



Role of Alkaline-Earth Metal-Catalyst: A Theoretical Study of Pyridines Hydroboration

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Density functional theory (DFT) calculations have been performed to investigate the mechanism of alkaline-earth-metal-catalyzed hydroboration of pyridines with borane. In this reaction, the active catalytic species is considered to be an alkaline earth metal hydride complex when the corresponding alkaline earth metal is used as the catalyst. The theoretical results reveal that initiation of the catalytic cycle is hydride transfer to generate a magnesium hydride complex when β -diimine alkylmagnesium is used as a pre-catalyst. The magnesium hydride complex can undergo coordination of the pyridine reactant followed by hydride transfer to form a dearomatized magnesium pyridine intermediate. Coordination of borane and hydride transfer from borohydride to magnesium then give the hydroboration product and regenerate the active magnesium hydride catalyst. The rate-determining step of the catalytic cycle is hydride transfer to pyridine with a free energy barrier of 29.7 kcal/mol. Other alkaline earth metal complexes, including calcium and strontium complexes, were also considered. The DFT calculations show that the corresponding activation free energies for the rate-determining step of this reaction with calcium and strontium catalysts are much lower than with the magnesium catalyst. Therefore, calcium and strontium complexes can be used as the catalyst for the reaction, which could allow mild reaction conditions.

Keywords: alkaline-earth-metals catalyst, theoretical study, hydroboration, dihydropyridine, metal hydride complex

INTRODUCTION

As an important derivative of pyridine, dihydropyridine is an important raw material to synthesize natural products. For instance, dihydropyridine is extensively used to synthesize nicotinamide adenine dinucleotide, antihypertensive drugs, and anti-inflammatory agents (Karrer et al., 1937; Mauzerall and Westheimer, 1955; Bossert et al., 1981; Schramm et al., 1983; Berg et al., 2002). In addition, because dihydropyridine can provide two hydrogen atoms, it is often used as a mild and efficient reducing agent with high selectivity in catalytic hydrogenation (Adolfsson, 2005; Connon, 2007). Dihydropyridine can be prepared by dearomatization of pyridine and its derivatives. However, application of this reaction is limited by its strict reaction conditions and unstable dearomatized

intermediates (Hantzsch, 1881; Stout and Meyers, 1982; Seyferth, 2009; Li Y. Y. et al., 2018). Synthesis of these compounds by homogeneous catalysis has seldom been reported (Harrod et al., 2001; Oshima et al., 2012a,b). In 1998, Harrod's research group (Hao et al., 1998) realized pyridine hydrosilylation and obtained the 1,2-dihydropyridine product with a titanocene derivative as the catalyst. In 2011, Nikonov's group (Gutsulyak et al., 2011) realized hydrosilylation of pyridine with ruthenium as the catalyst at room temperature and obtained a mixture of 1,2- and 1,4-borohydropyridine. However, application of these reactions in synthetic chemistry is greatly limited by the expensive transition metal catalyst (Yaroshevsky, 2006; Dobereiner and Crabtree, 2010; Osakada, 2011; Huang and Xia, 2015; Li et al., 2015; Qi et al., 2016, 2018; Yang et al., 2016; Yu et al., 2016; Xing et al., 2017; Liu et al., 2018; Luo et al., 2018; Zhu et al., 2018).

Alkaline-earth (Ae) metals, which are located in group IIA of the periodic table of elements, have attracted wide attention because of their low cost, availability, and abundant reserves in nature (Green et al., 2007). Ae metals, such as magnesium, calcium, strontium, and barium, are commonly used as homogeneous catalysts. Because the d^0 valence electron configuration at the center of the divalent cation (Ae^{2+}) in the Ae metal catalyst shows partial "lanthanide" characteristics, a similar catalytic cycle can be constructed in homogeneous catalysis (Li and Marks, 1996; Westerhausen, 2008; Kriek et al., 2009; Hill et al., 2016; Ma et al., 2016; Rochat et al., 2016; Rossin and Peruzzini, 2016; Xu et al., 2017a).

In the past few decades, many research groups have prepared series of organic Ae metal compounds, which have wide application prospects owing to their low cost and toxicity (Arrowsmith et al., 2011; Liu et al., 2012; Intemann et al., 2014; Schwamm et al., 2014; Hill et al., 2016; Rossin and Peruzzini, 2016). One of the most important applications is the hydrogen transfer reaction, in which Ae metal hydrides are usually used to transfer hydrogen atoms and they show unique catalytic activity (Dunne et al., 2011; Harder et al., 2011; Praneeth et al., 2012; Intemann et al., 2013; Liptrot et al., 2014; Anker et al., 2015; Weetman et al., 2016). The high catalytic activity of Ae metal hydrides can be ascribed to two factors. First, the hydrogen atoms in the Ae metal hydride have high electron density, which means that the hydrogen atoms can easily dissociate in the form of free hydride anions that exhibit Brønsted basicity. Second, Ae metal hydrides also exhibit Lewis acidity owing to the two formal positive charges carried by the metal ions (Rokob et al., 2013; Anker et al., 2014; Stepha, 2015; Hill et al., 2016). For example, the magnesium catalyst can catalyze the hydroboration reaction of borohydride compounds (pinacol–borane (HBpin), 9-borabicyclo [3.3.1]nonane (9-BBN), etc.) with various organic compounds (esters, ketones, amines, pyridines, imines, nitriles, and amides) to construct new C (hetero)–B bonds (Barrett et al., 2007; Hill et al., 2010; Arrowsmith et al., 2012; Butera et al., 2014; Schwamm et al., 2014; Lampland et al., 2015; Liptrot et al., 2015; Liu et al., 2017; Zhao et al., 2017; Jiang et al., 2018).

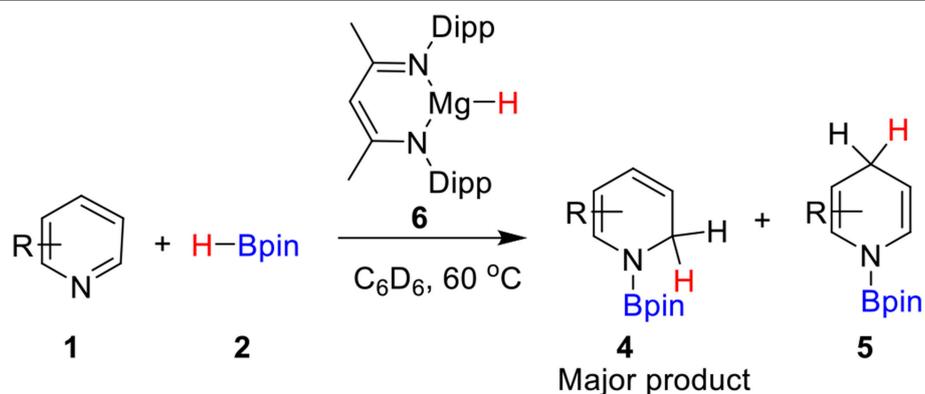
Hill and co-workers (Arrowsmith et al., 2011) first reported the magnesium-catalyzed hydroboration of Pyridines in 2011. In 2014, Harder's group (Intemann et al., 2014) reported hydroboration of pyridine catalyzed by the Ae metal magnesium

and obtained the 1,2-selective addition compound **4** as the major product (**Scheme 1**). Harder et al. suggested that magnesium hydride species **6** acts as a catalyst in the catalytic cycle. Based on the experimental observations and our previous theoretical studies of Ae catalysis, there are two possible reaction pathways. Raw material pyridine **1** coordinates with magnesium in active catalytic species **6** to give intermediate **7** (**Scheme 2**). The C = N double bond in pyridine then inserts into the Mg–H bond to give dearomatized magnesium amino intermediate **8**, which could coordinate with pinacolborane **2** to give nitrogen–boron compound **9**. Finally, magnesium hydride species **6** is regenerated by hydride transfer with the release of 1,2-borohydropyridine derivative **4**. Alternatively, intermediate **8** could be isomerized by 1,3-hydrogen migration to give intermediate **10**, which then coordinates to pinacolborane **2** to give nitrogen–boron complex **11**. After the corresponding hydride transfer, 1,4-borohydropyridine product **5** is obtained and active magnesium hydride species **6** is regenerated.

