)₃ (lut = 2,6-Lutidine, i.e. 2,6-dimethylpyridine); and three FLPs: carb/B(C₆F₅)₃, tBu₃P/B(C₆F₅)₃, Mes₃P/ BPh₃ (carb = N,N'-^tBu disubstituted imidazole-based carbene; Mes = 2,4,6-trimethylphenyl). This investigation identified two different types of TSs for H₂ splitting, which differ both in structure and in energy demand and were classified accordingly (Fig. S7). Low-energy TSs were characterized for short H–H distances of ca. 0.80 Å, being thus referred to as “early” TSs, whose geometrical configuration is closer to that of the reactant than that of the product. Conversely, high-energy TSs, associated with systems that are inactive for H₂ splitting (Me₃P–BF₃ and Mes₃P–BPh₃), were found to have a stronger “late” TS character (i.e. with a geometry closer to that of the product than the reactant), showing more stretched H–H distances ranging from 0.95 to 0.98 Å. Also, low-energy, ie “early” TSs were found to involve end-on H₂-LA interactions, whereas these interactions have more of a side-on character in high-energy “late” TSs, suggesting the existence of two different mechanisms. Relying on the fact that minor donation from the lone pair of the LB to the σ* orbital of H₂ would cause a prominent elongation of the H–H bond, the authors concluded that the ET model applies to high-energy, ie “late” TSs. On the contrary, the EF was proposed to play a more critical role in the splitting of H₂ by systems that operate through “early” TS structures, in which no sign of base→σ* donation was detected. Even though these results represent indeed a step forward towards the full understanding of FLP-assisted H₂ splitting processes, we believe that it is far from trivial to foresee whether a given FLP may activate H₂ through “early” or “late” TS. For such purpose, a much broader systematic analysis of the reactivity of different FLP families and LA/LB combinations and perhaps, with the assistance of state-of-the-art machine-learning tools, might be certainly required.

Finally, we wish to point out that while such a fundamental knowledge might be overlooked when targeting the construction of FLP-based heterogeneous catalysts, the above computational analyses point out that immobilized FLPs should exhibit a suitable orientation between the empty and occupied orbitals centred on the LB and LA sites to enable an effective polarisation and heterolytic splitting of H₂ for subsequent CO₂ hydrogenation.

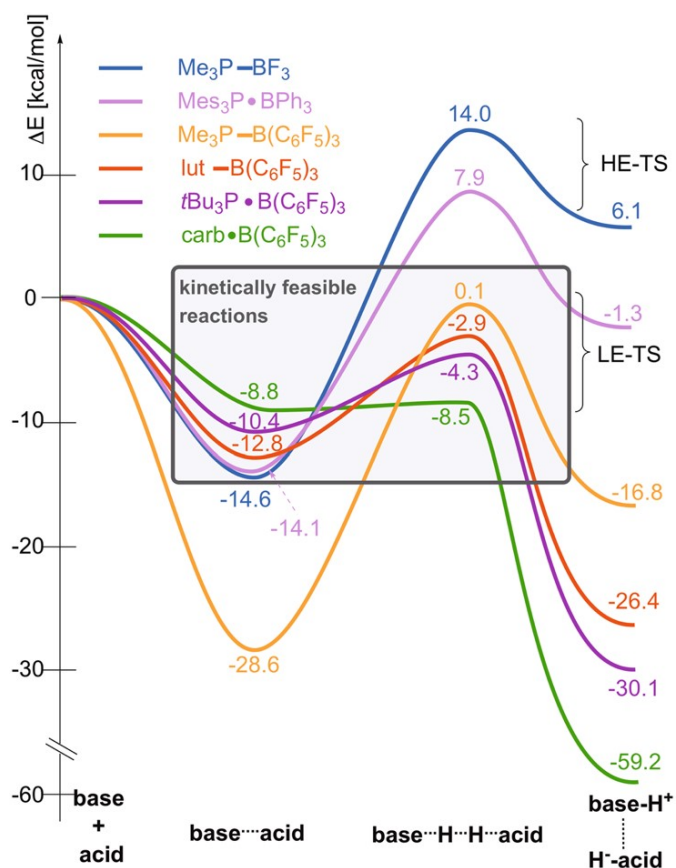


Fig. S7 Electronic energy profiles for the H₂ splitting promoted by a series of classical Lewis pairs (blue, orange and red lines) and FLPs (pink, purple and green lines), whereby transition states were characterised as low- or high-energy according to their relative energy but also to their “early” (LE-TS, LE= low energy) or “late” (HE-TS, HE=high energy) nature. Reprinted from ref. S46 (<http://creativecommons.org/licenses/by/4.0>).

