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Electrochemical hydrogenation with gaseous ammonia

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Abstract: As a carbon-free and sustainable fuel, ammonia serves as high energy density hydrogen storage material. It is important to develop new reactions able to utilize ammonia as hydrogen source directly. Herein, we report an electrochemical hydrogenation of alkenes, alkynes, and ketones using ammonia as the hydrogen source and carbon electrodes. A variety of heterocycles and functional groups, including for example sulfide, benzyl, benzyl carbamate and allyl carbamate were well tolerated. A fast stepwise electron transfer and proton transfer process were proposed to account for the transformation.

As one of the most highly produced industrial chemicals in the world, ammonia was used as fertilizer for one century. Most recently, ammonia was found to be one efficient and renewable energy storage material.^[1] In terms of energy density, safety in storage and transportation, ammonia acts as an ideal hydrogen source with nitrogen as the only side product and found applications in hydrogen-powered fuel cell devices.^[2] In the trends of sustainable chemistry, direct utilization of ammonia in organic synthesis is, therefore, desirable.^[3] One prominent protocol was Birch reduction, employing liquid ammonia solution with cryogenic or pressurized conditions and converting aromatic compounds to dearomatized products.^[4]

Electrochemical reactions are a fundamental tool for building molecules with efficient utilization of energy. Recently, electrochemical reactions have received a great deal of attention, and new reactivity and mechanisms have been reported.^[5] In particular, electrochemistry has been shown to be a powerful strategy for activating substrates in innovative ways.^[6] Tremendous progress has been achieved in various reactions to construct C-C,^[7] C-N,^[8] C-O,^[9] and C-halogen bonds,^[10] as well as multiple bonds.^[11] Ammonia showed fundamental compatibility with electrochemical conditions. Pioneering study by Thiebault^[12] and Bard^[13] achieved electrochemical Birch reduction of arenes in liquid ammonia. Most recently, Xu reported an novel example utilizing ammonia directly in build nitrogen-containing compounds, exhibiting the tremendous potential of ammonia in electrochemical synthesis.^[14]

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Herein, we report the first electrochemical hydrogenation of alkenes, alkynes, and ketones using gaseous ammonia as the proton source. This transformation was carried out at balloon pressure at room temperature with carbon anode and cathode. In contrast to established Birch reduction, arenes, such as phenyl and heterocycles, were well tolerated and a number of functional goups labile in transition-metal-catalyzed hydrogenation reaction were compatible in this reaction.

a) Birch reduction by Thiebault and Bard



b) Dehydrogenative synthesis of N-Heteroaromatics by Xu







Scheme 1 Direct application of ammonia in electrochemical reactions

We began by investigating the hydrogenation of substrate 1a in an undivided cell with two electrodes made of graphite felt (Table 1). Substrate 1a was chosen in part because transition-metalcatalyzed hydrogenation of this compound is challenging. For example, in the presence of Wilkinson's catalyst (entry 1) or Crabtree's catalyst (entry 2), hydrogenation of 1a under pressure did not occur, possibly because of the coordination ability of the pyridinyl group of the substrate. When Pd/C was the catalyst, the reaction was not regioselective, and a mixture of hydrogenated products was obtained (entry 3). In contrast, reaction of 1a in acetonitrile at room temperature under gaseous ammonia in a balloon at a cell potential of 5 V (cathode potential of -4.5 V vs SCE) and a Faraday efficiency of 54% afforded 2a as the sole product in 73% yield (entry 4). When ammonia was replaced with water as the hydrogen source, only a trace of 2a was detected (entry 5). In a protonic solvent (MeOH) instead of acetonitrile, an inferior yield of 61% was obtained (entry 6).