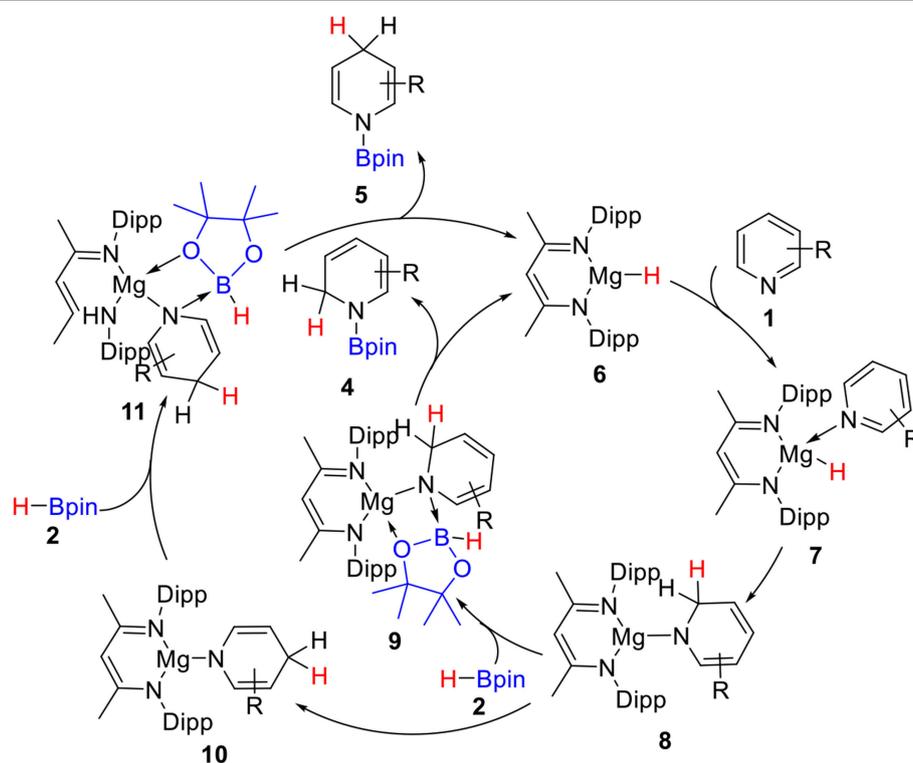
Here, we performed a theoretical mechanistic study of Ae catalysis and determined the trend of the reactivities of Ae-catalyzed hydrogenation reactions. The pyridine hydroboration reaction catalyzed by Ae metals reported by Harder's group was used as the template reaction for the theoretical calculations. The calculations were performed based on density functional theory (DFT) and the reaction mechanism is discussed to better understand the reaction process and provide theoretical guidance for subsequent organic reactions catalyzed by Ae metals.

COMPUTATIONAL METHODS

All of the DFT calculations were performed with the Gaussian 09 software package (Frisch et al., 2013). The B3-LYP (Lee et al., 1988; Becke, 1993; Stephens et al., 1994; Adamo and Barone, 1999) functional with the standard 6-31G(d) (Hehre et al., 1972; Francl et al., 1982) basis set (SDD Dolg et al., 1987 basis set for strontium atoms) was used for the geometry optimizations. Harmonic vibrational frequency calculations were performed for all of the stationary points to determine whether they are local minima or transition structures and to derive the thermochemical corrections for the enthalpies and free energies. The M11 (Peverati and Truhlar, 2011) functional with the 6-311+G(d) basis set (SDD for strontium atoms) was used to calculate the single-point energies, because it is expected that this strategy will provide more accuracy with regard to the energetic information (Peverati and Truhlar, 2012; Zhao et al., 2012; Yu and Lan, 2013; Cui et al., 2019). The solvent effect of benzene was considered by single-point calculations of the gas-phase stationary points with the solvation model based on the density (SMD), which is a continuous model (Cances et al., 1997; Marenich et al., 2009). The reported free energies are the M11-calculated Gibbs free energies in benzene solvent based on the B3-LYP-calculated geometries with thermodynamic corrections. The geometric configurations of the key reaction intermediates and transition states were generated with CYLview software (Legault, 2009). The total energies for all of the calculated structures are listed in **Supplementary Material**.



SCHEME 1 | Magnesium-catalyzed hydroboration of pyridines with borane.



