Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2014, **12**, 2137

Biomimetic aerobic oxidative hydroxylation of arylboronic acids to phenols catalysed by a flavin derivative†

Hana Kotoučová,[a,b] Iveta Strnadová,[b] Martina Kovandová,[a] Josef Chudoba,[c] Hana Dvořáková[c] and Radek Cibulka*[a]

Received 18th October 2013,
Accepted 23rd January 2014

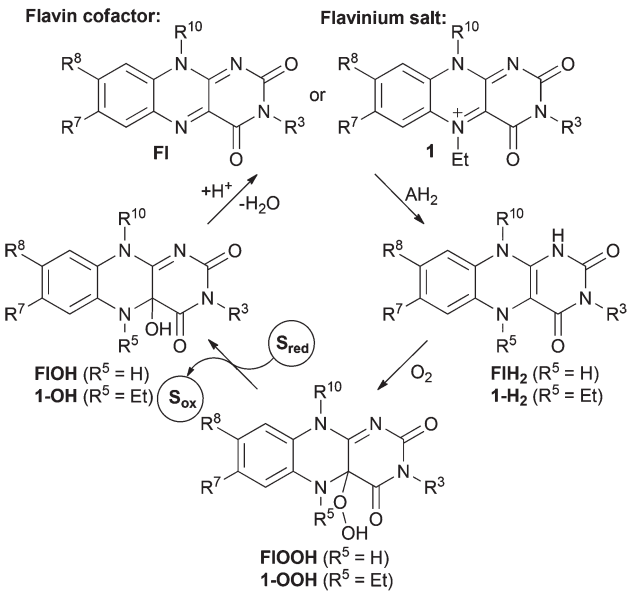
DOI: 10.1039/c3ob42081g

www.rsc.org/obc

Flavin-catalysed oxidative hydroxylation of substituted arylboronic acids by molecular oxygen with the assistance of hydrazine or ascorbic acid resulted in phenols in high yields. This mild organocatalytic protocol is compatible with a variety of functional groups and it is alternatively usable for transformation of alkylboronic acids to alcohols. Reaction takes place also in water and fulfils criteria for a green procedure.

Introduction

Design of biomimetic systems inspired by enzymatic catalytic processes usually yields new efficient green methodologies in organic synthesis.[1] Accordingly, oxygenation reactions occurring in flavin-dependent monooxygenases provided inspiration for artificial systems based on flavinium salts which are now used as powerful catalysts for chemoselective and stereoselective oxidations with oxygen or hydrogen peroxide.[2–4] In monooxygenases, flavin cofactor **Fl** (FMN or FAD) reduced by NADPH reacts with oxygen to give flavin-4a-hydroperoxide **FlOOH** (Scheme 1), which oxidizes a substrate. After oxygen transfer, the cofactor is regenerated by water elimination.[2,5] Artificial aerial oxidations catalysed by flavinium salts (*e.g.* by compound **1** in Scheme 1) in the presence of a sacrificial reducing agent proceed *via* the same mechanism.[2,4] The use of 5-alkylflavinium salts instead of neutral flavin is necessary because the 5-alkyl group stabilizes hydroperoxide **1-OOH** so that it can be utilized for oxidations.[2b,6] Despite their considerable potential, flavinium catalysts have still been tested only in O_2 oxidations of sulfides to sulfoxides,[4a,f] amines to *N*-oxides,[4f] and in Baeyer–Villiger (B.V.)[4e] and Dakin oxidations.[4c] Here, we report flavinium-catalysed oxidative hydroxylation of arylboronic acids, thus extending the portfolio of flavin-mediated oxidations and bringing an organocatalytic procedure for the transformation of arylboronic acids to phenols. Analogous biocatalytic oxidation of C–B bonds with Baeyer–Villiger oxygenases employing the flavin cofactor has been reported,[7] but with a substrate scope focused on alkylboronates.[7b]



Scheme 1 Mechanism of aerobic oxidations of substrate S catalysed by neutral flavin Fl (in enzymes) or flavinium salt 1 (in artificial systems) with the assistance of reductant AH_2.