Using the optimum conditions (Table 1, entry 4), we explored the substrate scope of this hydrogenation reaction by evaluating a variety of compounds with C–C double and triple bonds.(Scheme 2) We found that trisubstituted alkenes gave better yields than disubstituted alkenes, regardless of whether the pendant chain was *para* to the pyridine nitrogen (2b and 2c vs 2d) or *meta* or *ortho* to it (2e and 2f, respectively). That we were able

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to obtained **2g** (52% yield) showed that this protocol was compatible with a sulfide group. A steroid moiety remained intact under the reaction conditions: **2h** was obtained in 51% yield. Esters **2i–2n**, which contained other aryl groups (i.e., quinoline, indole, thiophene, or phenyl), were obtained in moderate to good yields. A product without a conjugated aryl group (**2o**) was prepared in 36% yield. Next, we subjected a variety of unsaturated amides to the protocol (Figure 3). When **Table 1** Hydrogenation and hydrogenation of alkene **1a**^[a]

corresponding alkyne precursors, and diphenyl acetylene could be converted to fully saturated product **2ag** in 88% yield. Product **2al** bearing a bromo atom could be prepared with 43% yield.

NHa



[a] GC-MS yields are provided. [b] Isolated yield.

cinnamide was used as the substrate, corresponding product 2p was obtained in 93% yield on a 0.2 mmol scale and in 87% yield on a 2.6 g scale. Amides 2q, 2r, and 2s could also be prepared, in yields ranging from 33% to 77%. Subsequently, we determined whether Boc, Cbz, and Aloc protecting groups could survive the reaction conditions. To our delight, desired products 2t, 2u, and 2v were obtained with their carbamate moieties intact. A substrate with a free hydroxyl group (2w) was also amenable to this transformation, and amino acid derivatives 2x and 2y could be obtained as well. An α , β -unsaturated nitrile substrate gave 2z in 92% yield. Compound 2aa, which is derived from a styrenyl pinacol borate, was generated in 37% yield. Subsequently, we found that tri- and diaryl-substituted alkenes were converted to corresponding saturated products 2ab-2ai in good to excellent yields. a-Methyl styrene underwent hydrogenation as well, affording 2aj in 60% GC yield and 46% isolated yield. Completely hydrogenated products 2ak and 2l could be obtained from the



Scheme 2. Hydrogenation of alkenes and alkynes. Conditions: **1** (0.2 mmol), NH₃ in balloon, LiClO₄ (0.1 mmol), MeCN (5 mL), graphite felt electrodes, 5 V, rt, 1.5 - 7 h; isolated yields are given.

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After exploring the reactivity of C–C double and triple bonds, we then explored substrates bearing C–O multiple bonds (Scheme 3), which are polarized. At a working voltage of 4 V in the presence of 0.5 mmol of LiClO₄ as a supporting electrolyte in DMF (method A), diphenyl ketone **3a** could be reduced to diphenyl methanol (**4a**) in 73% yield. Several ketones that are unable to tautomerize were successfully converted to the corresponding alcohols (**4b–4j**) in yields ranging from poor to good. In contrast, when the voltage was increased to 6 V (method B), **3a** was directly converted to diphenyl methanes **5b–5e** in moderate yields under the same conditions.



Scheme 3. hydrogenation of carbonyl compounds.^a Method A conditions: **3** (0.2 mmol), NH₃ balloon, LiClO₄ (0.5 mmol), DMF (5 mL), graphite felt electrodes, 4 V, rt, 4 – 10 h; isolated yields are given. Method B conditions: same as method A except that the working voltage was 6 V.