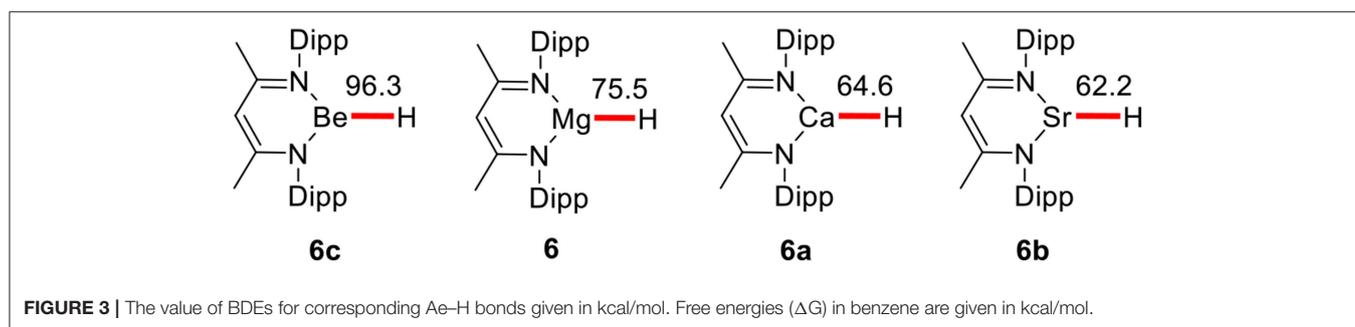
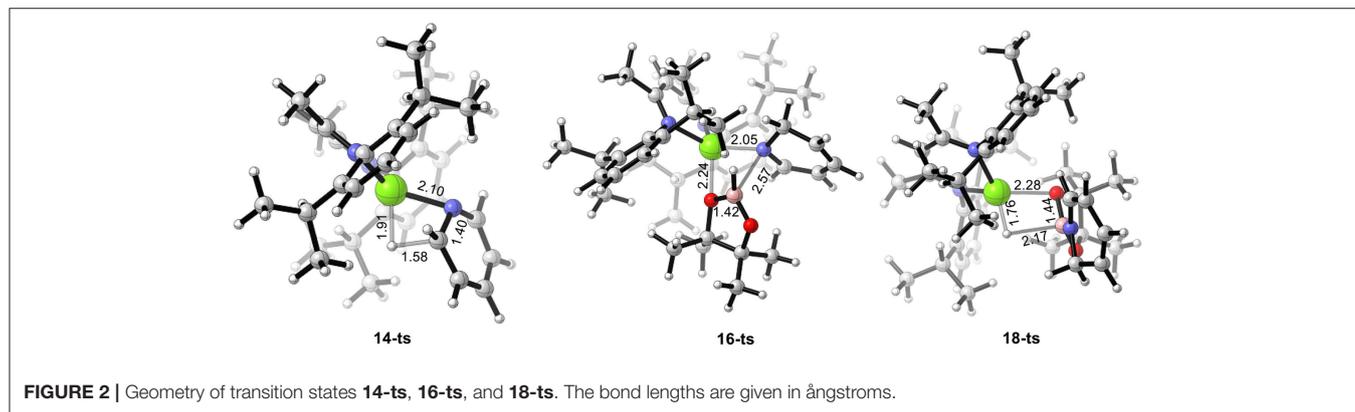
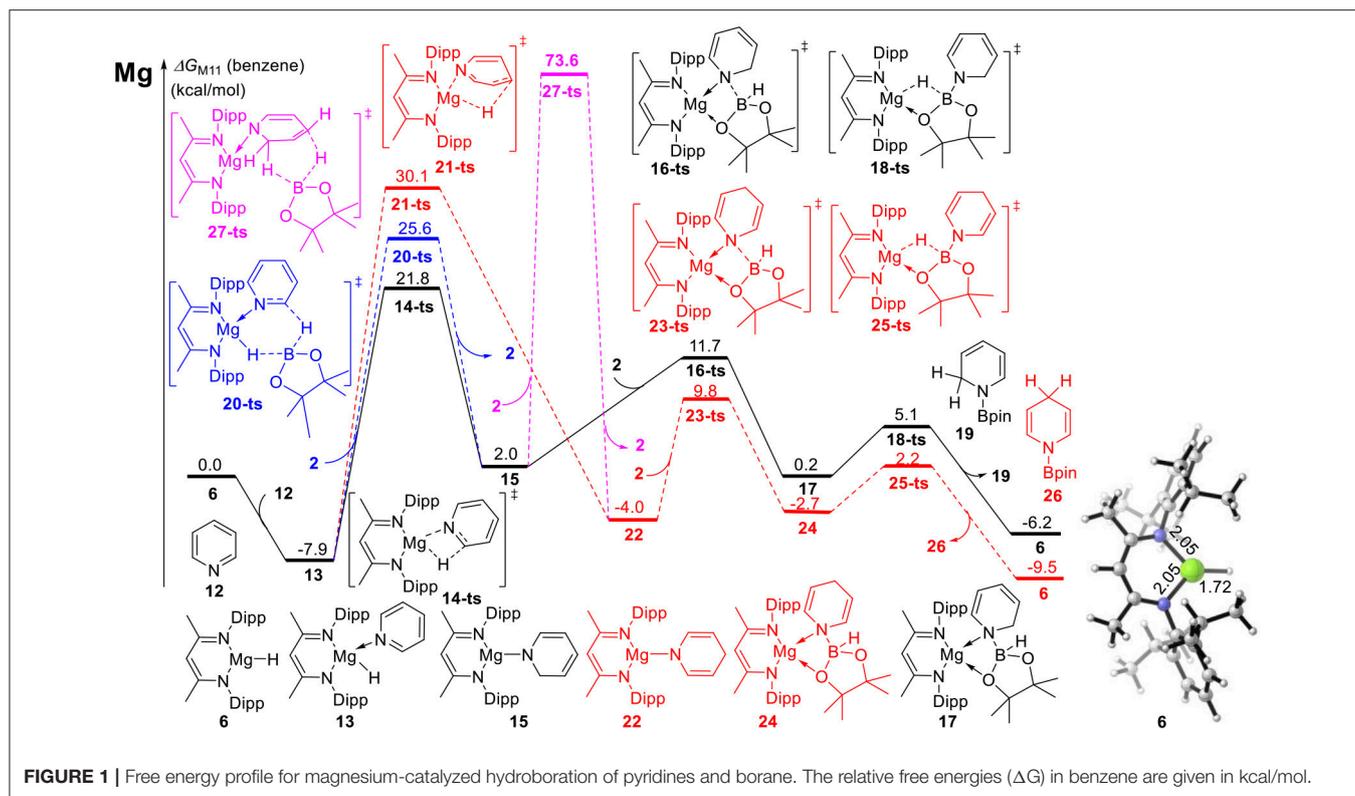
SCHEME 2 | Plausible mechanism for magnesium-catalyzed hydroboration of pyridines with borane.

RESULTS AND DISCUSSION

Mechanism of Pyridine Hydroboration Catalyzed by Magnesium-Hydrogen Species

DFT calculations were performed for hydroboration of pyridines catalyzed by magnesium (Scheme 2). We selected β -diimine magnesium hydride **6** as the relative zero point of the Gibbs free energy (Figure 1). Pyridine **12** coordinates with active magnesium hydride species **6** to form intermediate **13**. This

process is exergonic by 7.9 kcal/mol, indicating that the magnesium hydride species can be stabilized as the Lewis acid by the corresponding Lewis base. After pyridine is activated by the magnesium hydride species, the C=N double bond in pyridine **12** inserts into the Mg-H bond via transition state **14-ts**. The energy barrier of insertion step is 29.7 kcal/mol, indicating that this step is the rate-determining step of the catalytic cycle. The geometric structure of transition state **14-ts** is shown in Figure 2. The length of the C-H bond to be formed is 1.58 Å. The length of the Mg-H bond to be ruptured is 1.91 Å. The