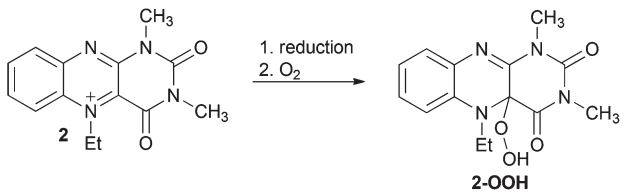
Currently, the hydroxylation of arylboronic acid represents a useful alternative to classical phenol synthesis methods, *i.e.* nucleophilic aromatic substitution of aryl halides or hydrolysis of arene diazonium salts, which often suffer from low functional group compatibility and poor accessibility of the starting compounds. Arylboronic acids can be hydroxylated by strong

[a]*Department of Organic Chemistry, Institute of Chemical Technology, Prague, Technická 5, 16628 Prague 6, Czech Republic. E-mail: cibulkar@vscht.cz; Fax: +420 220 444 288; Tel: +420 220 443 688*
[b]*Charles University of Prague, Faculty of Education, M. D. Rettigové 4, 116 39 Prague 1, Czech Republic*
[c]*Central Laboratories, Institute of Chemical Technology, Prague, Technická 5, 16628 Prague 6, Czech Republic*
† Electronic supplementary information (ESI) available: Synthesis and characterization of catalyst **2**, characterization of products of oxidative hydroxylations and NMR studies. See DOI: 10.1039/c3ob42081g

oxidizing agents such as hydrogen peroxide, oxone, or MCPBA which are usually used in stoichiometric amounts.[8] Because there is a need for mild and environmentally friendly oxidation methods tolerating other functionalities, catalytic oxidative hydroxylations of boronic acids became a subject of intensive research in the last decade.[9–12] As a result, oxidations with molecular oxygen catalysed by copper(II) or palladium(II) salts,[9] copper-promoted electrochemical hydroxylation,[10a] reaction with electrochemically generated superoxide anions,[10b] and photocatalytic aerobic oxidative hydroxylation mediated by a ruthenium or methylene blue sensitizer and visible light have been developed.[11] Recently, the metal-free mild oxidation with *N*-oxides has been reported, but it requires a stoichiometric amount of organic oxidant.[12] Unexpected phenol production from arylboronic acid in the presence of oxygen and naphthoquinone is still the only example of an organocatalytic aerobic process mentioned in the literature.[13]

Results and discussion

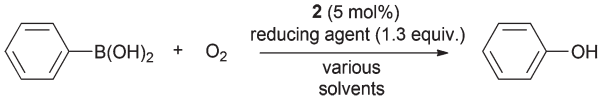
When searching for suitable conditions for the flavin-based oxidative hydroxylation of arylboronic acids, we evaluated a range of reducing agents and solvents from efficient protocols designed for aerobic sulfoxidations and B.V. oxidations.[4a,d–f] We used simple flavinium catalyst **2** (Scheme 2) which is readily available by a two-step procedure from commercial material.[4d] We initially employed the oxidation of phenylboronic acid (**3a**) with oxygen (1 atm., balloon) with 5 mol% of the catalyst as a model reaction (Table 1).



Scheme 2 Flavinium catalyst **2** and the corresponding hydroperoxide.

When hydrazine is used as a sacrificial reducing agent, the choice of solvent is essential (entries 1–4). In methanol, which dissolves phenylboronic acid well, only 5% conversion to phenol was observed after 10 min. Reaction in acetonitrile and in an acetonitrile–ethyl acetate–water mixture led to 35% and 12% conversions, respectively. Therefore we turned our attention to trifluoroethanol which is considered to be a suitable solvent for aerobic oxidations due to high solubility of oxygen.[4f] Addition of the methanol co-solvent was necessary to homogenize the reaction mixture. In the resulting trifluoroethanol–methanol (2 : 1) solvent system we observed the best result by far with a conversion of 95% after 10 min of oxidation (entry 4). As expected, lower catalyst loading as well as the use of air instead of oxygen led to deceleration of the process (entries 5 and 6). It is important to note that oxidation in the absence of the flavin catalyst does not take place (entry 7). Hydroxylation also proceeds with zinc or ascorbic acid as sacrificial reductants; however, the rates were lower than that with hydrazine under optimized conditions (entries 9–14). Reactions with zinc or ascorbic acid failed to accelerate either by changing the solvent or by adding sodium acetate to generate ascorbate with a higher reduction power[4a] and/or by generating the flavin hydroperoxide anion which is more powerful for nucleophilic oxidations[4e,14] (entries 11 and 13). Interestingly, flavin-based hydroxylations take place also in aqueous

Table 1 Oxidation of phenylboronic acid with oxygen catalyzed by alloxazinium salt **2**[a]