S1.3. Structure-activity relationships.

In addition to obtaining a detailed, atomistic picture of the reaction pathways underlying the H₂ splitting by FLPs, computational efforts have been also devoted to gain insight into the key factors that govern this process. Surely, the primary structural requirement of an active FLP is to offer a suitable LA...LB distance. By performing constrained potential-energy surface scans along the P...B distance of a P(^tBu)₃/B(C₆F₅)₃ FLP, Vankova and co-workers determined that optimal P...B distances for H₂ splitting lie within a range of 3 to 5 Å.^{S19} As for B/N FLPs, Corminboeuf and co-workers identified that the optimal B...N distance for H₂ splitting is found at ca. 2.9 Å, although the range of distances in which the energy of the TS varies within an energy range of 5 kcal mol⁻¹ spans from ca. 2.6–3.5 Å according to a fitting of the data to a Morse-like potential.^{S48}

From an experimental perspective, it has been shown that the electronic properties of the substituents on the LA and LB centres of an FLP have a strong impact on their H₂ splitting activity, as noted by Pápai and co-workers in ref S7. In the latter work, which may be regarded as the first attempt of establishing chemically-meaningful reactivity rules for this reaction, the authors carried out a comprehensive partition analysis of the Gibbs free energies for H₂ splitting promoted by a series of intra- and intermolecular FLPs, which gave access to several conclusions: i) the absence of H₂ splitting activity of some FLPs arises from unfavourable thermodynamics; the stabilization of the product is thus an essential requirement for reactivity; ii) the thermodynamics of the H₂ splitting correlates with the *cumulative acid-base strength* of the FLP partners; iii) linked or intramolecular FLPs suffer from a smaller entropic penalty along the reaction coordinate than intermolecular FLPs and thus, require of smaller cumulative acid-base strengths to be active; iv) acid-base strengths can be quantified from proton and hydride attachment energies; v) reaction free-energies for H₂ splitting by the analysed set of intramolecular FLPs can be linearly correlated with the reciprocal of the LA...LB distance, so that the shorter the donor-acceptor distance, the more exergonic the H₂ splitting is. Accessible reaction kinetics were also claimed to be compulsory, although owing to the Bell–Evans–Polanyi principle,^{S49,S50} low barriers are already triggered by favourable thermodynamics, as later proven.^{S51}

By analysing a set of intramolecular B/N FLPs represented in Fig. S8, Yepes *et al.*^{S11} also reported that their height of the barrier is very sensitive to the nature of the substituents on both the LA and LB centres, as they determine the degree of cooperative LB→σ*(H₂) and σ(H₂)→LA charge transfer as well as the strength of electrostatic attractions between the FLP partners along the reaction path. In particular, strong electron-withdrawing or soft/poor π-donor substituents at the LA moiety were found to be beneficial for the reaction kinetics. The above findings regarding the impact of the electronic properties of the substituents on the H₂-splitting activity of FLPs were further corroborated by Vankova and co-workers, who studied computationally along a series of experimentally-tested intermolecular FLPs along which the acid-base strength was systematically modified.^{S19}

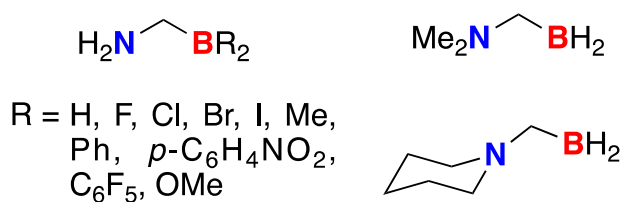


Fig. S8 Intramolecular B/N FLPs studied computationally for heterolytic H₂ splitting by Yepes *et al.*^{S11}