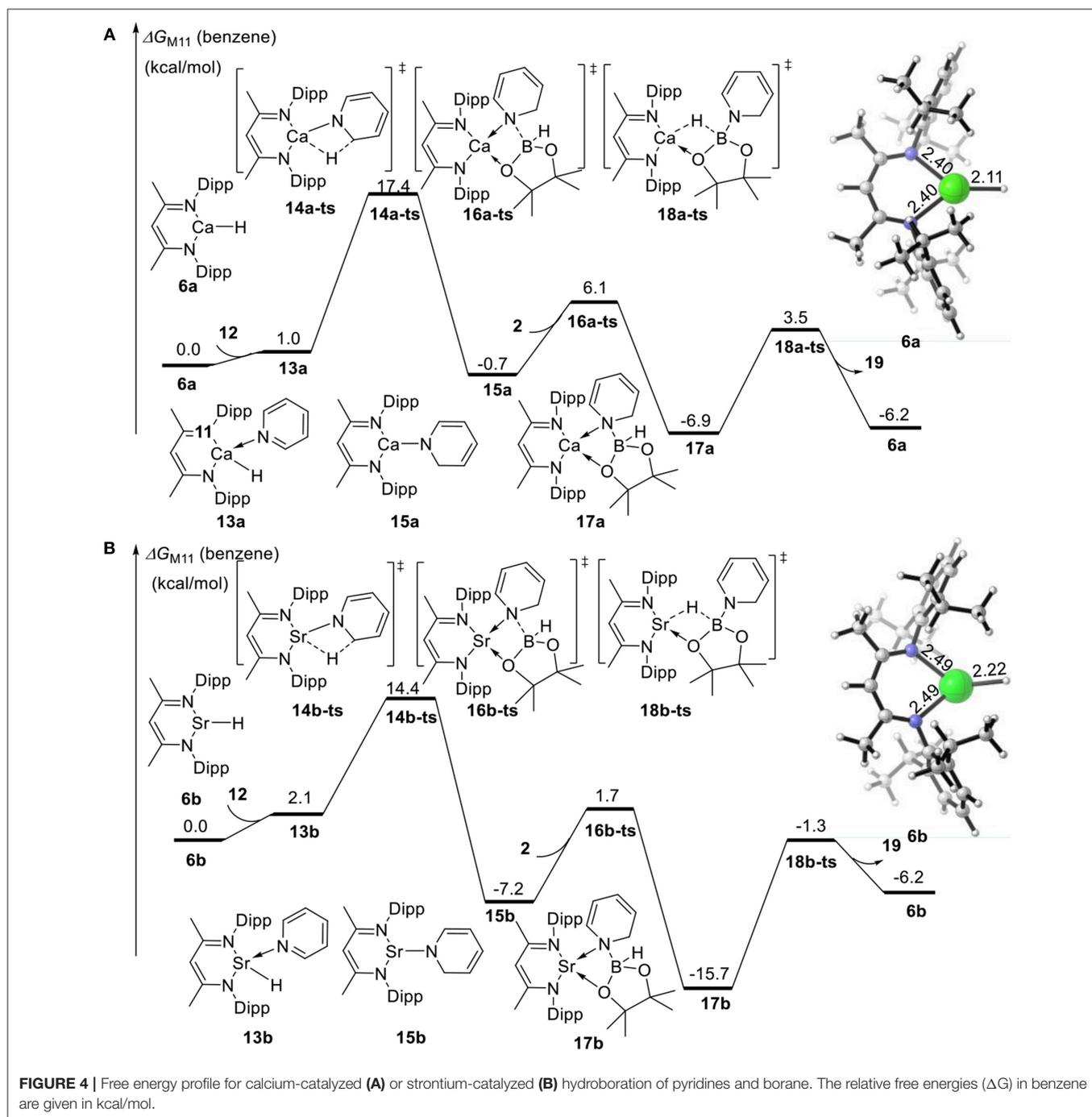


length of the C-N bond in pyridine involved in the reaction is 1.40 Å. The above data of the geometrical structure show that formation of the C-H bond and rupture of the Mg-H bond

simultaneously occur in this reaction. Intermediate **15** is obtained when C=N double insertion occurs. Because the aromaticity of pyridine in intermediate **15** is destroyed, its relative energy is

9.9 kcal/mol higher than that of intermediate **13**. In addition, we also considered another route to obtain intermediate **15**. With pinacolborane **2** acts as a bridge, the hydrogen atom migrates from magnesium to boron via hexatomic ring transition state **20-ts** and then transfers from boron to the ortho carbon of nitrogen to give intermediate **15**. The activation energy of this process is 33.5 kcal/mol, which indicates that it is a possible alternative pathway to generate intermediate **15**. In intermediate **15**, because the Mg–N covalent bond is formed

and there is a lone pair of electrons on the nitrogen atom, it can coordinate with pinacolborane **2** to give boron–nitrogen Lewis acid–base complex **17** via low-energy transition state **16-ts**. Interestingly, in intermediate **17**, there are also two lone pairs of electrons on each oxygen atom in pinacolborane **2**, so a coordination bond can form between oxygen and magnesium, increasing the stability of intermediate **17**. The pinacolborane **2** moiety of intermediate **17** is activated by the amino group, so hydride can migrate from boron to magnesium. Theoretical



calculations show that this process proceeds via transition state **18-ts** with an activation free energy of only 5.3 kcal/mol. After this step, 1,2-borohydropyridine product **19** is released and active catalytic species **6** is regenerated. The complete catalytic cycle is only exothermic by 6.2 kcal/mol. This indicates a weak thermodynamic driving force, which can be attributed to the aromaticity of pyridine being destroyed. Nevertheless, a stable N–B covalent bond is generated to drive the reaction.

Mechanism of Pyridine Hydroboration Catalyzed by Other Ae Metals

Harder's group only determined the catalytic activities of magnesium species. Followed these results, Harder and co-workers (Intemann et al., 2015) reported the calcium catalyzed hydrosilylation of pyridine, demonstrating that a beta-deketiminate calcium hydride is capable of faster selective 1,2-dearomatization in 2015. According to the basic rule of the periodic law of elements and our previous theoretical studies (Gao et al., 2016; Qi et al., 2017; Xu et al., 2017a,b; Li, Y. et al., 2018) elements of the same main group often have similar chemical properties (Cotton et al., 1988). After investigating the mechanism of pyridine hydroboration catalyzed by the magnesium catalyst, we performed M11 calculations to predict the catalytic activities of other Ae metals in the group. In the pyridine hydroboration reaction, the rate-determining step is considered to be pyridine C = N bond insertion with Mg–H

bond cleavage. Therefore, a weak metal–H covalent bond is favorable for this reaction. The calculated bond dissociation energies (BDEs) of Ae–H bonds are shown in **Figure 3**. The BDEs of Be–H, Mg–H, Ca–H, and Sr–H are 96.3, 75.5, 64.6, and 62.2 kcal/mol, respectively. Therefore, beryllium, which is in the same group as magnesium, has a small atomic radius, large steric hindrance, low metallic property, and strong Be–H bond. We believe that hydroboration cannot be catalyzed by beryllium hydride species. Furthermore, calcium and strontium could have higher catalytic activity than magnesium because of the weak metal–H covalent bonds owing to their larger atomic radii and lower electronegativities.

We also calculated the potential energy surfaces of the pyridine hydroboration reaction catalyzed by calcium and strontium hydride (**Figure 4**). In **Figure 4A**, active calcium hydride catalyst **6a** is selected as the relative zero of the Gibbs free energy. First, calcium hydride species **6a** coordinates with pyridine **12** to give intermediate **13a** with a relative Gibbs free energy of 1.0 kcal/mol. The pyridine C=N bond then inserts into the Ca–H covalent bond via transition state **14a-ts**. The energy barrier of this process is 17.4 kcal/mol, indicating that this step is the rate-determining step of the catalytic cycle. Compared with the corresponding reaction catalyzed by magnesium, the activation energy required for the rate-determining step decreases by 12.3 kcal/mol. Thus, we can conclude that the activity of the calcium catalyst is

