

Enhanced Reactivity of Aerobic Diimide Olefin Hydrogenation with Arylboronic Compounds: An Efficient One-Pot Reduction/Oxidation Protocol

Surojit Santra^[a] and Joyram Guin^{*[a]}

Keywords: Hydrogenation / Oxidative hydroxylation / Hydrazine hydrate / Oxygen / Alkenes

A catalyst-free and efficient method for simultaneous olefin hydrogenation and oxidation of arylboronate esters to phenols with hydrazine hydrate and molecular oxygen is presented. The process is based on the utilization of a readily available Lewis acidic arylboron compound, which evades common problems associated with the catalyst-free aerobic

simple procedure, the protocol smoothly delivers phenol derivatives and various alkanes in excellent yields with remarkable functional group compatibility. The method allows the reaction to be scaled up to 1 g of the starting materials.

hydrogenation of olefins with diimide. Using an operationally

Introduction

Transfer hydrogenation involving diimide (N_2H_2) represents a very useful alternative to established technology for hydrogenation with hydrogen gas (H_2).^[1,2] This approach is particularly attractive because diimide is able to carry out the hydrogenation of unsaturated carbon–carbon bonds with extremely high selectivity.^[1] Furthermore, diimide is particularly easy to synthesize either from hydrazine derivatives^[3] or by oxidation of hydrazine hydrate (N_2H_4 ·H₂O) with different nonhazardous and inexpensive oxidants,^[4] including molecular oxygen (O_2).^[1]

The generation of diimide by oxidation of hydrazine hydrate with molecular oxygen typically requires a catalyst to enhance the rate of the transformation. Accordingly, several catalytic approaches for the aerobic diimide reduction of olefins have been developed.^[5,6] Olefin hydrogenation with the use of hydrazine hydrate and oxygen gas has also been achieved without the use of catalysts, although it requires prolonged reaction times and an excess amount of hydrazine hydrate.^[7] Recently, the noncatalytic aerobic diimide reduction of olefins has been developed by using continuousflow technology.^[8] This approach has shortened the reaction time of this transformation; however, an elevated reaction temperature and a high pressure of oxygen gas are needed. Therefore, the search for an efficient, mild, and operationally simple method for the catalyst-free reduction of olefins with hydrazine hydrate and O2 remains highly desirable.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201501222.

In the course of diimide generation by oxidation of hydrazine hydrate with O_2 , the formation of a substantial quantity of hydrogen peroxide (H_2O_2) has been reported.^[9] This reactive species may be capable of decomposing diimide, which results in sluggish reactivity of the aerobic diimide reduction process in the absence of a catalyst. We therefore envisioned that effective trapping of in situ generated H₂O₂ with a suitable reagent could improve the reaction efficiency. Furthermore, it may also offer the opportunity to develop an aerobic oxygenation method. With the known reactivity of H₂O₂ toward Lewis acidic arylboron compounds,^[10] we anticipated that an efficient protocol for the aerobic diimide reduction of olefins could be designed by employing a stoichiometric amount of an arylboron species, which may eventually lead to the formation of the corresponding aromatic alcohols (Scheme 1).^[11] Herein, we report an efficient olefin hydrogenation method with hydrazine hydrate and O2 in the presence of arylboronate esters without the use of any catalyst at room temperature. The process does not require a longer reaction time or a large excess amount of the reagent. Furthermore, it proceeds with



Scheme 1. Concept of the simultaneous aerobic hydrogenation of olefins and oxygenation of arylboronic compounds.

 [[]a] Department of Organic Chemistry, Indian Association for the Cultivation of Science,
 2A & 2B Raja S. C. Mullick Road, Jadavpur, Kolkata 700032, India

E-mail: ocjg@iacs.res.in

http://www.iacs.res.in/ochem/ocjg/

SHORT COMMUNICATION

concomitant formation of phenols, which are pharmaceutically important compounds and frequently serve as versatile synthetic intermediates.^[12]