That is, both ^tBu₃P + B(*p*-C₆F₄H)₃ and Mes₃P + B(C₆F₅)₃ pairs, including either strong LB or LA component, respectively, were found to lead to non-reversible H₂ splitting; whereas no reaction could be attained with (C₆F₅)₃P + B(C₆F₅)₃ or ^tBu₃P + BMes₃ pairs, which consist of either a much less basic or a much less acidic partner. However, reversible H₂ splitting was observed with the (*o*-C₆H₄Me)₃P + B(*p*-C₆F₄H)₃ pair, which represents an intermediate situation in terms of LA and LB strength.^{S1, S52} Calculations supported that the ability of FLPs to split H₂ is governed by the thermodynamics of the reaction, which in turn, correlates with the cumulative acid-base strength.^{S19} As such, the reaction Gibbs free-energies were found to be highly negative for FLPs that activate H₂ in a non-reversible manner, supporting thus a highly exergonic process. Despite showing affordable kinetics, inactive FLPs with weak cumulative acid-base strengths were characterised by strongly endergonic H₂ activation energies. The reversible activation of H₂ by the FLP of moderate cumulative acid-base strength, namely (*o*-C₆H₄Me)₃P + B(*p*-C₆F₄H)₃, was consistently found to be almost ergoneutral. Similar conclusions were then reached by Neu *et al.* based on experimental investigations.^{S53} Recently, the concept of cumulative acid-base strength has been successfully applied to drive the design of FLPs for CO₂ hydrogenation, as we describe in more detail in section 3.2.2 of this review (see main text).

So far, the strengths of the LA and LB partners are largely accepted to be key factors governing the H₂ splitting process. However, the assessment of their relative impact on reaction energies and barriers remains largely unexplored. As described in section S1.1, Liu *et al.* characterised a stepwise mechanism for the H₂ splitting by a ^tBu₃P/B(C₆F₅)₃ pair through metadynamics simulations, in which the hydride transfer step to the LA was found to be rate-limiting, whereas the subsequent attachment of the proton to the LB occurs through a very small barrier and provides the thermodynamic driving force to the process. Thus, it was concluded that the acidity of the LA governs the kinetics of the reaction while the basicity of the LB partner determines its overall thermodynamics.^{S26, S37} However, it is important to clarify here that the acidity of the LA does play a role in the thermodynamics of the process. For the same LB, a stronger LA is expected to confer not only faster kinetics but also more favourable reaction energies than a weaker LA, as the shallow intermediate that precedes the stabilising protonation of the base will be already lower in energy. Berke and co-workers systematically analysed the activation of H₂ by a series of intermolecular B/N and B/P FLPs at the experimental level and concluded that the main factor controlling the reversibility of the process is the acidity of the LA, while the basicity of the LB was found to play a secondary role.^{S54}