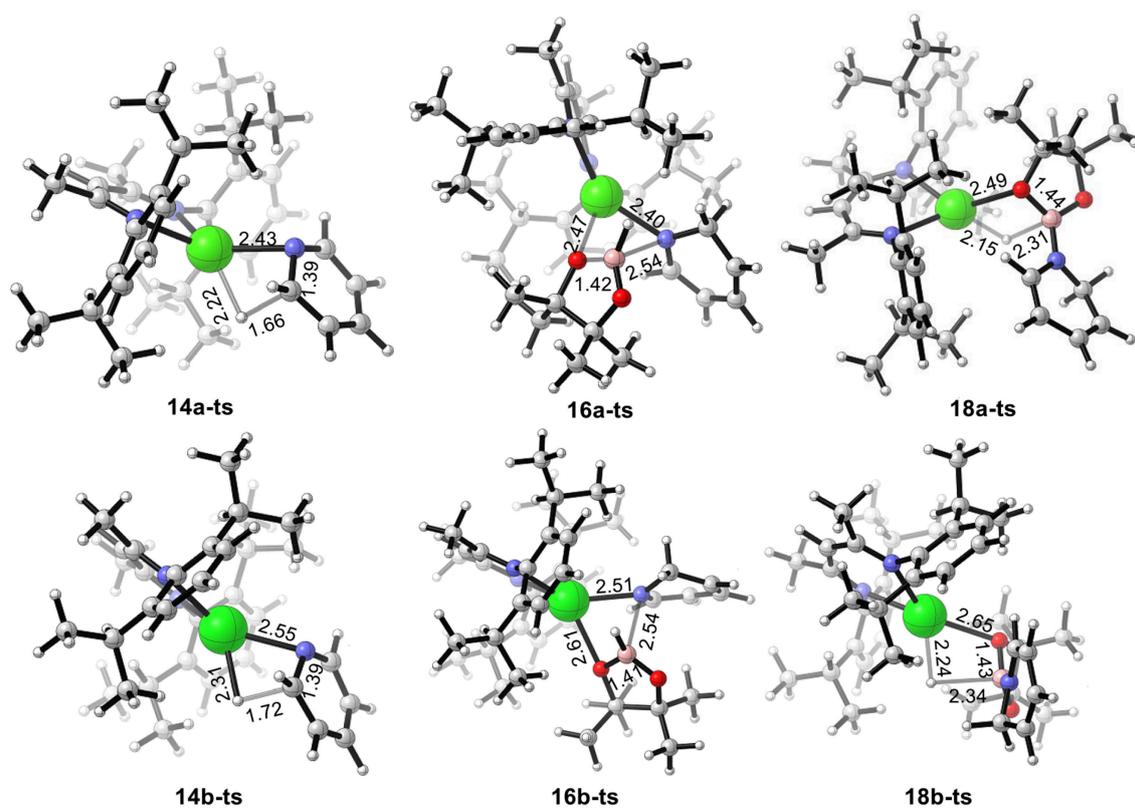


FIGURE 5 | Geometry of transition states **14a-ts**, **16a-ts**, **18a-ts**, **14b-ts**, **16b-ts**, and **18b-ts**. The bond lengths are given in Ångstroms.

higher than that of the magnesium catalyst. Intermediate **15a** coordinates with pinacolborane **2** via the corresponding low-energy transition state **16a-ts** to give boron–nitrogen Lewis acid–base complex **17a**. Finally, 1,2-borohydropyridine product **19** is released by hydride transfer with regeneration of active catalytic species **6a**. The geometric structures of **14a-ts**, **16a-ts**, and **18a-ts** are shown in **Figure 5**. The corresponding Ae metal transition states have similar structures.

Strontium hydride species **6b** can also coordinate with pyridine **12** to give intermediate **13b**, which is endergonic by 2.1 kcal/mol (**Figure 4B**). Intermediate **13b** is unstable and prone to react. The activation energy required for C=N bond insertion into the Sr–H bond via transition state **14b-ts** is 14.4 kcal/mol. However, intermediate **17b** generated by coordination to pinacolborane **2** is very stable, and its free energy is 9.5 kcal/mol lower than that of the 1,2-borohydropyridine product **19** and regenerated active catalyst **6b**. Therefore, the complete activation free energy for strontium catalysis of this reaction is 23.9 kcal/mol, which is 5.8 kcal/mol lower than that for magnesium catalysis, but 5.8 kcal/mol higher than that for calcium catalysis. Therefore, our theoretical calculations predict that the catalytic activities of the Ae metal complexes are calcium > strontium > magnesium.

CONCLUSION

The mechanism of pyridine hydroboration catalyzed by a series of Ae metals has been systematically investigated by DFT calculations. When a magnesium complex is used as the catalyst, the magnesium hydride intermediate is the active catalytic species for this reaction. According to the theoretical calculations, the reaction mechanism of this reaction is as follows. Pyridine first coordinates with the magnesium atom in the active catalyst, followed by the pyridine C=N double bond inserting into the Mg–H bond, resulting in dearomatization. The magnesium amino intermediate coordinates to pinacolborane and the magnesium hydride intermediate is regenerated by hydride transfer to release the product. The catalytic activities

of various Ae metals in the same group were predicted by DFT calculations. The trend of the Ae–H BDEs is Mg–H > Ca–H > Sr–H. The theoretical calculations indicate that when a calcium catalyst is used, there is a much lower activation free energy for C=N double bond insertion into the Ca–H bond, which is the rate-determining step of the catalytic cycle. However, because the boron–nitrogen Lewis acid–base complex with the strontium catalyst is very stable, the apparent activation free energy for the strontium catalyst is higher than that for the calcium catalyst, but lower than that for the magnesium catalyst. Therefore, we believe that milder reaction conditions could be used if a calcium or strontium complex is used as the catalyst.

AUTHOR CONTRIBUTIONS

The work was completed by cooperation of all authors. YyL, RB, and YL were responsible for the study of concept and design of the project. MW and HC searched the intermediates and transition states, JZ and DX analyzed the data and drew energy profiles. YyL, LQ, and YL drafted and revised the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fchem.2019.00149/full#supplementary-material>

