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Editor's Choice

Chiral Ammonium Hypoiodite-catalyzed Enantioselective Oxidative Dearomatization of 1-Naphthols Using Hydrogen Peroxide

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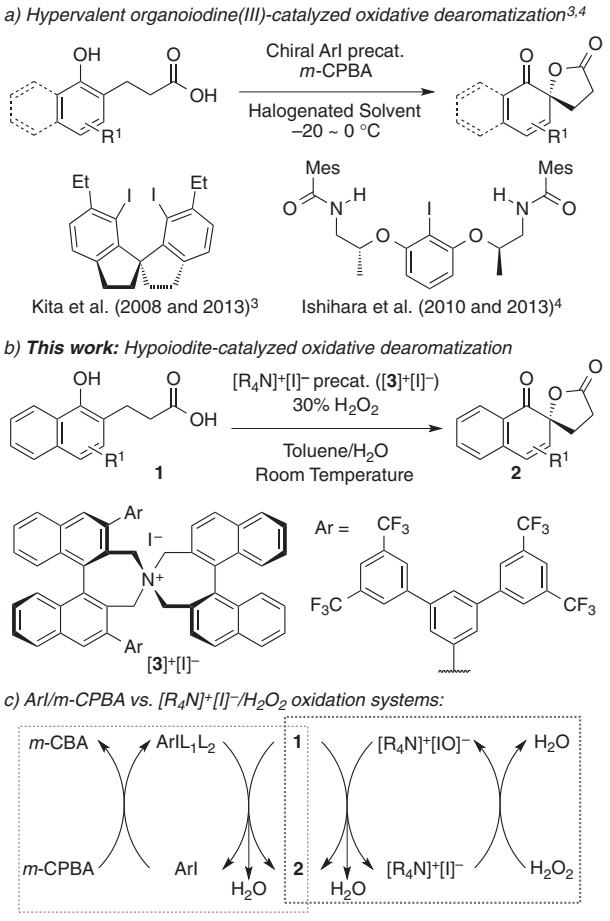
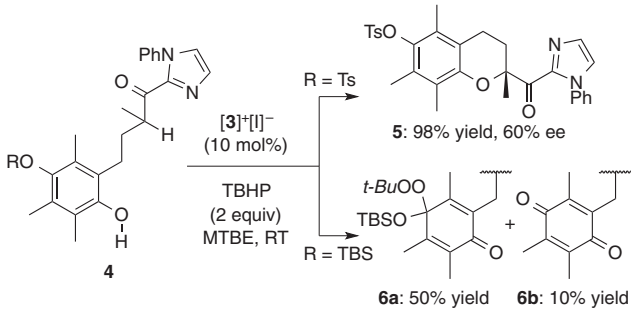
A highly enantioselective oxidative dearomatization of 1-naphthol derivatives (Kita spirolactonization) catalyzed by chiral hypoiodite species prepared in situ from chiral quaternary ammonium iodide in the presence of hydrogen peroxide is reported.

The oxidative dearomatization of phenol derivatives is an important pathway in the biosynthesis of many biologically active compounds.[1] As a consequence, the asymmetric oxidative dearomatization of phenols has emerged as a promising tool for the synthesis of various natural products.[2] Conventionally, enantioselective transition-metal catalysis has been used for these transformations.[2b,2d,2f] Recently, transition-metal-free oxidative dearomatization reactions[3–5] have been reported using chiral hypervalent organoiodines.[6] In particular, Kita's group[3] and our group[4] have developed highly enantioselective catalytic oxidative dearomatizations of phenol derivatives (Kita spirolactonization) using chiral iodoarenes (Scheme 1a). However, these chiral organoiodine(III) catalysts were prepared in situ from the corresponding iodoarenes and *meta*-chloroperbenzoic acid (*m*-CPBA), and *meta*-chlorobenzoic acid (*m*-CBA) was generated as a waste (Scheme 1c, left). Here, we report the enantioselective oxidative dearomatization of 1-naphthol derivatives **1** to spirolactones **2** using chiral ammonium hypoiodite catalysis[7,8] (Scheme 1b). The chiral hypoiodite active species is generated in situ from the corresponding chiral quaternary ammonium[9] iodide $[\mathbf{3}]^+[I]^-$ and aqueous hydrogen peroxide as a mild and inexpensive oxidant, and water is the only by-product generated from the oxidant (Scheme 1c, right). Moreover, the use of non-halogenated solvents such as toluene at ambient temperature is a major advantage over organoiodine(III)-catalyzed oxidation reactions, which often require halogenated solvents under low-temperature conditions.