Entry	Catalyst	Reducing agent	Solvent + additives	Conv.[b] 10 min. [%]
1	**2**	$N_2H_4{\cdot}H_2O$	CH_3OH	5
2	**2**	$N_2H_4{\cdot}H_2O$	CH_3CN	35
3	**2**	$N_2H_4{\cdot}H_2O$	CH_3CN–EtOAc–H_2O[d]	12
4	**2**	$N_2H_4{\cdot}H_2O$	CF_3CH_2OH–CH_3OH[e]	95
5	**2** (1 mol%)	$N_2H_4{\cdot}H_2O$	CF_3CH_2OH–CH_3OH[e]	10
6[c]	**2**	$N_2H_4{\cdot}H_2O$	CF_3CH_2OH–CH_3OH[e]	15
7	—	$N_2H_4{\cdot}H_2O$	CF_3CH_2OH–CH_3OH[e]	0(0)
8	**2**	$N_2H_4{\cdot}H_2O$	H_2O (pH = 7.8)	7(95)
9	**2**	Zn	CH_3OH	39
10	**2**	Zn	CH_3CN–EtOAc–H_2O[d]	12
11	**2**	Zn	CH_3CN–EtOAc–H_2O[d] + CH_3COONa (1 equiv.)	13
12	**2**	Ascorbic acid	CF_3CH_2OH–CH_3OH–H_2O[f]	6
13	**2**	Ascorbic acid	CF_3CH_2OH–CH_3OH–H_2O[f] + CH_3COONa (1 equiv.)	8
14	**2**	Ascorbic acid	H_2O (pH = 7.8)	27

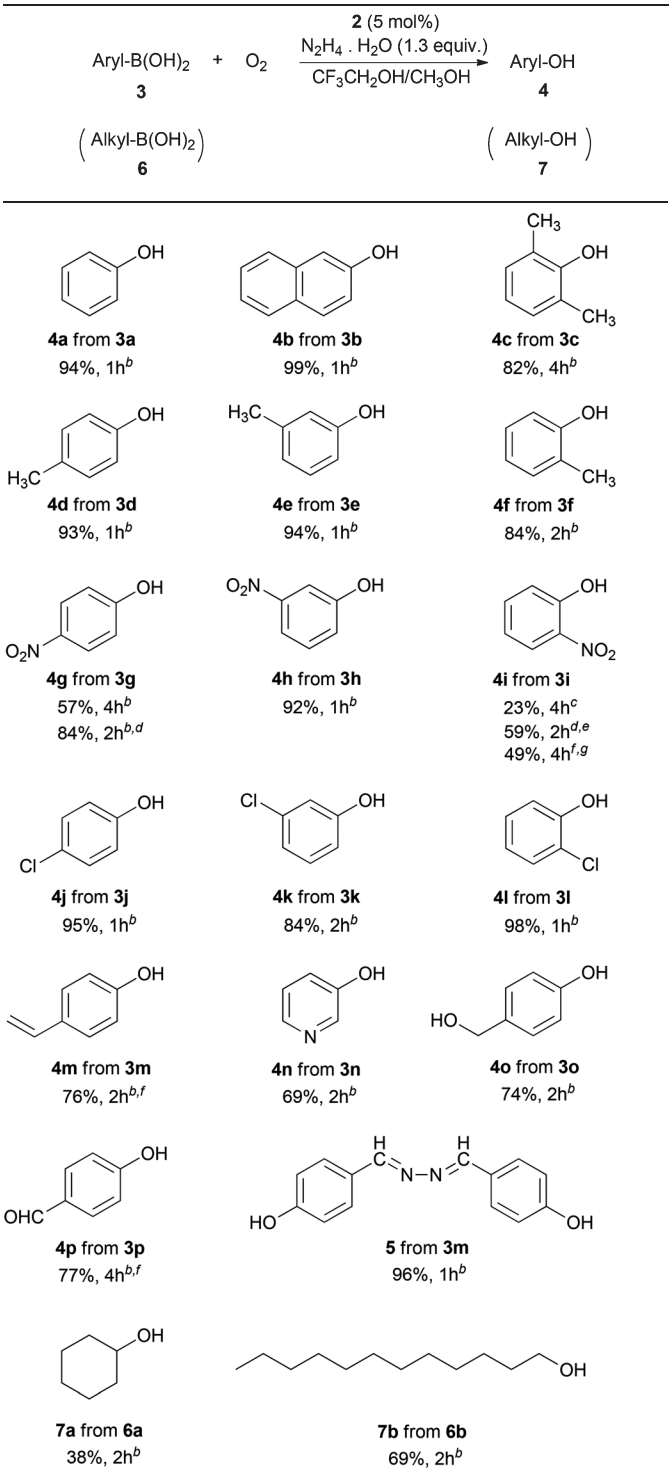
[a] Conditions: phenylboronic acid (0.079 mmol), **2** (5 mol% unless otherwise indicated), reducing agent (0.106 mmol), oxygen (1 atm., balloon), solvent 0.6 mL, R.T. (for details see procedure A in the Experimental section). [b] Conversion after 10 minutes (conversion after 3 hours in brackets) determined by ^{1}H NMR. [c] Air (1 atm., balloon) used instead of oxygen. [d] 8 : 1 : 1. [e] 2 : 1. [f] 7 : 3 : 2.