REFERENCES

- Adamo, C., and Barone, V. (1999). Toward reliable density functional methods without adjustable parameters: the PBE0 model. *J. Chem. Phys.* 110, 6158–6170. doi: 10.1063/1.478522
- Adolfsson, H. (2005). Organocatalytic hydride transfers: a new concept in asymmetric hydrogenations. *Angew. Chem. Int. Ed.* 44, 3340–3342. doi: 10.1002/anie.200500827
- Anker, M. D., Arrowsmith, M., Bellham, P., Hill, M. S., Kociok-Köhn, G., Liptrot, D. J., et al. (2014). Selective reduction of CO₂ to a methanol equivalent by B(C₆F₅)₃-activated alkaline earth catalysis. *Chem. Sci.* 5, 2826–2830. doi: 10.1039/C4SC00885E
- Anker, M. D., Hill, M. S., Lowe, J. P., and Mahon, M. F. (2015). Alkaline-Earth-Promoted CO homologation and reductive catalysis. *Angew. Chem. Int. Ed.* 54, 10009–10011. doi: 10.1002/anie.201505851
- Arrowsmith, M., Hadlington, T. J., Hill, M. S., and Kociok-Köhn, G. (2012). Magnesium-catalysed hydroboration of aldehydes and ketones. *Chem. Commun.* 48, 4567–4569. doi: 10.1039/c2cc30565h
- Arrowsmith, M., Hill, M. S., and Hadlington, T. G. (2011). Kociok-Köhn, Weetman, C. Magnesium-Catalyzed Hydroboration of Pyridines. *Organometallics* 30, 5556–5559. doi: 10.1021/om2008138
- Barrett, A. G., Crimmin, M. R., S., Hill, M., Hitchcock, P. B., and Procopiou, P. A. (2007). Calcium-Catalyzed Intermolecular Hydrophosphination. *Organometallics* 26, 4076–4079. doi: 10.1021/om070083t
- Becke, A. D. (1993). Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* 98, 5648–5652. doi: 10.1063/1.464913
- Berg, J. M., Tymoczko, J. L., and Stryer, L. (2002). *Biochemistry, 5th ed.*; W. Philadelphia, PA: H. Freeman.
- Bossert, F., Meyer, H., and Wehinger, E. (1981). 4-Aryldihydropyridines, a new class of highly active calcium antagonists. *Angew. Chem. Int. Ed.* 20, 762–769. doi: 10.1002/anie.198107621
- Butera, V., Russo, N., and Sicilia, E. (2014). Hydrogen release from dialkylamine-boranes promoted by Mg and Ca complexes: a DFT analysis of the reaction mechanism. *Chem. Eur. J.* 20, 5967–5976. doi: 10.1002/chem.201304329
- Cances, E., Mennucci, B., and Tomasi, J. (1997). A new integral equation formalism for the polarizable continuum model: theoretical background and applications