Recently, we developed an in situ-generated chiral quaternary ammonium hypoiodite catalysis for the enantioselective oxidative cyclization of ketophenols to 2-acyl-2,3-dihydrobenzofurans or 2-acylchromans with the use of hydrogen peroxide or *tert*-butyl hydroperoxide (TBHP) as oxidants.[7] In these reactions, the chemoselective α-oxidation of carbonyl moieties preferentially proceeded, and phenol moieties served as intramolecular nucleophiles. However, during our studies on six-membered oxidative cyclization to chromans (Scheme 2),[7b] we found that tuning of the acidity of the phenol moiety of substrates with electron-withdrawing protective groups is crucial for chemoselective oxidative carbon–oxygen coupling (i.e., **4** to **5**), since electron-rich phenol moieties are easily dearomatized (i.e., **4** to **6**). Based on these preliminary findings, we envisioned that the hypoiodite oxidation system could be applied to the

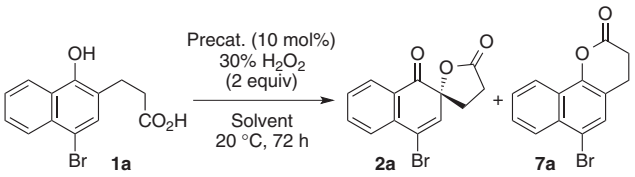


Scheme 1. Oxidative dearomatization of phenols.



Scheme 2. Preliminary findings for the oxidative dearomatization of phenols using hypoiodite catalysis.[7b]

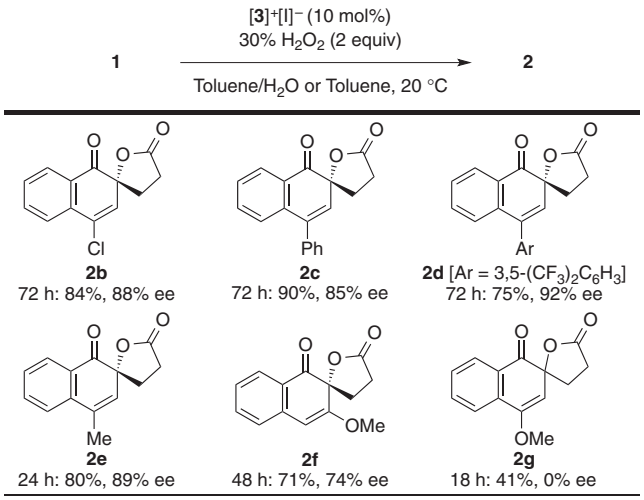
Table 1. Hypoiodite-catalyzed oxidative dearomatization of **1a**[a]



Entry	Precat.	Solvent	**2a** (**7a**) Yield/%[b]	**2a** ee/%[c]
1	$[Bu_4N]^+[I]^-$	Toluene	69 (13)	—
2	—[d]	Toluene	52 (14)	—
3	—[d]	Toluene/H_2O[e]	<1 (28)	—
4	$[Bu_4N]^+[I]^-$	Toluene/H_2O[e]	38 (21)	—
5	$[\mathbf{3}]^+[I]^-$	Toluene/H_2O[e]	72 (<5)	88
6	$[\mathbf{3}]^+[Cl]^-$	Toluene/H_2O[e]	<1 (10)	—

[a]Unless otherwise noted, a solution of **1a** (0.1 mmol) and 30 wt % H_2O_2 (0.2 mmol) in solvent was stirred in the presence of catalyst at 20 °C. [b]Isolated yield of **2a** is shown. The yield of **7a** shown in parentheses was determined by NMR analysis. [c]Enantiomeric excess and absolute configuration of **2a** were determined by HPLC analysis based on the literature.[4] [d]In the absence of catalyst. [e]Toluene/H_2O (2:1 v/v).

Table 2. Substrate scope[a]



[a]A solution of **1** (0.1 mmol) and 30 wt % H_2O_2 (0.2 mmol) in toluene–H_2O (for **2b**–**2d**) or toluene (for **2e**–**2g**) was stirred in the presence of $[\mathbf{3}]^+[I]^-$ at 20 °C. The reaction time, isolated yield, and enantiomeric excess of **2** are shown. Intramolecular condensation by-products **7** were obtained in less than 5% yield in each case. For details, see Supporting Information.

oxidative spirolactonization of 1-naphthols tethered to a carboxylic acid moiety at the 2-position (Scheme 1b).