solutions (entries 8 and 14). The reaction is slower compared to that in trifluoroethanol. Most probably, the reaction rate in water is negatively influenced by low solubility of oxygen which is approx. 10 times lower as compared with organic and fluorinated solvents.[15] Even so, quantitative conversion was almost observed in aqueous medium with hydrazine as the reductant after extended time (3 h).

Series of boronic acids with an electron-withdrawing or electron-donating group were screened in preparative experiments to investigate the substrate scope of the reaction (Table 2; see the Experimental section and ESI† for details). Most substituted phenols **4** were obtained in quantitative conversion and with good to excellent yields from arylboronic acids **3** using our optimized protocol, *i.e.* the $2/O_2$ (1 atm.)/hydrazine system in trifluoroethanol–methanol. It should be mentioned that the procedure is suitable also for *ortho*-substituted and even for *ortho*,*ortho*′-disubstituted derivatives with only longer reaction time being required. The reaction is slower also for *ortho*- and *para* nitro derivatives **3g** and **3i**. For oxidation of *o*-nitrophenylboronic acid (**3i**), 51% conversion was only observed even after extended reaction time. This is probably caused (in addition to a steric effect in the case of **3i**) by relatively high acidity of the resulting nitrophenols[16] which are able to protonate hydrazine. Hydrazine acts as a flavin reducing agent and a base generating flavinhydroperoxide anion. Both these processes could be decelerated by hydrazinium/hydrazine equilibrium. Addition of a weak base,[18] *e.g.* sodium bicarbonate or sodium acetate, speeds up the reaction significantly: quantitative and 85% conversion was detected for **3g** and **3i**, respectively, in the presence of 5 equivalents of sodium acetate after 2 h.

Special attention has been paid to arylboronic acids possessing moieties sensitive to oxidation: aldehyde group, pyridine nitrogen, double bond and (hydroxymethyl)phenyl group. As expected, hydrazine is not compatible with aldehyde function and hydrazone **5** is formed by the original protocol from *p*-formylphenylboronic acid (**3p**). On the other hand, the procedure with ascorbic acid gave *p*-hydroxybenzaldehyde (**4p**) in an almost quantitative yield. This indicates that the $2/O_2$/ascorbic acid system is also useful on the preparative scale and, moreover, the procedure is chemoselective leaving the aldehyde function non-oxidized.[19] The protocol with ascorbic acid was efficiently applied also to hydroxylation of *o*-nitrophenylboronic acid (**3i**) and 4-vinylphenylboronic acid (**3m**). The hydrazine based procedure is excluded for **3m** to avoid double bond reduction by diimide which can be formed from hydrazine by the action of flavinium salts.[20] On the other hand, the procedure with hydrazine succeeded in producing corresponding hydroxy derivatives from pyridin-3-ylboronic acid (**3n**) and 4-(hydroxymethyl)phenylboronic acid (**3o**) in quantitative conversion and with good yields. No side-oxidation of the double bond, pyridine nitrogen, as well as (hydroxymethyl)phenyl group was ever observed. Finally, cyclohexyl- (**6a**) and dodecylboronic acid (**6b**) were oxidized to the corresponding alcohols **7a** and **7b** by the unchanged protocol with hydrazine showing its applicability to alkylboronic acids.