- to isotropic and anisotropic dielectrics. *J. Chem. Phys.* 107, 3032–3041. doi: 10.1063/1.474659
- Connon, S. J. (2007). Asymmetric organocatalytic reductions mediated by dihydropyridines. *Org. Biomol. Chem.* 5, 3407–3417. doi: 10.1039/b711499k
- Cotton, F. A., Wilkinson, G., Murillo, C. A., and Bochmann, M. (1988). *Advanced Inorganic Chemistry, 6th Edn.* New York, NY: A Wiley-interscience publication.
- Cui, C. X., Xu, D., Ding, B. W., Qu, L. B., Zhang, Y. P., and Lan, Y. (2019). Benchmark study of popular density functionals for calculating binding energies of three-center two-electron bonds. *J. Comput. Chem.* 40, 657–670. doi: 10.1002/jcc.25752
- Dobereiner, G. E., and Crabtree, R. H. (2010). Dehydrogenation as a substrate-activating strategy in homogeneous transition-metal catalysis. *Chem. Rev.* 110, 681–703. doi: 10.1021/cr900202j
- Dolg, M., Wedig, U., Stoll, H., and Preuss, H. (1987). Energy-adjusted *ab initio* pseudopotentials for the first row transition elements. *J. Chem. Phys.* 86, 866–872. doi: 10.1063/1.452288
- Dunne, J. F., Neal, S. R., Engelkemier, J., Ellern, A., and Sadow, A. D. (2011). Tris(oxazolonyl)boratomagnesium-Catalyzed Cross-Dehydrocoupling of Organosilanes with amines, hydrazine, and ammonia. *J. Am. Chem. Soc.* 133, 16782–16785. doi: 10.1021/ja207641b
- Francl, M. M., Pietro, W. J., Hehre, W. J., Stephen Binkley, Gordon, M. S., DeFrees, D. J., et al. (1982). Self-consistent molecular orbital methods. XXIII. A polarization-type basis set for second-row elements. *J. Chem. Phys.* 77, 3654–3665. doi: 10.1063/1.444267
- Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., Cheeseman, J. R., et al. (2013). *Gaussian 09, Revision D.01*, Gaussian, Inc., Wallingford, CT: The full author list is shown in the ESI.
- Gao, B., Liu, S., Lan, Y., and Huang, H. (2016). Rhodium-catalyzed cyclocarbonylation of ketimines via C-H bond activation. *Organometallics* 35, 1480–1487. doi: 10.1021/acs.organomet.6b00072
- Green, S. P., Jones, C., and Stasch, A. (2007). Stable Magnesium(I) Compounds with Mg-Mg Bonds. *Science* 318, 1754–1757. doi: 10.1126/science.1150856
- Gutsulyak, D. V., van der Est, A., and Nikon, G. I. (2011). Facile catalytic hydrosilylation of pyridines. *Angew. Chem. Int. Ed.* 50, 1384–1387. doi: 10.1002/anie.201006135
- Hantzsch, A. (1881). Condensationsprodukte aus Aldehydammoniak und ketonartigen Verbindungen. *Ber. Dtsch. Chem. Ges.* 14, 1637–1638. doi: 10.1002/cber.18810140214
- Hao, L., Harrod, J. F., Lebus, A. M., Mu, Y., Shu, R., Samuel, E., et al. (1998). Homogeneous catalytic hydrosilylation of pyridines. *Angew. Chem. Int. Ed.* 37, 3126–3129. doi: 10.1002/(SICI)1521-3773(19981204)37:22<3126::AID-ANIE3126>3.0.CO;2-Q
- Harder, S., Spielmann, J., Intemann, J., and Bandmann, H. (2011). Hydrogen storage in magnesium hydride: the molecular approach. *Angew. Chem. Int. Ed.* 50, 4156–4160. doi: 10.1002/anie.201101153
- Harrod, J. F., Shu, R. G., Woo, H., and Samuel, E. (2001). Titanocene(III) catalyzed homogeneous hydrosilylation-hydrogenation of pyridines. *Can. J. Chem.* 79, 1075–1185. doi: 10.1139/v00-191
- Hehre, W. J., Ditchfield, R., and Pople, J. A. (1972). Self-consistent molecular orbital methods. XII. further extensions of Gaussian-type basis sets for use in molecular orbital studies of organic molecules. *J. Chem. Phys.* 56, 2257–2261. doi: 10.1063/1.1677527
- Hill, M. S., Liprot, D. J., and Weetma, C. (2016). Alkaline earths as main group reagents in molecular catalysis. *Chem. Soc. Rev.* 45, 972–988. doi: 10.1039/C5CS00880H
- Hill, M. S., MacDougall, D. J., and Mahon, M. F. (2010). Group 2 promoted hydrogen release from $\text{NMe}_2\text{H}\cdot\text{BH}_3$: intermediates and catalysis. *Dalton Trans.* 39, 11129–11131. doi: 10.1039/c0dt01246g
- Huang, G. P., and Xia, Y. Z. (2015). Catalyst-controlled C-C σ bond cleavages in metal halide-catalyzed cycloisomerization of 3-acylcyclopropenes via a formal 1,1-halometalation mechanism: insights from quantum chemical calculations. *ACS Catal.* 5, 859–868. doi: 10.1021/cs501738p
- Intemann, J., Bauer, H., Pahl, J., Maron, L., and Harder, S. (2015). Calcium hydride catalyzed highly 1,2-selective pyridine hydrosilylation. *Chem. Eur. J.* 21, 11452–11461. doi: 10.1002/chem.201501072
- Intemann, J., Lutz, M., and Harder, S. (2014). Multinuclear magnesium hydride clusters: selective reduction and catalytic hydroboration of pyridines. *Organometallics* 33, 5722–5729. doi: 10.1021/om500469h
- Intemann, J., Spielmann, J., Sirsch, P., and Harder, S. (2013). Well-defined molecular magnesium hydride clusters: relationship between size and hydrogen-elimination temperature. *Chem. Eur. J.* 19, 8478–8489. doi: 10.1002/chem.201300684
- Jiang, Y. Y., Liu, T. T., Zhang, R. X., Xu, Z. Y., Sun, X., and Bi, S. (2018). Mechanism and rate-determining factors of amide bond formation through acyl transfer of mixed carboxylic-carbamic anhydrides: a computational study. *J. Org. Chem.* 83, 2676–2685. doi: 10.1021/acs.joc.7b03107
- Karrer, P., Ringier, B. H., J., Büchi, Fritzsche, H., and Solmssen, U. (1937). Modellversuche betreffend die wasserstoffübertragenden Wirkungsgruppen der Cofermente. *Helv. Chim. Acta.*, 20, 55–71. doi: 10.1002/hlca.19370200106
- Krieck, S., Görls, H., Yu, L., Reiher, M., and Westerhausen, M. (2009). Stable “Inverse” sandwich complex with unprecedented organocalcium(I): crystal structures of $[(\text{thf})_2\text{Mg}(\text{Br})\text{-C}_6\text{H}_2\text{-2,4,6-Ph}_3]$ and $[(\text{thf})_3\text{Ca}\{\mu\text{-C}_6\text{H}_3\text{-1,3,5-Ph}_3\}\text{Ca}(\text{thf})_3]$. *J. Am. Chem. Soc.* 131, 2977–2985. doi: 10.1021/ja808524y
- Lampland, N. L., Hovey, M., Mukherjee, D., and Sadow, A. D. (2015). Magnesium-catalyzed mild reduction of tertiary and secondary amides to amines. *ACS Catal.* 5, 4219–4226. doi: 10.1021/acscatal.5b01038
- Lee, C., Yang, W., and Robert, G. (1988). Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B.* 37, 785–789. doi: 10.1103/PhysRevB.37.785
- Legault, C. Y. (2009). *CYLVView, 1.0b*, Université de Sherbrooke, Canada, Available online at: <http://www.cylview.org/>
- Li, Y., Liu, S., Qi, Z., Qi, X., Li, X., and Lan, Y. (2015). The mechanism of N-O bond cleavage in rhodium-catalyzed C-H bond functionalization of quinoline N-oxides with Alkynes: a computational study. *Chem. Eur. J.* 21, 10131–10137. doi: 10.1002/chem.201500290
- Li, Y., Zou, L., Bai, R., and Lan, Y. (2018). Ni(I)–Ni(III) vs. Ni(II)–Ni(IV): mechanistic study of Ni-catalyzed alkylation of benzamides with alkyl halides. *Org. Chem. Front.* 5, 615–622. doi: 10.1039/C7QO00850C
- Li, Y. W., and Marks, T. J. (1996). Diverse mechanistic pathways and selectivities in organo-F-element-catalyzed hydroamination. Intermolecular Organolanthanide-Catalyzed Alkyne and Alkene Hydroamination. *Organometallics* 15, 3770–3772. doi: 10.1021/om960293y
- Li, Y. Y., Chen, Y., Shan, C. H., Zhang, J., Xu, D. D., Bai, R. P., et al. (2018). Recent advances in alkaline-earth-metal-catalyzed hydrofunctionalization reactions. *Chin. J. Org. Chem.* 38, 1885–1896. doi: 10.6023/cjoc201804031
- Liprot, D. J., Hill, M. S., and Mahon, M. F. (2014). Accessing the single-electron manifold: magnesium-mediated hydrogen release from silanes. *Angew. Chem. Int. Ed.* 53, 6224–6227. doi: 10.1002/anie.201403208
- Liprot, D. J., Hill, M. S., Mahon, M. F., and Wilson, A. S. (2015). Alkaline-earth-catalyzed dehydrocoupling of amines and boranes. *Angew. Chem. Int. Ed.* 54, 13362–13365. doi: 10.1002/anie.201505949
- Liu, B., Roisnel, T., Carpentier, J. F., and Sarazin, Y. (2012). When bigger is better: intermolecular hydrofunctionalizations of activated alkenes catalyzed by heteroleptic alkaline earth complexes. *Angew. Chem. Int. Ed.* 51, 4943–4946. doi: 10.1002/anie.201200364
- Liu, S., Qi, X. T., Qu, L. B., Bai, R. P., and Lan, Y. (2018). C-H bond cleavage occurring on a Rh(V) intermediate: a theoretical study of Rh-catalyzed arene azidation. *Catal. Sci. Technol.* 8, 1645–1651. doi: 10.1039/C7CY02367G
- Liu, Y. X., Tang, Y. N., Jiang, Y. Y., Zhang, X. M., Li, P., and Bi, S. W. (2017). Mechanism and Origin of $\text{Et}_2\text{Al}(\text{OEt})$ -induced chemoselectivity of nickel-catalyzed three-component coupling of one diketene and two alkynes. *ACS Catal.* 7, 1886–1896. doi: 10.1021/acscatal.6b03543
- Luo, Y., Liu, S., Xu, D., Qu, L.-B., Luo, X., Bai, R., et al. (2018). Counterion effect and directing group effect in Rh-mediated C-H bond activation processes: a theoretical study. *J. Organomet. Chem.* 864, 148–153. doi: 10.1016/j.jorganchem.2018.03.016
- Ma, M. T., Wang, W. F., and Yao, W. W. (2016). Synthesis of magnesium(I) complexes and their applications. *Chin. J. Org. Chem.* 36, 72–82. doi: 10.6023/cjoc201507015
- Marenich, A. V., Cramer, C. J., and Truhlar, D. G. (2009). Universal solvation model based on solute electron density and on a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions. *J. Phys. Chem. B.* 113, 6378–6396. doi: 10.1021/jp810292n
- Mauzerall, D., and Westheimer, F. (1955). H. 1-Benzylidihydrocinotinamide-a model for reduced DPN. *J. Am. Chem. Soc.* 77, 2261–2264. doi: 10.1021/ja01613a070