Results and Discussion

In accordance with our concept presented in Scheme 1, we began our study by investigating the hydrogenation of olefin **1a** by employing hydrazine hydrate and atmospheric pressure of O₂ at 32 °C in the presence of various arylboronic compounds (Table 1). Arylboronic acid 2a indeed promoted the hydrogenation of **1a**, although a long reaction time (16 h) and an excess amount of hydrazine hydrate were required to obtain good yields of corresponding alkane 3a and substituted phenol 4 (Table 1, entries 1 and 2). With this initial result, various readily available arylboronic compounds were examined for the transformation. Interestingly, a significant rate acceleration was observed by using a neutral catechol complex of arylboronic acid 2a, and this could be attributed to the enhanced Lewis acidity of the neutral cyclic arylboronate compound.^[13] Accordingly, the hydrogenation of olefin 1a in combination with ester 2b was completed in 2.5 h by using 4.0 equivalents of hydrazine hydrate, which delivered the desired products in nearly quantitative yields (Table 1, entry 3). Importantly, the reaction could be performed by reducing the amount of hydrazine hydrate even further, although alkane 3a and phenol 4 were isolated in slightly lower yields after a fairly long reaction time (Table 1, entries 4 and 5). Comparable results were obtained with ester 2c and with potassium phenyltrifluoroborate 2d (Table 1, entries 6 and 7). However, only moderate yields of the expected products were obtained with boronate ester 2e (Table 1, entry 8). Arylboronate ester 2f rendered rather unsatisfactory results (Table 1, entry 9). The use of pure oxygen gas was essential, as both the alkane and phenol were obtained in much lower yields in the presence of air (Table 1, entry 10).

We then directed our focus toward exploring the substrate scope with various olefins and arylboronate ester 2b or 2c under the optimized reaction conditions. A wide range of terminal and internal olefins were readily transformed into the corresponding alkanes in excellent yields in the presence of a several sensitive functional groups (Table 2). Substituted styrenes having nitro, bromo, methoxy, and tert-butyl groups were readily converted into corresponding alkanes 3b-e in excellent yields (89-94%). A $C \equiv C$ bond was also hydrogenated in nearly quantitative yield to afford alkane 3f. Substituted allyl aryl ethers underwent smooth hydrogenation through this process. Excellent yields of expected alkanes 3g-k were obtained with free amine, nitro, alcohol, and protected amine functionalities. Importantly, the benzyloxycarbonyl (Cbz, see product 31) protecting group was well tolerated in this method, even though it is labile to the transition-metal-catalyzed hydrogenation process. Although a slightly modified reaction procedure was necessary (see the Supporting Information), ketone- and aldehyde-functionalized alkanes 3m

Table 1. Evaluation of boron compounds and optimization of the reaction. $\ensuremath{^{[a]}}$



[a] Reaction conditions: Olefin (0.1 mmol), arylboronic compound **2b–f** (0.1 mmol), acetonitrile (0.3 M), 32 °C; yields of the isolated products are given. [b] Reaction was performed on 0.2 mmol scale. [c] Reaction was performed in air.

and 3n were obtained in good yields. Allyl sulfide and allylamine furnished products 30 and 3p in yields of 94 and 93%, respectively. N.N-Diallylaniline underwent complete hydrogenation to afford the product in good yield (3q, 85%). Gratifyingly, α,β - and α,α -disubstituted olefins bearing methoxy, alcohol, and ester groups furnished hydrogenated products 3r-w in excellent yields (92-95%). Interestingly, an azide-substituted olefin was converted into corresponding alkane 3x in 91% yield, and the azide moiety remained intact. Heteroaromatic functionalities were equally tolerated in this method. Accordingly, 2-vinylpyridine was fully converted into 2-ethylpyridine (3y), and quinine furnished hydrogenated product 3z in moderate yield. It is noteworthy that the aerobic oxygenation of arylboronate ester 2b or 2c took place concomitantly to deliver corresponding phenol 4 or 5, respectively, in nearly quantitative vield for almost all of the substrates (see the Supporting Information). The isolation of both products (i.e., alkane and phenol) was performed by using regular column chromatography without any difficulties.

To demonstrate the practical synthetic potential of this methodology, the reaction was performed on a preparative scale. Accordingly, 1.1 g of olefin 1a and 1.2 g of ester 2c were subjected to the one-pot aerobic hydrogenation/oxy-genation protocol, for which 1.0 g of corresponding alkane

Table 2. Substrate scope.^[a,b]



[a] Reaction conditions: Olefin (0.1 mmol), boronate ester **2b** (0.1 mmol), hydrazine hydrate (0.4 mmol), acetonitrile (0.3 M), 32 °C. [b] Yields of the isolated products are given. [c] Conversion (indicated in parentheses) was determined by analysis of the crude mixture by ¹H NMR spectroscopy upon performing the reaction in the absence of boronate ester. [d] Reaction was performed with boronate ester **2c**. [e] Hydrazine hydrate (5.0 equiv.). [f] Hydrazine hydrate (6.0 equiv.). [g] Reaction was conducted on 0.2 mmol scale. [h] Hydrazine hydrate (9.0 equiv.). [i] Conversion was determined by analysis of the crude mixture by ¹H NMR spectroscopy.