Table 2 Isolated yields and reaction times for oxidative hydroxylations of arylboronic (and alkylboronic) acids on a preparative scale[a]



[a] Conditions: boronic acid (0.79 mmol), catalyst **2** (5 mol%), hydrazine (1.06 mmol), oxygen (1 atm., balloon), CF_3CH_2OH–CH_3OH (2 : 1, 6 mL), R.T. (see procedure B in the Experimental section). [b] Conversion >95%. [c] Conversion 51%. [d] 5 equiv. of sodium acetate added (see procedure D in the Experimental section). [e] Conversion 85%. [f] Ascorbic acid + sodium acetate instead of hydrazine (see procedure C in the Experimental section). [g] Conversion 76%.

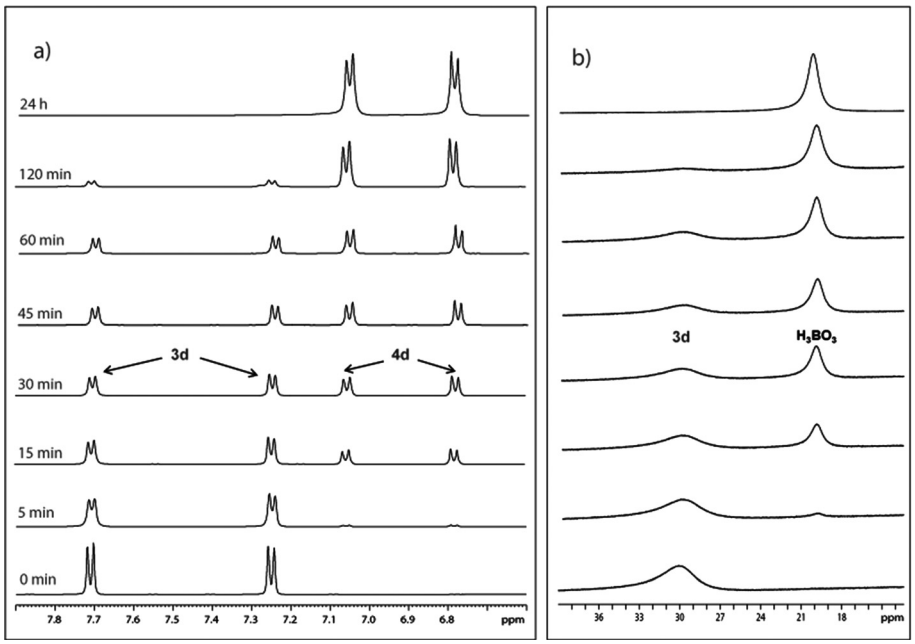


Fig. 1 Course of aerial oxidation of **3d** to **4d** mediated by the **2**/ascorbic acid/CH_3COONa system in CF_3CH_2OH–CD_3CN–D_2O (7 : 4 : 3) monitored by ^1H (a) and ^{11}B (b) NMR; for full spectra, see ESI.†

In a preliminary mechanistic study on the course of oxidative hydroxylation, we tried to vary the amount of hydrazine relative to the substrate. We observed the quantitative production of phenol with only 0.5 equivalent of hydrazine showing that, similar to sulfoxidations,[4d,f] one equivalent of hydrazine generates two equivalents of dihydroflavine (the precursor of flavin hydroperoxide) in the catalytic cycle. During the first reduction step, hydrazine is oxidized to diimide which is still strong enough to reduce the second molecule of flavinium salt while it itself is oxidized to molecular nitrogen.[4d] ^1H and ^{11}B NMR monitoring of the *p*-methylphenylboronic acid (**3d**) hydroxylation mediated by the **2**/ascorbic acid/CH_3COONa system[21] in CF_3CH_2OH–CD_3CN–D_2O revealed a simple reaction course with no by-products (Fig. 1; see also ESI†). It also shows that the likely intermediates, *e.g.* adduct of **2-OOH** on arylboronic acid and the corresponding arylborate, are readily converted to the reaction products (phenol and boric acid). Similarly, a simple course of hydroxylation was observed in aqueous solution (see ESI† for details).

Conclusions

In conclusion, flavinium salt **2**, in the presence of a sacrificial reducing agent, catalysed the oxidative hydroxylation of arylboronic acids to phenols with molecular oxygen which is a new synthetic application for the flavin-based biomimetic systems. The flavinium-based method is organocatalytic, thus distinguishing it from other catalytic procedures for the hydroxylation of arylboronic acids. The method is characterized by a broad substrate scope, including *ortho*-substituted arylboronic acids and derivatives with groups sensitive to oxidation. It is also applicable for the transformation of alkylboronic acids to alcohols. The reaction is performed under mild conditions with potential use of water as a solvent. The use of oxygen as a stoichiometric oxidant and hydrazine as a sacrificial reducing agent producing water and nitrogen as the only by-products ranks this method among the green procedures. The efficiency of the described catalytic system should be further increased by optimizing the structure of the flavin catalyst, and this is now underway in our laboratory.