- Osakada, K. (2011). 1,4-hydrosilylation of pyridine by ruthenium catalyst: a new reaction and mechanism. *Angew. Chem. Int. Ed.* 50, 3845–3846. doi: 10.1002/anie.201008199
- Oshima, K., Ohmura, T., and Sugimoto, M. (2012a). Regioselective synthesis of 1,2-dihydropyridines by rhodium-catalyzed hydroboration of pyridines. *J. Am. Chem. Soc.*, 134, 3699–3702. doi: 10.1021/ja3002953
- Oshima, K., Ohmura, T., and Sugimoto, M. (2012b). Dearomatizing conversion of pyrazines to 1,4-dihydropyridazine derivatives via transition-metal-free dimerization, silaboration, and hydroboration. *Chem. Commun.* 48, 8571–8573. doi: 10.1039/c2cc34086k
- Peeverati, R., and Truhlar, D. G. (2011). M11-L: a local density functional that provides improved accuracy for electronic structure calculations in chemistry and physics. *J. Phys. Chem. Lett.* 2, 2810–2817. doi: 10.1021/jz201170d
- Peeverati, R., and Truhlar, D. G. (2012). Performance of the M11 and M11-L density functionals for calculations of electronic excitation energies by adiabatic time-dependent density functional theory. *Phys. Chem. Chem. Phys.* 14, 11363–11370. doi: 10.1039/c2cp41295k
- Praneeth, V. K., Ringenburg, M. R., and Ward, T. R. (2012). Redox-Active Ligands in Catalysis. *Angew. Chem. Int. Ed.* 51, 10228–10234. doi: 10.1002/anie.201204100
- Qi, X., Bai, R., Zhu, L., Jin, R., Lei, A., and Lan, Y. (2016). Mechanism of synergistic Cu(II)/Cu(I)-mediated alkyne coupling: dinuclear 1,2-reductive elimination after minimum energy crossing point. *J. Org. Chem.* 81, 1654–1660. doi: 10.1021/acs.joc.5b02797
- Qi, X., Li, Y., Bai, R., and Lan, Y. (2017). Mechanism of Rhodium-Catalyzed C-H Functionalization: advances in theoretical investigation. *Acc. Chem. Res.* 50, 2799–2808. doi: 10.1021/acs.accounts.7b00400
- Qi, X. T., Liu, X. F., Qu, L. B., Liu, Q., and Lan, Y. (2018). Mechanistic insight into cobalt-catalyzed stereodivergent semihydrogenation of alkynes: the story of selectivity control. *J. Catal.* 362, 25–34. doi: 10.1016/j.jcat.2018.03.016
- Rochat, R., Lopez, M. J., Tsurugi, H., and Mashima, K. (2016). Recent developments in homogeneous organomagnesium catalysis. *Chem. Cat. Chem.* 8, 10–20. doi: 10.1002/cctc.201500853
- Rokob, T. A., Bakó, I., Stirling, A., Hamza, A., and Pápai, I. (2013). Reactivity models of hydrogen activation by frustrated lewis pairs: synergistic electron transfers or polarization by electric field? *J. Am. Chem. Soc.* 135, 4425–4437. doi: 10.1021/ja312387q
- Rossin, A., and Peruzzini, M. (2016). Ammonia–borane and amine–borane dehydrogenation mediated by complex metal hydrides. *Chem. Rev.* 116, 8848–8872. doi: 10.1021/acs.chemrev.6b00043
- Schramm, M., Thomas, G., Towart, R., and Franckowiak, G. (1983). Novel dihydropyridines with positive inotropic action through activation of Ca²⁺ channels. *Nature* 303, 535–537. doi: 10.1038/303535a0
- Schwamm, R. J., Day, B. M., Mansfield, N. E., Knowelden, W., Hitchcock, P. B., and Coles, M. P. (2014). Catalytic bond forming reactions promoted by amidinate, guanidinate and phosphoguanidinate compounds of magnesium. *Dalton Trans.* 43, 14302–14314. doi: 10.1039/C4DT01097C
- Seyferth, D. (2009). The grignard reagents. *Organometallics.* 28, 1598–1605. doi: 10.1021/om900088z
- Stepha, D. W. (2015). Frustrated lewis pairs. *J. Am. Chem. Soc.* 137, 10018–10032. doi: 10.1021/jacs.5b06794
- Stephens, P. J., Devlin, F. J., Chabalowski, C. F., and Frisch, M. J. (1994). *Ab initio* calculation of vibrational absorption and circular dichroism spectra using density functional force fields. *J. Phys. Chem.* 98, 11623–11627. doi: 10.1021/j100096a001
- Stout, D. M., and Meyers, A. I. (1982). Recent advances in the chemistry of dihydropyridines. *Chem. Rev.* 82, 223–243. doi: 10.1021/cr00048a004
- Weetman, C., Anker, M. D., Arrowsmith, M., Hill, M. S., Kociok-Köhne, G., Liptrout, D. J., et al. (2016). Magnesium-catalysed nitrile hydroboration. *Chem. Sci.* 7, 628–641. doi: 10.1039/C5SC03114A
- Westerhausen, M. (2008). Molecular magnesium(I) compounds: from curiosity to kudos. *Angew. Chem. Int. Ed.* 47, 2185–2187. doi: 10.1002/anie.200705758
- Xing, Y. Y., Liu, J. B., Sheng, X. H., Sun, C. Z., Huang, F., and Chen, D. Z. (2017). Solvent mediating a switch in the mechanism for rhodium(III)-catalyzed carboamination/cyclopropanation reactions between N-enoxypthalimides and alkenes. *Inorg. Chem.* 56, 5392–5401. doi: 10.1021/acs.inorgchem.7b00450
- Xu, D. D., Shan, C. H., Bai, R. P., and Lan, Y. (2017b). Mechanism of alkaline earth metal catalyzed hydroboration of carbodiimides: a theoretical study. *Chin. J. Org. Chem.* 37, 1231–1236. doi: 10.6023/cjoc201701033
- Xu, D. D., Shan, C. H., Li, Y. Z., Qi, X. T., Luo, X. L., Bai, R. P., et al. (2017a). Bond dissociation energy controlled σ -bond metathesis in alkaline-earth-metal hydride catalyzed dehydrocoupling of amines and boranes: a theoretical study. *Inorg. Chem. Front.* 4, 1813–1820. doi: 10.1039/C7QI00459A
- Yang, Y. F., Houk, K. N., and Wu, Y. D. (2016). Computational exploration of Rh^{III}/Rh^V and Rh^{III}/Rh^I catalysis in Rhodium(III)-Catalyzed C-H activation reactions of N-Phenoxyacetamides with Alkynes. *J. Am. Chem. Soc.* 138, 6861–6868. doi: 10.1021/jacs.6b03424
- Yaroshevsky, A. A. (2006). Abundances of chemical elements in the Earth's crust. *Geochem. Int.* 44, 48–55. doi: 10.1134/S001670290601006X
- Yu, Z., and Lan, Y. (2013). Mechanism of rhodium-catalyzed carbon–silicon bond cleavage for the synthesis of benzosilole derivatives: a computational study. *J. Org. Chem.* 78, 11501–11507. doi: 10.1021/jo402070f
- Yu, Z., Qi, X., Li, Y., Liu, S., and Lan, Y. (2016). Mechanism, chemoselectivity and enantioselectivity for the rhodium-catalyzed desymmetric synthesis of hydrobenzofurans: a theoretical study. *Org. Chem. Front.* 3, 209–216. doi: 10.1039/C5QO00334B
- Zhao, Y., Ng, H. T., Peeverati, R., and Truhlar, D. G. (2012). Benchmark database for ylidic bond dissociation energies and its use for assessments of electronic structure methods. *J. Chem. Theory Comput.* 8, 2824–2834. doi: 10.1021/ct300457c
- Zhao, Y., Zou, S. L., Jiang, Y. Y., and Bi, S. W. (2017). Theoretical study of the Cl-initiated atmospheric oxidation of methyl isopropenyl ketone. *RSC Adv.* 7, 52801–52811. doi: 10.1039/C7RA09445K
- Zhu, L., Ye, J. H., Duan, M., Qi, X. T., Yu, D. G., Bai, R. P., et al. (2018). The mechanism of copper-catalyzed oxytrifluoromethylation of allylamines with CO₂: a computational study. *Org. Chem. Front.* 5, 633–639. doi: 10.1039/C7QO00838D

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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