We then turned to investigate if the reaction only proceeds as an room temperature version of Birch reaction (Scheme 4). As the electrode material was important in electrochemical reactions, we compared the electrode used in this work and previous electrochemical Birch reaction. As that noted by Thiebault, the Mg anode and AI cathode were crucial in achieving the desired Birch reduction of arenes. If carbon electrodes were applied in a controlled reaction, the corresponding transformation did not occurr.^[12] In Bard's electrochemical Birch reduction of C60, Pt electrodes were adopted.^[13] A standard reaction (Table 1, entry 4) employing Pt cathode was carried out and desired hydrogenation did not take place (Scheme 4a). Subsequently, radical clock substrates 1am and 1an were evaluated and 2am and 2an were detected as the only products, respectively, suggesting a radical intermediate might be too transient to trigger a ring opening of cycloproyl group in this electrochemical process (Scheme 4b). In addition, (E)-1ao gave 2ao as a 1.0:1.9 syn/anti mixture, and an almost identical result was obtained when (Z)-1ao was used as the starting material, suggesting the hydrogenation process was stepwise. This assumption was confirmed with two interrupted reaction using alkynes **1ap** and **1aq** as substrate. In both cases, alkene **1I** or **1ag** with *E* configuration was detected as the only isomer. In another reaction, by treating an interrupted reaction mixture with 4-bromobenzaldehyde, we were able to confirm the formation of hydrazine (as indicated by the formation of product **6**, Scheme 4c). A controlled reaction showed the hydrazine could serve as a hydrogen source under standard reaction condition, giving hydrogenation product **2ah** from **1ah** as well. Next, alkyne **1aq** was subject to the hydrogenation reaction in CD₃CN, a 15% D incorporation in product **2ag** was observed. a) Comparison of electodes





Scheme 4. Control experiments and trapping of intermediate

On the basis of the above-described results, a plausible pathway of hydrogenation of alkene via a fast stepwise process was proposed in Scheme 5. At first, an electron transfer from cathode to substrate is coupled with a proton transfer from ammonia. The resulting intermediate **A** then undergoes the second electron transfer from cathode and proton transfer from ammonia to furnish hydrogenation product. The amide anion side products undergo oxidation at the anode, forming hydrazine

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which in turn, reduces the substrate and generates dinitrogen via diimide \mathbf{B} , another plausible reducing reagent. In addition, the direct generation of hydrazine from ammonia and consequent hydrogenation of substrates may operate in this transformation as well (path b).



Scheme 5. A plausible pathway of electrochemical hydrogenation reaction

In summary, we have developed a convenient, transition-metalfree electrochemical protocol for hydrogenation of alkenes, alkynes and ketones with gaseous ammonia as hydrogen source. This protocol was compatible with a variety of functional groups, including unconjugated alkenes; benzyl, Boc, Cbz, Alloc, sulfide, silyl, and borate groups, and heterocycles. The ammonia, which is safe to use in an electrochemical setting, organic-solventcompatible, and an environmentally friendly bulk chemical, provides a new and complementary approach for hydrogenation reactions employing hydrogen.

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- J. G. Chen, R. M. Crooks, L. C. Seefeldt, K. L. Bren, R. M. Bullock, M. Y. Darensbourg, P. L. Holland, B. Hoffman, M. J. Janik, A. K. Jones, M. G. Kanatzidis, P. King, K. M. Lancaster, S. V. Lymar, P. Pfromm, W. F. Schneider, R. R. Schrock, *Science* 2018, *360*, eaar6611.
- [2] R. F. Service, *Science* **2018**, *361*, 120-123.
- [3] a) J. Zhao, A. S. Goldman, J. F. Hartwig, *Science* 2005, *307*, 1080-1082;
 b) M. J. Bezdek, S. Guo, P. J. Chirik, *Science* 2016, *354*, 730-733.
- [4] H. E. Zimmerman, Acc. Chem. Res. 2012, 45, 164-170.
- [5] a) R. Francke, R. D. Little, *Chem. Soc. Rev.* 2014, *43*, 2492-2521; b) M. Yan, Y. Kawamata, P. S. Baran, *Chem. Rev.* 2017, *117*, 13230-13319; c) Y. Jiang, K. Xu, C. Zeng, *Chem. Rev.* 2018, *118*, 4485-4540; d) K. D. Moeller, *Chem. Rev.* 2018, *118*, 4817-4833; e) A. Wiebe, T. Gieshoff, S. Möhle, E. Rodrigo, M. Zirbes, S. R. Waldvogel, *Angew. Chem. Int. Ed.* 2018, *57*, 5594-5619; f) J.-i. Yoshida, A. Shimizu, R. Hayashi, *Chem. Rev.* 2018, *118*, 4702-4730.

