JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Nicotinic acid as an efficient organo-catalyst in the synthesis of phenols via ipso hydroxylation

Balaji P. Kotkar

Research Student, Department of chemistry, Savitribai Phule Pune University, Ganeshkhind Road, Ganeshkhind, Pune, Maharashtra 411007.

Abstract

Herein, we report an efficient protocol for the oxidative hydroxylation of arylboronic acids to phenols using nicotinic acid as organo-catalyst and aqueous H_2O_2 as an oxidant. This synthetic method features mild condition, simplicity and high yields.

IndexTerms - Ipso hydroxylation, Organo-catalyst, Nicotinic acid, phenols, Arylboronic acids

Introduction

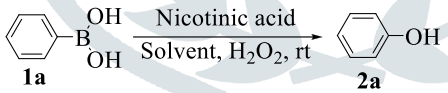
The phenol ring constitutes a key structural unit in many agrochemicals, natural products[1] and pharmaceuticals.[2-4] The traditional methods used to synthesise phenols usually involve the use transition-metal catalysts, complex ligands and harsh reaction conditions.[5] In view of the easy availability, lower toxicity and higher stability the application of organoboronic acid for the synthesis of phenol derivatives is a highly efficient and advantageous strategy. As a consequence of this, efforts have been made for the transformation of arylboronic acids into phenols via *ipso* hydroxylation by using Oxone,[6] NH_2OH,[7] N-oxides,[8] potassium peroxymonosulphate,[9] HOF,[10] *m*CPBA,[11] CuNP,[12] I_2-H_2O_2,[13] biosilica-H_2O_2,[14] lactic acid-H_2O_2,[15] organic hypervalent iodine (III)[16] etc. However, these methods plagued by certain disadvantages like use of strong oxidising agent, commercially unavailable metal catalysts, ligand, higher temperature and harmful organic solvents. Therefore, to overcome these drawbacks development of simple, efficient and greener protocols is still in demand.

Herein, we present the organocatalyst, nicotinic acid for ipso-hydroxylation of arylboronic acids to phenols in aqueous environment without the use of toxic metal, base and problematic solvent.

Results and discussion

Table 1

Optimization of nicotinic acid catalyzed ipso-hydroxylation



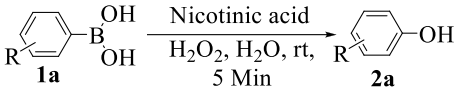
1a 2a

Entry	Nicotinic acid (mg)	H_2O_2 (ml)	Solvent (2ml)	Time (min)	Yield (%)[b]
1	100	0.50	H_2O	5	96
2	50	0.50	H_2O	5	96
3	25	0.50	H_2O	5	89
4	50	0.50	MeOH	5	84
5	50	0.50	^{i}PrOH	5	87
6	50	0.50	CH_3CN	5	81
7	50	0.50	THF	5	77
8	50	-	H_2O	60	-
9	-	0.50		60	trace
10	50	0.25	H_2O	5	87

[a] Reaction condition: Phenylboronic acid (1 mmol), H_2O_2 (30% aq.), Nicotinic acid catalyst.
[b] Isolated yields.

Table 1

Synthesis of phenols catalysed by nicotinic acid[a]



Entry	R	Yield[b] (%)
1	H	96
2	*m*-CN	95
3	*p*-I	92
4	*o*-Me	88
5	*p*-NO_2	92
6	*m*-NO_2	89
7	*p*-Cl	92
8	α-Naphthol	91
9	β-Naphthol	93
10	*p*-COOH	90
11	*p*-CHO	88
12	*p*-$COCH_3$	95
13	*m*-CN	93
14	*p*-Br	91

[a] Reaction condition: Phenylboronic acid (1 mmol), 0.5 mL of H_2O_2 (30% aq), 50 mg of Nicotinic acid catalyst.
[b] Isolated yields

In the initial screening, we used to react phenylboronic acid (1a, 1 mmol) with H_2O_2 (0.5 mL) in the presence 25 mg nicotinic acid in 2 mL of water at rt and observed the formation of phenol (2a) in 89% yield in 5 min (Table 1, entry 3). Increasing the catalyst loading from 25 mg to 50 mg resulted into a gradual enhancement in the yield of phenol (entries 3–9). However, further increase in catalyst loading does not improve the yield of desired product (entry 10). The effect of concentration of H_2O_2 used in the present experimental conditions was also investigated (entry 5, Table 1). The hydroxylation reaction of arylboronic acids could not be performed in the absence of H_2O_2 and catalyst (Table 1, entry 8, 9). A range of solvents such as MeOH, *i*PrOH, CH_3CN, THF and H_2O were evaluated (entries 4-8, Table 1) and H_2O was found to be the most effective solvent.