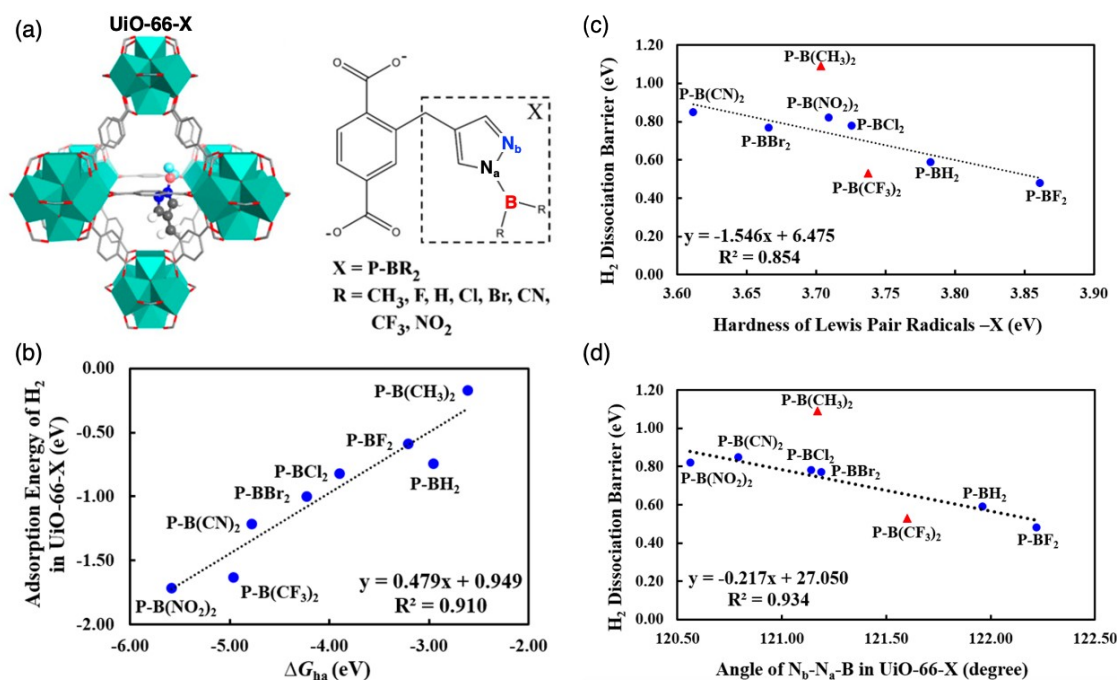


Fig. S9 (a) Octahedral cage of the UiO-66 Metal-Organic Framework bearing a linker functionalized with a Lewis Pair (X). (b) Adsorption energy of H₂ in UiO-66-X plotted against the free-energy of hydride attachment to the B centre of the Lewis pair. BEP relationships between the H₂ dissociation barrier on X and the chemical hardness of the Lewis pairs (c) and the N_b-N_a-B angle in the bare UiO-66-X structure (d). Reprinted with permission from ref. S55. Copyright 2015, Wiley-VCH.

Ye and Johnson noticed that even though some qualitative trends relating to the H₂ splitting ability of FLPs and their molecular structure had been reported in the literature (vide supra), clear structure-activity relationships were yet to be established.^{S55} In an original approach to explore computationally the immobilization of intramolecular FLPs in UiO-66, a porous MOF matrix, for CO₂ hydrogenation - which is discussed in detail in section 3.3 of this review - Ye and Johnson aimed to set the very first structure-activity relationships between the structure of FLPs and their ability to activate H₂, as well as to subsequently hydrogenate CO₂ in the gas phase under a stream of H₂ and CO₂. In this section, we focus only on their findings regarding the initial H₂ splitting step. As their ultimate goal relates to the covalent grafting of FLPs to the organic linkers of the MOF, the authors selected a set of 8 FLPs, which on paper, can be installed on the terephthalate linkers of the MOF. As shown in Fig. S9a, these consist of a pending pyrazole functionalized with a BR₂ moiety (R = CH₃, F, H, Cl, Br, CN, CF₃, NO₂), that leads to a series of intramolecular B/N FLPs of increasing LA acidity. Computing electronic energy profiles for all systems, the authors tried to find Brønsted–Evans–Polanyi (BEP) relationships^{S50,S56} between energetic parameters (reaction energies and barriers) and a set of molecular descriptors. The latter include the acidity of the LA, the basicity of the LB, the electronegativity, chemical hardness and softness of the FLP sites, atomic charges and structural parameters of both the bare FLP and the zwitterionic hydrogenated intermediate. The strength of the LA and the LB were estimated as the hydride and proton attachment free energies, respectively; electronegativity was calculated from the ionisation potential and electron affinity of the FLP using the Mulliken formula,^{S57} whereas hardness and

softness were also derived from the aforementioned measurable magnitudes employing the Parr and Pearson's formula.^{S58}

The dissociative H₂ adsorption energy (i.e. heterolytic H₂ splitting on the FLP) was found to correlate linearly with the hydride attachment energy as shown in Fig. S9b, so that as the LA strength increases, so does the H₂ dissociative adsorption energy.^{S55} Notably, no correlation was found with the proton attachment energy, which is in line with the experimental findings of Berke and co-workers.^{S54} Nevertheless, the computational work of Ye and Johnson only addressed the impact of the substituents at the LA boron centre, resulting in a rather narrow range of proton attachment energies. That is, the analysed FLPs do not significantly differ in terms of LB basicity, and therefore, the impact of this parameter remained uncharted. Furthermore, a linear BEP relationship was identified between the energy barrier for H₂ splitting and the chemical hardness of the LA (Fig. S9c).^{S55} Increasing the hardness of the LA decreases the barrier for H₂ dissociation in accordance with Pearson's theory, as this is a process along which the LA binds a hydride. We wish to stress here that, unlike the H₂ adsorption energy, this barrier was found not to correlate with the acidity of the LA. This may be interpreted as that the Bell–Evans–Polanyi principle does not fully apply to this process, given the absence of a linear correlation between reaction energies and barriers; and that some other factors affect the kinetics but not the thermodynamics of the reaction. Another BEP relationship was found between the H₂ splitting barrier and the bond angle conformed by N_b, N_a and B centres (see Fig. S9d) in the bare FLP, which was ascribed to the fact that larger angles induce strain in the FLP, lowering the barrier for H₂ splitting. The height of the reverse barrier for H₂ release, however, was found to be inversely proportional to the H₂ adsorption and to the hydride attachment energies, which as mentioned above, correlate linearly to one another. It is also relevant for the present review, that the MOF environment was not found to significantly affect the adsorption energy of H₂ on the FLP, as similar reaction energies were obtained from both isolated and in-MOF FLP models.