Experimental

Materials and methods

NMR spectra were recorded on a Varian Mercury Plus 300 (299.97 MHz for ^1H, and 75.44 MHz for ^{13}C) and a Bruker Avance DRX 500 (500.13 MHz for ^1H, 125.77 MHz for ^{13}C and 160.4 MHz for ^{11}B) at 298 K unless otherwise indicated. Chemical shifts δ are given in ppm using residual solvent or tetramethylsilane as an internal standard for ^1H and ^{13}C NMR and $BF_3{\cdot}Et_2O$ as an external standard for ^{11}B. Elemental analyses (C, H, N) were performed on a Perkin-Elmer 240 analyser. High-resolution mass spectra were obtained on an LTQ Orbitrap Velos (Thermo Fisher Scientific), equipped with an orbitrap mass analyzer. The mass spectrometer was operated in ESI mode (ESI source temperature 250 °C, potential 3000 V) with a mass range from 200 to 2000 a.m.u. TLC analyses were carried out on a DC Alufolien Kieselgel 60 F254 (Merck). Preparative column chromatography separations were performed on a silica gel Kieselgel 60 (0.040–0.063 mm) (Merck). Melting points were measured on a Boetius melting point apparatus and are uncorrected. Starting materials, reagents and substrates were obtained from

commercial suppliers and used without further purification. The solvents were purified and dried using standard procedures. Catalyst **2** was prepared according to the modified protocol from the literature[4d] (see ESI† for details and characterization).

General procedures for oxidative hydroxylations

Oxidations carried out on an analytical scale – general procedure A. Boronic acid (7.9×10^{-5} mol) and a reducing agent (10.6×10^{-5} mol) were dissolved or suspended in 0.6 mL of solvent. Then catalyst **2** (0.4×10^{-5} mol) was added and the reaction mixture was shaken for 10 min in a small flask under oxygen (balloon, 1 atm.). The solvents were evaporated and the residue was dissolved in CD_3OD for NMR measurement.

Preparative oxidations – general procedure B (hydrazine hydrate used as a reducing agent). Boronic acid (7.9×10^{-4} mol) and hydrazine hydrate (7.92 mL, 10.6×10^{-4} mol) were dissolved in trifluoroethanol (4.0 mL) and methanol (2.0 mL). Then catalyst **2** (0.4×10^{-4} mol) was added and the reaction mixture was shaken in a flask under oxygen (balloon, 1 atm.). The solvents were evaporated and the crude product was purified by column chromatography.

Preparative oxidations – general procedure C (ascorbic acid used as a reducing agent). Boronic acid (7.9×10^{-4} mol), natrium acetate (131.2 mg, 16.0×10^{-4} mol) and ascorbic acid (218.8 mg, 16.0×10^{-4} mol) were dissolved in trifluoroethanol (3.5 mL), water (1.0 mL) and methanol (1.5 mL). Then catalyst **2** (14.8 mg, 0.4×10^{-4} mol) was added and the reaction mixture was shaken in a flask under oxygen (balloon, 1 atm.). The solvents were evaporated and the residue was dissolved/suspended in water (20 mL). The resulting mixture was extracted with dichloromethane (3 × 15 mL) and dried over magnesium sulfate. After evaporation of solvents, the crude product was purified by column chromatography.

Preparative oxidations – general procedure D (procedure B with the application of a base). Boronic acid (7.9×10^{-4} mol), natrium acetate (162 mg, 3.95×10^{-4} mol) and hydrazine hydrate (81.4 mg, 16.0×10^{-4} mol) were dissolved in trifluoroethanol (4.0 mL) and methanol (2.0 mL). Then catalyst **2** (14.8 mg, 0.4×10^{-4} mol) was added and the reaction mixture was shaken in a flask under oxygen (1 atm.) for 2 hours. The solvents were evaporated, the residue was dissolved/suspended in water (20 mL) and the mixture was acidified with hydrochloric acid (pH = 1). The resulting mixture was extracted with dichloromethane (3 × 15 mL) and dried over magnesium sulfate. After evaporation of solvents, the crude product was purified by column chromatography.