- [6] a) T. Morofuji, A. Shimizu, J.-i. Yoshida, J. Am. Chem. Soc. 2015, 137, 9816-9819; b) Z.-W. Hou, Z.-Y. Mao, J. Song, H.-C. Xu, ACS Catal. 2017, 7, 5810-5813; c) A. Wiebe, T. Gieshoff, S. Mohle, E. ROdrigo, M. Zirbes, S. R. Waldvogel, Angew. Chem. Int. Ed. 2018, 57, 5594-5619; d) N. Sauermann, R. Mei, L. Ackermann, Angew. Chem. Int. Ed. 2018, 57, 5090-5094; e) S. Tang, S. Wang, Y. Liu, H. Cong, A. Lei, Angew. Chem. Int. Ed. 2018, 57, 4737-4741; f) Y. Qiu, C. Tian, L. Massignan, T. Rogge, L. Ackermann, Angew. Chem. Int. Ed. 2018, 57, 5818-5822.
- [7] a) D. Hayrapetyan, R. K. Rit, M. Kratz, K. Tschulik, L. J. Gooßen, *Chem. Eur. J.* 2018; b) A. J. J. Lennox, S. L. Goes, M. P. Webster, H. F. Koolman, S. W. Djuric, S. S. Stahl, *J. Am. Chem. Soc.* 2018, *140*, 11227-11231; c) R. R. Merchant, K. M. Oberg, Y. Lin, A. J. E. Novak, J. Felding, P. S. Baran, *J. Am. Chem. Soc.* 2018, *140*, 7462-7465; d) L. Sebastian, F.-U. B. Antonio, D. Maurice, S. Dieter, F. Robert, W. S. R., *Chem. Eur. J.* 2018, *24*, 6057-6061. e) S. Lips, D. Schollmeyer, R. Franke, S. R. Waldvogel, *Angew. Chem. Int. Ed.* 2018, *57*, 13325-13329.
- a) R. Hayashi, A. Shimizu, J.-i. Yoshida, J. Am. Chem. Soc. 2016, 138, [8] 8400-8403; b) N. Fu, G. S. Sauer, A. Saha, A. Loo, S. Lin, Science 2017, 357, 575-579; c) C. Li, Y. Kawamata, H. Nakamura, J. C. Vantourout, Z. Liu, Q. Hou, D. Bao, J. T. Starr, J. Chen, M. Yan, P. S. Baran, Angew. Chem. Int. Ed. 2017, 56, 13088-13093; d) C. Tian, L. Massignan, H. T. Meyer, L. Ackermann, Angew. Chem. Int. Ed. 2018, 57, 2383-2387; e) X. Gao, P. Wang, L. Zeng, S. Tang, A. Lei, J. Am. Chem. Soc. 2018, 140, 4195-4199; f) S. Herold, D. Bafaluy, K. Muñiz, Green Chemistry 2018, 20, 3191-3196; g) Z. W. Hou, Z. Y. Mao, Y. Y. Melcamu, X. Lu, H. C. Xu, Angew. Chem. Int. Ed. 2018, 57, 1636-1639; h) J. Li, W. Huang, J. Chen, L. He, X. Cheng, G. Li, Angew. Chem. Int. Ed. 2018, 57, 5695-5698; i) D.-Z. Lin, J.-M. Huang, Org. Lett. 2018, 20, 2112-2115; j) S. Tang, S. Wang, Y. Liu, H. Cong, A. Lei, Angew. Chem. Int. Ed. 2018, 57, 4737-4741; k) Q.-L. Yang, X.-Y. Wang, J.-Y. Lu, L.-P. Zhang, P. Fang, T.-S. Mei, J. Am. Chem. Soc. 2018, 140, 11487-11494; I) S. Zhang, L. Li, M. Xue, R. Zhang, K. Xu, C. Zeng, Org. Lett. 2018, 20, 3443-3446; m) H.-B. Zhao, P. Xu, J. Song, H.-C. Xu, Angew. Chem. Int. Ed., doi:10.1002/anie.201809679.
- [9] a) Y. Kawamata, M. Yan, Z. Liu, D.-H. Bao, J. Chen, J. T. Starr, P. S. Baran, J. Am. Chem. Soc. 2017, 139, 7448-7451; b) N. Sauermann, T. H. Meyer, C. Tian, L. Ackermann, J. Am. Chem. Soc. 2017, 139, 18452-18455; c) W. Fei, R. Mohammad, S. S. S., Angew. Chem. Int. Ed. 2018, 57, 6686-6690; d) K. A. M., S. Miriam, C. Raanan, N. Ronny, Angew. Chem. Int. Ed. 2018, 57, 5403-5407; e) A. Shrestha, M. Lee, A. L. Dunn, M. S. Sanford, Org. Lett. 2018, 20, 204-207; f) S. Tang, D. Wang, Y. Liu, L. Zeng, A. Lei, Nat. Commun. 2018, 9, 798; g) S. Zhang, L. Li, H. Wang, Q. Li, W. Liu, K. Xu, C. Zeng, Org. Lett. 2018, 20, 252-255.