Two years later, Ye *et al.* revisited the factors that influence the thermodynamics of H₂ splitting on FLPs using four families of intramolecular FLPs, which include B/N and B/P pairs attached to structurally distinct scaffolds.^{S59} Besides discussing CO₂ hydrogenation (see section 3.2.3 in the main text), the authors drew relevant conclusions about the dependence of H₂ splitting energies on FLP parameters that are worth commenting here. Firstly, Ye *et al.* attempted to correlate H₂ binding energies with hydride attachment free energies, finding quantitative linear correlations for each individual FLP family (with $r^2 > 0.95$), as shown above, but not for all FLP families together ($r^2 = 0.834$). This evidenced that besides hydride attachment free energies, there are other factors that influence the binding energy of H₂. Through in-depth screening of a variety of molecular descriptors, the authors identified the following, reasonably accurate scaling relationship (eq. 1):

$$\Delta E = (0.184 d_1 + 0.273) \Delta G_{\text{ha}} + (0.990 d_1 + 0.010 \Delta \vartheta - 0.400) \quad (1)$$

where ΔE is the energy of H₂ splitting on the FLP; d_1 is the LA...LB distance in the bare FLP; ΔG_{ha} is the free-energy of hydride attachment on the LA site; and $\Delta \vartheta$ stands for

the variation of the angles concerning the LA/LB sites and the two consecutive atoms of the scaffold in the direction of the FLP partner upon H₂ binding.

Zhang *et al.* used DFT calculations to analyse the splitting of H₂ by four B/N FLPs of similar structure.^{S60} These include the inactive Piers' *ansa*-aminoborane^{S61} and three more active derivatives based on the same scaffold that have been reported by Repo and co-workers,^{S62,S63} which differ in the electronic properties of the substituents on both B and N centres. In line with previous findings,^{S54,S55} the authors concluded that the acidity of the LA has an important effect on the thermodynamics of the H₂ splitting, correlating with the Hammett constants of the substituents for a series of compounds bearing a -B(*p*-C₆F₄R)₂ LA moiety whereby R is modified systematically, as shown in Fig. S10. Tussing *et al.* also used the Hammett parameter to set semi-logarithmic relationships with rate constants for FLP-catalysed imine hydrogenation reactions.^{S64}

However, among the FLPs studied by Zhang *et al.*, the acidity of the LA was found not to influence the reaction barrier. The latter was proposed to be more significantly affected by the strength of the LB site.^{S60} The authors also pointed out that increasing the polarity of the solvent is beneficial for the thermodynamics of the reaction, owing to the strongly polarized nature of the zwitterionic hydrogenated product.

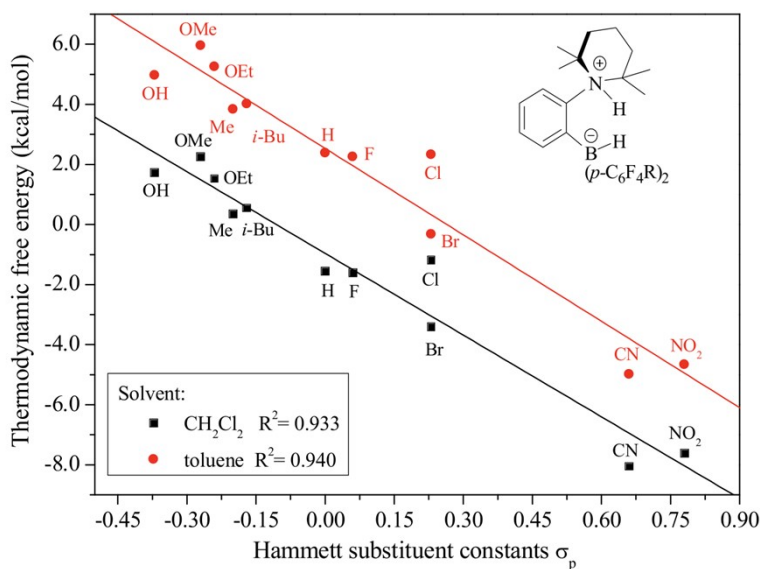


Fig. S10 Relationship between the reaction Gibbs free-energy for H₂ splitting by an intramolecular FLP (shown in the inset) and the Hammett constants of the substituents. Reprinted with permission from ref. S60. Copyright 2018, Elsevier.