A mixture of 4-bromo-1-naphthol derivative **1a** and 30 wt % aqueous hydrogen peroxide (2 equivalents) in toluene was stirred in the presence of 10 mol % of $[Bu_4N]^+[I]^-$ at 20 °C to give the desired spirolactone **2a** and intramolecular condensation by-product **7a** in respective yields of 69% and 13% (Table 1, Entry 1). Surprisingly, **2a** was also obtained in the absence of catalyst under the same conditions (Entry 2).[10] To prevent an uncatalyzed background reaction, the reaction conditions were investigated and almost no oxidation reaction occurred in a toluene–water biphasic system in the absence of catalyst (Entries 3 and 4). Next, the enantioselective oxidation reaction was performed using chiral ammonium iodide $[\mathbf{3}]^+[I]^-$, and **2a** was obtained in 72% yield with 88% ee (Entry 5). Importantly, high enantioselectivity could be achieved in the present oxidative dearomatization even in the absence of an imidazolyl auxiliary, which was required for our previous oxidation reactions.[7] Additionally, we confirmed that iodide is essential for the present reaction, since no oxidation reaction occurred in the presence of ammonium chloride $[\mathbf{3}]^+[Cl]^-$ instead of $[\mathbf{3}]^+[I]^-$ (Entry 6).

To explore the scope of the present dearomatization reaction, several 1-naphthol derivatives **1** were examined as substrates under optimized conditions (Table 2).[11] The oxidation of 4-substituted **1b**–**1e** and 3-OMe-substituted **1f** gave the corresponding spirolactones **2b**–**2f** in good to high yields with good to high enantioselectivities. However, the oxidation of 4-methoxynaphthol derivative **1g** gave racemic **2g**, as did a previous organoiodine(III) system.[3,4] Unfortunately, no satisfactory results were obtained for the oxidation of simple phenols under these conditions.

In summary, we have achieved a chiral hypoiodite-catalyzed enantioselective oxidative dearomatization of 1-naphthol derivatives using hydrogen peroxide as a mild and inexpensive oxidant. The most important advantages of the present method are: (1) milder reaction conditions (non-halogenated solvent), (2) operational simplicity (ambient temperature), and (3) water is the only by-product derived from the oxidant used. These results highlight the substantial scope of chiral hypoiodite catalysis in place of organoiodine catalysis.

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Supporting Information is available electronically on J-STAGE.

References and Notes

1 S. K. Jackson, K.-L. Wu, T. R. R. Pettus, in *Biomimetic Organic Synthesis*, ed. by E. Poupon, B. Nay, Wiley-VCH, Weinheim, **2011**, Chap. 20. doi:10.1002/9783527634606.ch20.

2 Selected reviews: a) C.-C. Liao, R. K. Peddinti, *Acc. Chem. Res.* **2002**, *35*, 856. b) D. Magdziak, S. J. Meek, T. R. R. Pettus, *Chem. Rev.* **2004**, *104*, 1383. c) L. Pouységu, D. Deffieux, S. Quideau, *Tetrahedron* **2010**, *66*, 2235. d) S. P. Roche, J. A. Porco, Jr., *Angew. Chem., Int. Ed.* **2011**, *50*, 4068. e) A. Bartoli, F. Rodier, L. Commeiras, J.-L. Parrain, G. Chouraqui, *Nat. Prod. Rep.* **2011**, *28*, 763. f) C.-X. Zhuo, W. Zhang, S.-L. You, *Angew. Chem., Int. Ed.* **2012**, *51*, 12662. g) M. Uyanik, K. Ishihara, *J. Synth. Org. Chem., Jpn.* **2012**, *70*, 1116. h) A. M. Harned, *Tetrahedron Lett.* **2014**, *55*, 4681.

3 a) T. Dohi, A. Maruyama, N. Takenaga, K. Senami, Y. Minamitsuji, H. Fujioka, S. B. Caemmerer, Y. Kita, *Angew. Chem., Int. Ed.* **2008**, *47*, 3787. b) T. Dohi, N. Takenaga, T.