a) N. Fu, G. S. Sauer, S. Lin, *J. Am. Chem. Soc.* 2017, *139*, 15548-15553; b) M. Rafiee, F. Wang, D. P. Hruszkewycz, S. S. Stahl, *J. Am. Chem. Soc.* 2018, *140*, 22-25.

- [11] a) X. Hu, G. Zhang, F. Bu, A. Lei, Angew. Chem. Int. Ed. 2018, 57, 1286-1290; b) L. Li, S. Luo, Org. Lett. 2018, 20, 1324-1327; c) R. Mei, N. Sauermann, J. C. A. Oliveira, L. Ackermann, J. Am. Chem. Soc. 2018, 140, 7913-7921; d) J. C. Siu, G. S. Sauer, A. Saha, R. L. Macey, N. Fu, T. Chauviré, K. M. Lancaster, S. Lin, J. Am. Chem. Soc. 2018; e) P. Xiong, H.-H. Xu, J. Song, H.-C. Xu, J. Am. Chem. Soc. 2018, 140, 2460-2464; f) K.-Y. Ye, G. Pombar, N. Fu, G. S. Sauer, I. Keresztes, S. Lin, J. Am. Chem. Soc. 2018, 140, 2468-2441; g) L. Zeng, H. Li, S. Tang, X. Gao, Y. Deng, G. Zhang, C.-W. Pao, J.-L. Chen, J.-F. Lee, A. Lei, ACS Catal. 2018, 8, 5448-5453; h) Z.-J. Wu, S.-R. Li, H.-C. Xu, Angew. Chem. Int. Ed., 10.1002/anie.201807683.
- [12] J. Chaussard, C. Combellas, A. Thiebault, *Tetrahedron Lett.* 1987, 28, 1173-1174.
- [13] F. Zhou, C. Jehoulet, A. J. Bard, J. Am. Chem. Soc. 1992, 114, 11004-11006.
- [14] H.-B. Zhao, Z.-J. Liu, J.Song, H.-C. Xu, Angew. Chem. Int. Ed. 2017, 56, 12732-12735.

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Entry for the Table of Contents

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Ammonia was used as a renewable and carbon-free fuel and applied as a high density hydrogen storage material. A room temperature electrochemical hydrogenation of alkene, alkyne and ketones was achieved with ammonia gas at balloon pressure at room temperature with carbon electrodes.



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