3a was isolated in 92% yield in combination with 0.52 g of phenol **5** in 90% yield [Equation (1)].^[14]

$$\begin{array}{c} & & & \\$$

To obtain insight into the reaction mechanism, several control experiments were performed (see the Supporting Information). Accordingly, the reduction of olefin 1a was performed under an argon atmosphere with the use of hydrazine hydrate and H₂O₂ and by varying their mol ratios. Whereas complete consumption of olefin 1a was achieved with 2.0 equivalents of hydrazine hydrate and 3.0 equivalents of H2O2, the use of an excess amount of H2O2 essentially inhibited the reaction, which suggests that H₂O₂ plays a role in the diimide decomposition process. On the contrary, upon repeating this experiment in the presence of boronate ester 2b, an improved result was obtained. Also, very sluggish reactivity was realized if the aerobic diimide reduction was performed in the absence of ester 2b.^[15] Furthermore, time-dependent ¹H NMR spectroscopy experiments revealed that the reduction of olefin 1a with diimide in the presence of arylboronate ester 2b took place at a much faster rate than that with arylboronic acid 2a. Presumably, arylboronate ester 2b contributes to the olefin hydrogenation step of the process. On the basis of these observations, we propose a cooperative mechanism in which in situ generated H₂O₂ initially forms Lewis adduct I with the arylboronate ester (Scheme 2). Complex I then interacts with diimide through hydrogen bonding to form reactive species II.^[6e] Subsequent hydrogen transfer from activated diimide complex II to the olefin delivers the corresponding alkane with the expulsion of N_2 . Finally, the H_2O_2 -arylboronate complex furnishes the corresponding phenol derivative and the diol that could be reused in boronate ester synthesis.



Scheme 2. Proposed reaction mechanism.

SHORT COMMUNICATION

Conclusions

In conclusion, we developed an efficient method for a one-pot hydrogenation/oxygenation process to give access to functionalized alkanes and phenol derivatives. Several relatively inactive terminal and internal olefins with varying substituents were hydrogenated in excellent yields, and arylboronate compounds were simultaneously oxidized to substituted phenols with equal efficiency. The use of O_2 as the oxidant and the formation of the ultimately safe byproducts N₂ and B(OH)₃ make the process environmentally attractive. The practical utility of this method was further demonstrated by performing a gram-scale experiment. Remarkable rate acceleration of the aerobic diimide reduction of olefins in the presence of a mild Lewis acidic arylboronate ester is an attractive feature of this transformation. Hydrogenbonding activation of diimide was implicated in the reaction pathway. Further studies toward expanding the scope of this transformation with other classes of substrates are currently being pursued in our group.

Supporting Information (see footnote on the first page of this article): Experimental details, characterization data, and copies of the ¹H NMR and ¹³C NMR spectra of all key intermediates and final products.

Acknowledgments

We gratefully acknowledge generous financial support from the Science and Engineering Research Board, India (grant number SB/S1/ OC-52/2013), and the Council of Scientific and Industrial Research (CSIR), New Delhi for a fellowship to S. S. J. G. sincerely thanks Dr. T. K. Paine for various insightful discussions.

- Reviews on diimide reduction: a) S. Hünig, H. R. Müller, W. Thier, Angew. Chem. Int. Ed. Engl. 1965, 4, 271; Angew. Chem. 1965, 77, 368; b) C. E. Miller, J. Chem. Educ. 1965, 42, 254; c) W. M. N. Ratnayake, J. S. Grossert, R. G. Ackman, J. Am. Oil Chem. Soc. 1990, 67, 940; d) D. J. Pasto, R. T. Taylor, Org. React. 1991, 40, 91; e) P. A. Chaloner, M. A. Esteruleas, L. A. O. F. Joó, Homogeneous Hydrogenation, Kluwer, Dordrecht, The Netherlands, 1994; f) D. Sellmann, A. Hennige, Angew. Chem. Int. Ed. Engl. 1997, 36, 276; Angew. Chem. 1997, 109, 270; g) E. W. Schmidt, Hydrazine and Its Derivatives: Preparation, Properties, and Applications, 2nd ed., Wiley, New York, 2001; h) J. G. de Vries, C. J. Elsevier (Eds.), Handbook of Homogeneous Hydrogenation, Wiley-VCH, Weinheim, Germany, 2007, vols. 1–3.
- [2] Reviews on olefin reduction with organic hydrogen donors: a)
 G. Zassinovich, G. Mestroni, S. Gladiali, *Chem. Rev.* 1992, 92, 1051; b) R. Noyori, S. Hashiguchi, *Acc. Chem. Res.* 1997, 30, 97; c) C. Zhu, K. Saito, M. Yamanaka, T. Akiyama, *Acc. Chem. Res.* 2015, 48, 388.
- [3] a) E. J. Corey, W. L. Mock, D. J. Pasto, *Tetrahedron Lett.* 1961, 2, 347; b) E. J. Corey, D. J. Pasto, W. L. Mock, *J. Am. Chem. Soc.* 1961, 83, 2957; c) R. S. Dewey, E. E. van Tamelen, *J. Am. Chem. Soc.* 1961, 83, 3729; d) S. Hünig, H.-R. Müller, W. Thier, *Tetrahedron Lett.* 1961, 2, 353; e) E. E. van Tamelen, R. S. Dewey, R. J. Timmons, *J. Am. Chem. Soc.* 1961, 83, 3725.
- [4] a) J. M. Hoffman, R. H. Schlessinger, J. Chem. Soc., Chem. Commun. 1971, 1245; b) K. Mori, M. Ohki, A. Sato, M. Matsui, Tetrahedron 1972, 28, 3739; c) M. Christl, G. Brüntrup, Chem. Ber. 1974, 107, 3908; d) K. Kondo, S. Murai, N. Son-