Finally, we have screened electronically diverse arylboronic acids for ipso-hydroxylation under optimized conditions (Table 2). For substrates containing an electron-donating group such as -OMe, -NH_2, -Me, -OH, -I and electron withdrawing groups like -Cl, -CHO, -NO_2, -$COCH_3$, -CN provided undoubtedly impressive results irrespective of their positions.

Conclusion

In conclusion, a novel and versatile protocol has been put forward for the hydroxylation of arylboronic acids to phenols. Our approach was to find a practical way to promote this transformation, by utilizing aqueous hydrogen peroxide as the oxidant and a cheap and commercially available nicotinic acid as the catalyst. A variety of arylboronic acids transformed to the corresponding phenols in good yields.

General procedure for the synthesis of phenols

To the mixture of arylboronic acid 1a (1 mmol), 30% H_2O_2 (0.50 ml) in water (2 mL) in a round-bottom flask was added nicotinic acid (25 mg) at room temperature. The completion of the reaction was monitored by TLC. After the completion of the reaction, water (10 mL) was added and it was worked up using diethylether (2 x 10 mL), washed with brine. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo to give the crude mass. The crude compound was then purified by column chromatography on silica-gel (100-200) to afford the phenol 2a in pure form.

ACKNOWLEDGMENT

B.P.K is thankful to UGC, New Dehli, for the award of research fellowship.

Selected experimental data

3-hydroxybenzonitrile (Table 2, entry 2): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.34 (m, 1H), 7.24-7.22 (m, 1H), 7.11-7.05 (m, 2H), 5.25 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 130.5, 124.5, 120.6, 118.9, 118.5, 113.1.

4-Chlorophenol (Table 2, entry 7): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.18 (m, 2H), 6.79-6.74 (m, 2H), 4.97 (s,1 H). ^{13}C NMR (100 MHz, CDCl3) δ 154.2, 129.5, 125.7, 116.9.

Naphthalen-2-ol (Table 2, entry 7): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.74 (m, 2H), 7.69 (d, J = 8.2 Hz, 1H), 7.45-7.42 (m, 1H), 7.34-7.31 (m, 1H), 7.14 (d, J = 2.5 Hz, 1H), 7.11 (dd, J = 8.8, 2.5 Hz, 1H), 4.89 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 134.7, 129.9, 129.2, 127.7, 126.5, 126.4, 123.7, 117.9, 109.5.

4-Bromophenol (Table 2, entry 14): ^{1}H NMR (400 MHz, $CDCl_3$) δ7.37-7.25 (m,2H), 6.75-6.71 (m, 2H), 4.67 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 132.7, 117.2, 113.2.

REFERENCES

1. J. H. P. Tyman, Synthetic and Natural Phenols, vol 52, Elsevier: New york, 1996.
2. S. Nandi, M. Vracko, M. C. Bagchi, Chem. Biol. Drug Des. 2007, 70, 424–436.
3. Z. Rappoport, The Chemistry of Phenols, Wiley-VCH: Weinheim, 2003.
4. B. Badhani, N. Sharma, R. Kakkar, RSC Adv. 2015, 5, 27540–27557.
5. (a) J. H. P. Tyman, Synthetic and Natural Phenols, Elsevier, New York, 1996; (b) H. Hock, S. Lang, Ber. Dtsch. Chem. Ges. B 1944, 77, 257–264. (c) A. Tlili, N. Xia, F. Monnier and M. Taillefer, Angew. Chem., Int. Ed., 2010, 48, 8725–8728.
6. Webb KS, Levy D. Tetrahedron Lett. 1995, 36, 5117–5118.
7. Kinmehr E, Yahyaee M, Tabatabai K. Tetrahedron Lett. 2007, 48, 2713–2715.
8. Zhu C, Wang R, Falck JR. *Org Lett*. 2012, 14, 3494–3497.
9. Webb, K. S.; Levy, D. Tetrahedron Lett.1995, 36, 5117-5118.
10. Gatenyo, J., Vints, I., Rozen, S. Chem. Commun. 2013, 7379–7381.
11. Chen, D. S., Huang, J. M. Synlett 2013, 499–501.
12. A. Affrose, I.A. Azath, A. Dhakshinamoorthy, K. Pitchumani, J. Mol. Catal. A Chem. 2014, 395, 500–505.
13. A. Gogoi, U. Bora, Synlett. 2012, 23, 1079-1081
14. A. Mahanta, P. Adhikari, U. Bora, A.J. Thakur, Tetrahedron Lett. 2015, 56, 1780-1783.
15. S. Gupta, P. Chaudhary, L. Seva, S. Sabiah, J. Kandasamy, RSC Adv. 2015, 5, 89133-89138.
16. N. Chatterjee, A. Goswami, Tetrahedron Lett. 2015, 56, 1524-1527.