Characterization of products of oxidative hydroxylations

Phenols **4a–4p** and **5** and alcohols **7a** and **7b** resulting from oxidative hydroxylations of boronic acids were characterized by ^1H and ^{13}C NMR and the HR-MS technique. Spectral data correspond to those published in the literature (see ESI† for details).

Acknowledgements

This work was financially supported by the Czech Science Foundation (grant no. P207/12/0447).

Notes and references

1 L. Marchetti and M. Levine, *ACS Catal.*, 2011, **1**, 1090–1118.
2 Applications of flavinium salts in catalysis are reviewed in: (*a*) G. de Gonzalo and M. W. Fraaije, *ChemCatChem*, 2013, **5**, 403–415; (*b*) F. G. Gelalcha, *Chem. Rev.*, 2007, **107**, 3338–3361; (*c*) Y. Imada and T. Naota, *Chem. Rec.*, 2007, **7**, 354–361.
3 Very recent papers on H_2O_2 oxidations catalyzed by flavinium salts: (*a*) Y. Imada, T. Kitagawa, S. Iwata, N. Komiya and T. Naota, *Tetrahedron*, 2014, **70**, 495–501; (*b*) P. Ménová, H. Dvořáková, V. Eigner, J. Ludvík and R. Cibulka, *Adv. Synth. Catal.*, 2013, **355**, 3451–3462; (*c*) R. Jurok, J. Hodačová, V. Eigner, H. Dvořáková, V. Setnička and R. Cibulka, *Eur. J. Org. Chem.*, 2013, 7724–7738; (*d*) M. J. Pouy, E. M. Milczek, T. M. Figg, B. M. Otten, B. M. Prince, T. B. Gunnoe, T. R. Cundari and J. T. Groves, *J. Am. Chem. Soc.*, 2012, **134**, 12920–12923; (*e*) A. T. Murray, P. Matton, N. W. G. Fairhurst, M. P. John and D. R. Carbery, *Org. Lett.*, 2012, **14**, 3656–3659; (*f*) P. Ménová and R. Cibulka, *J. Mol. Catal. A: Chem.*, 2012, **363–364**, 362–370; (*g*) T. Hartman, V. Herzig, M. Buděšínský, J. Jindřich, R. Cibulka and T. Kraus, *Tetrahedron: Asymmetry*, 2012, **23**, 1571–1583.
4 Papers on aerial oxidations catalyzed by flavinium salts: (*a*) Y. Imada, T. Kitagawa, H.-K. Wang, N. Komiya and T. Naota, *Tetrahedron Lett.*, 2013, **54**, 621–624; (*b*) S. Chen, M. S. Hossain and F. W. Foss, *ACS Sust. Chem. Eng.*, 2013, **1**, 1045–1051; (*c*) S. Chen and F. W. Foss, *Org. Lett.*, 2012, **14**, 5150–5153; (*d*) Y. Imada, H. Iida, S. Ono, Y. Masui and S.-I. Murahashi, *Chem.–Asian. J.*, 2006, **1**, 136–147; (*e*) Y. Imada, H. Iida, S.-I. Murahashi and T. Naota, *Angew. Chem., Int. Ed.*, 2005, **44**, 1704–1706; (*f*) Y. Imada, H. Iida, S. Ono and S.-I. Murahashi, *J. Am. Chem. Soc.*, 2003, **125**, 2868–2869.
5 C. T. Walsh and T. A. Wencewicz, *Nat. Prod. Rep.*, 2012, 175–200.
6 G. Merenyi and J. Lind, *J. Am. Chem. Soc.*, 1991, **113**, 3146–3153.
7 (*a*) B. P. Branchaud and C. T. Walsh, *J. Am. Chem. Soc.*, 1985, **107**, 2153–2161; (*b*) P. B. Brondani, H. Dudek, J. S. Reis, M. W. Fraaije and L. H. Andrade, *Tetrahedron: Asymmetry*, 2012, **23**, 703–708.
8 (*a*) D.-S. Chen and J.-M. Huang, *Synlett*, 2013, 499–501; (*b*) N. Mulakayala, Ismail, K. M. Kumar, R. K. Rapolu, B. Kandagatla, P. Rao, S. Oruganti and M. Pal, *Tetrahedron Lett.*, 2012, **53**, 6004–6007; (*c*) A. Gogoi and U. Bora, *Synlett*, 2012, 1079–1081; (*d*) G. K. S. Prakash, S. Chacko, C. Panja, T. E. Thomas, L. Gurung, G. Rasul, T. Mathew and G. A. Olah, *Adv. Synth. Catal.*, 2009, **351**, 1567–1574; (*e*) B. R. Travis, B. P. Ciaramitaro and B. Borhan, *Eur. J. Org.*