oda, *Tetrahedron Lett.* **1977**, *18*, 3727; e) T. G. Back, S. Collins, R. G. Kerr, *J. Org. Chem.* **1981**, *46*, 1564; f) R. A. Roberts, V. Schuell, L. A. Paquette, *J. Org. Chem.* **1983**, *48*, 2076.

- [5] For the metal-catalyzed diimide reduction of olefins, see: a) J. W. Wilt, G. Gutman, W. J. Ranus, A. R. Zigman, J. Org. Chem. 1967, 32, 893; b) B. M. Trost, S. Schneider, J. Am. Chem. Soc. 1989, 111, 4430; c) W. R. Roush, L. K. Hoong, M. A. J. Palmer, J. A. Straub, A. D. Palkowitz, J. Org. Chem. 1990, 55, 4117; d) M. Shokouhimehr, Y. Piao, J. Kim, Y. Jang, T. Hyeon, Angew. Chem. Int. Ed. 2007, 46, 7039; Angew. Chem. 2007, 119, 7169; e) A. Dhakshinamoorthy, M. Alvaro, H. Garcia, Adv. Synth. Catal. 2009, 351, 2271; f) Y. Jang, S. Kim, S. W. Jun, B. H. Kim, S. Hwang, I. K. Song, B. M. Kim, T. Hyeon, Chem. Commun. 2011, 47, 3601; g) E. Kim, S. Kim, B. M. Kim, Bull. Korean Chem. Soc. 2011, 32, 3183; h) M. Lamani, G. S. Ravikumara, K. R. Prabhu, Adv. Synth. Catal. 2012, 354, 1437; i) A. Dhakshinamoorthy, S. Navalon, D. Sempere, M. Alvaro, H. Garcia, Chem. Commun. 2013, 49, 2359.
- [6] For the organocatalytic diimide reduction of olefins, see: a) C. Smit, M. W. Fraaije, A. J. Minnaard, J. Org. Chem. 2008, 73, 9482; b) Y. Imada, T. Kitagawa, T. Ohno, H. Iida, T. Naota, Org. Lett. 2010, 12, 32; c) Y. Imada, H. Iida, T. Kitagawa, T. Naota, Chem. Eur. J. 2011, 17, 5908; d) B. J. Marsh, E. L. Heath, D. R. Carbery, Chem. Commun. 2011, 47, 280; e) M. Lamani, R. S. Guralamata, K. R. Prabhu, Chem. Commun. 2012, 48, 6583.
- [7] a) H. Chen, J. Wang, X. Hong, H.-B. Zhou, C. Dong, *Can. J. Chem.* 2012, *90*, 758; b) M. P. Feth, K. Rossen, A. Burgard, *Org. Process Res. Dev.* 2013, *17*, 282; c) D. Leow, Y.-H. Chen, T.-H. Hung, Y. Su, Y.-Z. Lin, *Eur. J. Org. Chem.* 2014, 7347; d) N. Menges, M. Balci, *Synlett* 2014, *25*, 671.
- [8] a) A. S. Kleinke, T. F. Jamison, Org. Lett. 2013, 15, 710; b) B.
 Pieber, S. T. Martinez, D. Cantillo, C. O. Kappe, Angew. Chem. Int. Ed. 2013, 52, 10241; Angew. Chem. 2013, 125, 10431; c) B.
 Pieber, T. Glasnov, C. O. Kappe, Chem. Eur. J. 2015, 21, 4368.
- [9] E. C. Gilbert, J. Am. Chem. Soc. 1929, 51, 2744.
- [10] For the H₂O₂-mediated hydroxylation of arylboronic acids, see:
 a) H. G. Kuivila, J. Am. Chem. Soc. 1955, 77, 4014; b) M. Hawthorne, J. Org. Chem. 1957, 22, 1001; c) H. G. Kuivila, A. G. Armour, J. Am. Chem. Soc. 1957, 79, 5659; d) J. Simon, S. Salzbrunn, G. K. Surya Prakash, N. A. Petasis, G. A. Olah, J. Org. Chem. 2001, 66, 633; e) A. Gogoi, U. Bora, Synlett 2012, 23, 1079; f) N. Mulakayala, Ismail, K. M. Kumar, R. K. Rapolu, B. Kandagatla, P. Rao, S. Oruganti, M. Pal, Tetrahedron Lett. 2012, 53, 6004; g) L. Wang, D.-Y. Dai, Q. Chen, M.-Y. He, Asian J. Org. Chem. 2013, 2, 1040; h) M. Gohain, M. du Plessis, J. H. van Tonder, B. C. B. Bezuidenhoudt, Tetrahedron Lett. 2014, 55, 2082.