Nakae, Y. Toyoda, M. Yamasaki, M. Shiro, H. Fujioka, A. Maruyama, Y. Kita, *J. Am. Chem. Soc.* **2013**, *135*, 4558.
4 a) M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem., Int. Ed.* **2010**, *49*, 2175. b) M. Uyanik, T. Yasui, K. Ishihara, *Tetrahedron* **2010**, *66*, 5841. c) M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem., Int. Ed.* **2013**, *52*, 9215.
5 a) J. K. Boppisetti, V. B. Birman, *Org. Lett.* **2009**, *11*, 1221. b) S. Quideau, G. Lyvinec, M. Marguerit, K. Bathany, A. Ozanne-Beaudenon, T. Buffeteau, D. Cavagnat, A. Chénedé, *Angew. Chem., Int. Ed.* **2009**, *48*, 4605. c) K. A. Volp, A. M. Harned, *Chem. Commun.* **2013**, *49*, 3001. d) C. Bosset, R. Coffinier, P. A. Peixoto, M. El Assal, K. Miqueu, J.-M. Sotiropoulos, L. Pouységu, S. Quideau, *Angew. Chem., Int. Ed.* **2014**, *53*, 9860.
6 Selected recent examples for the enantioselective oxidation reactions using chiral hypervalent organoiodines: a) S. M. Altermann, R. D. Richardson, T. K. Page, R. K. Schmidt, E. Holland, U. Mohammed, S. M. Paradine, A. N. French, C. Richter, A. M. Bahar, B. Witulski, T. Wirth, *Eur. J. Org. Chem.* **2008**, 5315. b) N. Jalalian, B. Olofsson, *Tetrahedron* **2010**, *66*, 5793. c) M. Fujita, Y. Yoshida, K. Miyata, A. Wakisaka, T. Sugimura, *Angew. Chem., Int. Ed.* **2010**, *49*, 7068. d) C. Röben, J. A. Souto, Y. González, A. Lishchynskyi, K. Muñiz, *Angew. Chem., Int. Ed.* **2011**, *50*, 9478. e) J. Yu, J. Cui, X.-S. Hou, S.-S. Liu, W.-C. Gao, S. Jiang, J. Tian, C. Zhang, *Tetrahedron: Asymmetry* **2011**, *22*, 2039. f) A. Rodríguez, W. J. Moran, *Synthesis* **2012**, *44*, 1178. g) A.-A. Guilbault, B. Basdevant, V. Wanie, C. Y. Legault, *J. Org. Chem.* **2012**, *77*, 11283. h) U. Farid, T. Wirth, *Angew. Chem., Int. Ed.* **2012**, *51*, 3462. i) M. Shimogaki, M. Fujita, T. Sugimura, *Eur. J. Org. Chem.* **2013**, 7128. j) S. Brenet, F. Berthiol, J. Einhorn, *Eur. J. Org. Chem.* **2013**, 8094. k) W. Kong, P. Feige, T. de Haro, C. Nevado, *Angew. Chem., Int. Ed.* **2013**, *52*, 2469. l) C. Röben, J. A. Souto, E. C. Escudero-Adán, K. Muñiz, *Org. Lett.* **2013**, *15*, 1008. m) H. Wu, Y.-P. He, L. Xu, D.-Y. Zhang, L.-Z. Gong, *Angew. Chem., Int. Ed.* **2014**, *53*, 3466. n) P. Mizar, A. Laverny, M. El-Sherbini, U. Farid, M. Brown, F. Malmedy, T. Wirth, *Chem.—Eur. J.* **2014**, *20*, 9910.
7 a) M. Uyanik, H. Okamoto, T. Yasui, K. Ishihara, *Science* **2010**, *328*, 1376. b) M. Uyanik, H. Hayashi, K. Ishihara, *Science* **2014**, *345*, 291. c) We also reported the hypoiodite-catalyzed intra- and intermolecular direct α-oxyacylation of carbonyl compounds: M. Uyanik, D. Suzuki, T. Yasui, K. Ishihara, *Angew. Chem., Int. Ed.* **2011**, *50*, 5331.
8 Selected reviews: a) M. Uyanik, K. Ishihara, *Chim. Oggi* **2011**, *29*, 18. b) M. Uyanik, K. Ishihara, *ChemCatChem* **2012**, *4*, 177. c) P. Finkbeiner, B. J. Nachtsheim, *Synthesis* **2013**, *45*, 979. d) X.-F. Wu, J.-L. Gong, X. Qi, *Org. Biomol. Chem.* **2014**, *12*, 5807.
9 a) T. Ooi, K. Maruoka, *Angew. Chem., Int. Ed.* **2007**, *46*, 4222. b) S. Shirakawa, K. Maruoka, *Angew. Chem., Int. Ed.* **2013**, *52*, 4312.
10 Among the substrates examined, uncatalyzed background reaction was observed only for **1a**.[11] The reason for this result is not yet clear.
11 For details, see the Supporting Information.