Chem., 2002, 3429–3434; (*f*) J. Simon, S. Salzbrunn, G. K. Surya Prakash, N. A. Petasis and G. A. Olah, *J. Org. Chem.*, 2000, **66**, 633–634; (*g*) K. S. Webb and D. Levy, *Tetrahedron Lett.*, 1995, **36**, 5117–5118; (*h*) M. Hawthorne, *J. Org. Chem.*, 1957, **22**, 1001–1001.

9 (*a*) H. Yang, Y. Li, M. Jiang, J. Wang and H. Fu, *Chem.–Eur. J.*, 2011, **17**, 5652–5660; (*b*) K. Inamoto, K. Nozawa, M. Yonemoto and Y. Kondo, *Chem. Commun.*, 2011, **47**, 11775–11777; (*c*) A. D. Chowdhury, S. M. Mobin, S. Mukherjee, S. Bhaduri and G. K. Lahiri, *Eur. J. Inorg. Chem.*, 2011, **2011**, 3232–3239; (*d*) J. Xu, X. Wang, C. Shao, D. Su, G. Cheng and Y. Hu, *Org. Lett.*, 2010, **12**, 1964–1967.

10 (*a*) H.-L. Qi, D.-S. Chen, J.-S. Ye and J.-M. Huang, *J. Org. Chem.*, 2013, **78**, 7482–7487; (*b*) K. Hosoi, Y. Kuriyama, S. Inagi and T. Fuchigami, *Chem. Commun.*, 2010, **46**, 1284–1286.

11 (*a*) Y.-Q. Zou, J.-R. Chen, X.-P. Liu, L.-Q. Lu, R. L. Davis, K. A. Jørgensen and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 784–788; (*b*) S. P. Pitre, C. D. McTiernan, H. Ismaili and J. C. Scaiano, *J. Am. Chem. Soc.*, 2013, **135**, 13286–13289.

12 C. Zhu, R. Wang and J. R. Falck, *Org. Lett.*, 2012, **14**, 3494–3497.

13 A. N. Cammidge, V. H. M. Goddard, C. P. J. Schubert, H. Gopee, D. L. Hughes and D. Gonzalez-Lucas, *Org. Lett.*, 2011, **13**, 6034–6037.

14 S.-I. Murahashi, S. Ono and Y. Imada, *Angew. Chem., Int. Ed.*, 2002, **41**, 2366–2368.

15 S. L. Murov, I. Carmichael and G. L. Hug, *Handbook of Photochemistry*, New York, 2nd edn, 1993.

16 pK_a values for **3g**, **3h**, **3i** and hydrazinium are 7.23, 8.40, 7.15 and 8.10, respectively; see ref. 17.

17 (*a*) M. D. Liptak, K. C. Gross, P. G. Seybold, S. Feldgus and G. C. Shields, *J. Am. Chem. Soc.*, 2002, **124**, 6421–6427; (*b*) S. P. Mezyk, M. Tateishi, R. MacFarlane and D. M. Bartels, *J. Chem. Soc., Faraday Trans.*, 1996, **92**, 2541–2545.

18 Stronger bases, *e.g.* sodium carbonate, caused decomposition of flavinium catalyst.

19 Oxidation of aromatic aldehydes to carboxylic acids or corresponding phenols (Dakin oxidation) mediated by flavins has been described; see ref. 3*b* and 4*c*.

20 (*a*) Y. Imada, H. Iida and T. Naota, *J. Am. Chem. Soc.*, 2005, **127**, 14544–14555; (*b*) C. Smit, M. W. Fraaije and A. J. Minnaard, *J. Org. Chem.*, 2008, **73**, 9482–9485; (*c*) Y. Imada, T. Kitagawa, T. Ohno, H. Iida and T. Naota, *Org. Lett.*, 2010, **12**, 32–35; (*d*) J. F. Teichert, T. den Hartog, M. Hanstein, C. Smit, B. ter Horst, V. Hernandez-Olmos, B. L. Feringa and A. J. Minnaard, *ACS Catal.*, 2011, **1**, 309–315.

21 Since hydrazine interaction with boronic acid results in signal broadening (see ESI†), we used ascorbic acid as a reducing agent.