- [11] For the aerobic hydroxylation of arylboronic acids, see: a) L. Zhang, G. Zhang, M. Zhang, J. Cheng, J. Org. Chem. 2010, 75, 7472; b) A. N. Cammidge, V. H. M. Goddard, C. P. J. Schubert, H. Gopee, D. L. Hughes, D. Gonzalez-Lucas, Org. Lett. 2011, 13, 6034; c) A. D. Chowdhury, S. M. Mobin, S. Mukherjee, S. Bhaduri, G. K. Lahiri, Eur. J. Inorg. Chem. 2011, 3232; d) H. Yang, Y. Li, M. Jiang, J. Wang, H. Fu, Chem. Eur. J. 2011, 17, 5652; e) H. Jiang, L. Lykke, S. U. Pedersen, W.-J. Xiao, K. A. Jørgensen, Chem. Commun. 2012, 48, 7203; f) Y.-Q. Zou, J.-R. Chen, X.-P. Liu, L.-Q. Lu, R. L. Davis, K. A. Jørgensen, W.-J. Xiao, Angew. Chem. Int. Ed. 2012, 51, 784; Angew. Chem. 2012, 124, 808; g) S. P. Pitre, C. D. McTiernan, H. Ismaili, J. C. Scaiano, J. Am. Chem. Soc. 2013, 135, 13286; h) W. Ding, J.-R. Chen, Y.-Q. Zou, S.-W. Duan, L.-Q. Lu, W.-J. Xiao, Org. Chem. Front. 2014, 1, 151; i) M. Jiang, Y. Li, H. Yang, R. Zong, Y. Jin, H. Fu, RSC Adv. 2014, 4, 12977; j) H. Kotoucova, I. Strnadova, M. Kovandova, J. Chudoba, H. Dvorakova, R. Cibulka, Org. Biomol. Chem. 2014, 12, 2137; k) L. Yang, F. Wang, R. Lee, Y. Lv, K.-W. Huang, G. Zhong, Org. Lett. 2014, 16, 3872; 1) I. G. T. M. Penders, Z. Amara, R. Horvath, K. Rossen, M. Poliakoff, M. W. George, RSC Adv. 2015, 5, 6501.



- [12] a) J. H. P. Tyman, Synthetic and Natural Phenols, Elsevier, New York, 1996; b) Z. Rappoport, The Chemistry of Phenols, Wiley-VCH, Weinheim, Germany, 2003.
- [13] a) J. O. Edwards, G. C. Morrison, V. F. Ross, J. W. Schultz, J. Am. Chem. Soc. 1955, 77, 266; b) M. T. Reetz, C. M. Niemeyer, K. Harms, Angew. Chem. Int. Ed. Engl. 1991, 30, 1472; Angew. Chem. 1991, 103, 1515; c) G. Springsteen, B. Wang, Tetrahedron 2002, 58, 5291; d) J. Yan, G. Springsteen, S. Deeter, B. Wang, Tetrahedron 2004, 60, 11205.
- [14] Efficient gas-liquid mixing was particularly important to obtain an excellent result in the gram-scale experiment. Therefore, the reaction was performed in a 500 mL Erlenmeyer flask.
- [15] The reduction of olefin 1a without the use of arylboronate ester under otherwise optimized reaction conditions required >24 h to achieve nearly full conversion of olefin 1a, see also ref.^[7d] Received: September 22, 2015

Published Online: October 22, 2015