In 2020, Heshmat and Ensing published a comprehensive computational study using 75 intermolecular FLPs, which was aimed at disclosing the impact of the electronic and steric effects of LA and LB components on the kinetics and thermodynamics of H₂ splitting.^{S65} The array of analysed FLPs consisted of combinations of 12 experimentally reported, borane-derived LAs with two families of LB partners, including strong phosphines (*t*Bu₃P and Me₃P) and less basic ethereal solvents (tetrahydrofuran and Ph₂O). Their main conclusions can be summarised as follows. The thermodynamics of the reaction can be tuned by modifying both the electrophilicity of the LA and the

nucleophilicity of the LB, further supporting the previously proposed relationship between the reaction free energies and the cumulative acid-base strength.^{S7,S19} O-based LBs lead to strong cation-anion interactions in the hydrogenated FLP adduct, which manifests into short $\text{H}^- \cdots \text{H}^+$ distances. This feature was hence proposed to hamper the dissociation of the adduct for further hydrogenation of substrates. Being stronger LBs, P-based compounds were found to yield more stable hydrogenated products, rendering the H_2 splitting processes more exergonic. Yet at the same time, P-based LBs display longer $\text{H}^- \cdots \text{H}^+$ distances in the product easing the dissociation of cation-anion products for further reactivity. This was ascribed to the presence of stronger P-H bonds, which are a consequence of the increased nucleophilicity of the LBs as well as of their bulkiness, allowing for larger cation \cdots anion separation. Furthermore, several factors were identified to affect reaction kinetics: i) both stronger LA and LB partners decrease the height of the barrier; ii) bulky LBs lead to early TSs to decrease the steric repulsion with the LA partner, resulting in lower barriers as found by Skara *et al.*^{S46}; iii) conversely, bulkiness and structural congestion around LAs hinder the accessibility of the B centre and increases the height of the barrier. From the joint analysis of the free-energy profiles obtained for such a large set of intermolecular FLPs, the authors also concluded that the reported reactivity trends are in accordance with the BEP principle mentioned above, as the free-energy barriers were found to correlate fairly well with the reaction free energies. It is important to note though, that such an agreement cannot be inferred from the set of intramolecular FLPs studied by Ye and Johnson,^{S55} which might suggest the existence of differences between intra- and intermolecular FLPs that are still not fully understood.

Overall, this section highlights that despite the complexity of FLP reactivity, computational methods have significantly contributed over the years to the generation of valuable knowledge that can be used to guide the experimental design of FLPs to conduct H_2 splitting. Still, several points still lack of a quantitative or unambiguous answer. For instance, the exact structural and electronic parameters that determine whether an intermolecular FLP operates through an intra- or an intermolecular mechanism, the relative weights of the impact of electric field polarisation and orbital overlap on H_2 splitting and how they depend on the FLP nature and structure, are aspects of the H_2 splitting by FLPs that remain controversial or unclear nowadays. Also, although a set of molecular parameters of FLPs have been recognised to influence H_2 splitting kinetics and thermodynamics, generic, clear quantitative structure-activity relationships are still to be established. Most likely, this is because besides eventual exceptions, the series of FLPs analysed in each work are constrained to a single family of FLPs and quite often, account for a rather limited number of structures. Moreover, within the present context of using FLPs not only for H_2 splitting but also for subsequent hydrogenation of CO_2 , one should also consider balancing the energetics of H_2 splitting with those of the following hydrogenation reaction. This adds an extra layer of complexity to the design challenge, which goal drifts from minimising energy barriers or optimising thermodynamics for a single elementary step process to identifying the molecular descriptors and the sometimes-overlooked experimental conditions that simultaneously optimise the performance of two distinct processes.

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