This article was downloaded by: [Heriot-Watt University] On: 27 December 2014, At: 10:33 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



# Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lsyc20

# Successful Application of Indirect Electrooxidation for the Transformation of Biaryl Methanols to the Corresponding Biaryl Ketones

Mitsuhiro Okimoto $^{\rm a}$ , Takashi Yoshida $^{\rm a}$ , Masayuki Hoshi $^{\rm a}$ , Tomohito Chiba $^{\rm a}$  & Kei Maeo $^{\rm a}$ 

<sup>a</sup> Department of Biotechnology and Environmental Chemistry , Kitami Institute of Technology , Kitami , Hokkaido , Japan Published online: 27 Jul 2011.

To cite this article: Mitsuhiro Okimoto , Takashi Yoshida , Masayuki Hoshi , Tomohito Chiba & Kei Maeo (2011) Successful Application of Indirect Electrooxidation for the Transformation of Biaryl Methanols to the Corresponding Biaryl Ketones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 41:21, 3134-3139, DOI: 10.1080/00397911.2010.517369

To link to this article: <u>http://dx.doi.org/10.1080/00397911.2010.517369</u>

# PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing,

systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <a href="http://www.tandfonline.com/page/terms-and-conditions">http://www.tandfonline.com/page/terms-and-conditions</a>



*Synthetic Communications*<sup>®</sup>, 41: 3134–3139, 2011 Copyright © Taylor & Francis Group, LLC ISSN: 0039-7911 print/1532-2432 online DOI: 10.1080/00397911.2010.517369

## SUCCESSFUL APPLICATION OF INDIRECT ELECTROOXIDATION FOR THE TRANSFORMATION OF BIARYL METHANOLS TO THE CORRESPONDING BIARYL KETONES

### Mitsuhiro Okimoto, Takashi Yoshida, Masayuki Hoshi, Tomohito Chiba, and Kei Maeo

Department of Biotechnology and Environmental Chemistry, Kitami Institute of Technology, Kitami, Hokkaido, Japan

**GRAPHICAL ABSTRACT** 



**Abstract** Various biaryl methanols were electrooxidized into the corresponding biaryl ketones in good yields and under very mild reaction conditions. Because of the relatively high oxidation potential, bulky structure, and somewhat poor solubility, biaryl methanols do not readily undergo direct electrooxidative transformations as a synthetic step toward the corresponding biaryl ketones. Herein, we report the successful indirect electrooxidation of secondary biaryl methanols featuring the use of a slight excess amount of KI (1.2 equivalents, relative to the substrate) in MeOH.

Keywords Biaryl ketones; biaryl methanols; electron transfer; iodine ion; oxidation

#### INTRODUCTION

The oxidation of secondary alcohols into the corresponding ketones has served as an important, fundamental, and practical transformation in organic synthesis. Accordingly, there has been numerous reports of such oxidations via indirect electrooxidative methods that involve various mediators as the electron carrier.<sup>[1-16]</sup> To the best of our knowledge, however, the indirect electrooxidation of widespread biaryl methanols (1) to the corresponding biaryl ketones (2) has yet to be reported. Shono and coworkers have carried out pioneering studies on the indirect electrooxidation of secondary aliphatic alcohols to the corresponding ketones in aqueous solutions, with *tert*-butanol or *tert*-butanol/*n*-hexane as the cosolvent, and in the presence of a

Received December 6, 2009.

Address correspondence to Mitsuhiro Okimoto, Department of Biotechnology and Environmental Chemistry, Kitami Institute of Technology, Koen-cho 165, Kitami, Hokkaido 990-8507, Japan. E-mail: okimotmt@mail.kitami-it.ac.jp

catalytic amount of iodide ions (0.10-0.25 equivalents, relative to the substrate) as the mediator.<sup>[17]</sup> Their studies, however, did not include the electrooxidation of sterically hindered secondary aromatic alcohols such as biaryl methanols 1. In fact, their similar reaction conditions, the oxidation of diphenyl methanol (1a) resulted in a poor yield (less than 60%) of diphenyl ketone (2a). On the other hand, because ketones that possess an  $\alpha$ -hydrogen immediately undergo electrooxidation to give  $\alpha$ -hydroxydimethylacetals or their derivatives, the corresponding aliphatic and alkyl aromatic ketones could not be obtained by the indirect electrooxidation of secondary aliphatic and  $\alpha$ -alkyl benzyl alcohols in MeOH using iodide ion as mediator.<sup>[18,19]</sup> During the course of our studies on the preparative-scale indirect electrooxidation of several organic compounds in the presence of iodide ions, [20-26] we discovered that our methodology can be successfully applied toward the electrooxidation of a wide range of biaryl methanols 1 to the corresponding biaryl ketones 2 in good to excellent yields. The reactions were carried out in MeOH and involved the use of excess amounts (versus catalytic amounts) of the iodide ion source (KI) as the mediator. Initially, the optimal reaction conditions for the indirect electrooxidation were examined using diphenyl methanol (1a) as the model substrate. The types of the supporting electrolytes along with the corresponding yields of the resulting diphenyl ketone (2a) are listed in Table 1. Remarkably, the use of merely 1.2 equivalents of KI (relative to 1a) was effective in the formation of 2a in a reasonable yield of 79%(entry 11), which was improved to nearly 90% by the addition of NaOMe (2.0 equivalents, entry 5).

In contrast, the use of a catalytic amount of KI (0.6 equivalent, relative to 1a) actually decreased the yield of 2a (entry 4). Substitution of KI (entry 5) with KBr

OH I electrooxidatior Ph-CH-Ph <b>1a</b> in MeOH	n ► Ph−	0 <sup>II</sup> C <b>–</b> Ph <b>2a</b>	
		Yield (%)	
ry Supporting electrolytes (mmol)		Unreacted 1a <sup>b</sup>	
p-TsON(Et) <sub>4</sub> (10)-KI (6)	63	36	
NaOAc (10)-KI (6)	77	22	
NaOH (10)-KI (6)	82	15	
NaOMe (10)-KI (3)	45	53	
NaOMe $(10)$ -KI $(6)$		10	
NaOMe $(10)$ -KI $(9)$		10	
<i>t</i> -BuOK (10)–KI (6)		17	
NaOMe $(10)$ -KBr $(6)$		80	
NaOMe $(10)$ -KCl $(6)$		68	
NaOMe (10)-none		69	
None-KI (6)	79	20	
	$\begin{array}{c} \begin{array}{c} \begin{array}{c} OH\\ I\\ Ph-CH-Ph\\ \mathbf{1a} \end{array} & \begin{array}{c} \begin{array}{c} \begin{array}{c} electrooxidation\\ in \ MeOH \end{array} \end{array} \end{array}$	$\begin{array}{c} \begin{array}{c} \begin{array}{c} OH \\ I \\ Ph-CH-Ph \\ 1a \end{array} & \begin{array}{c} \begin{array}{c} electrooxidation \\ in MeOH \end{array} & Ph-Ph \\ \hline \end{array} \\ \end{array} \\ \begin{array}{c} \begin{array}{c} \\ Supporting electrolytes (mmol) \end{array} & \begin{array}{c} 2a^b \\ \hline \end{array} \\ \end{array} \\ \hline \end{array} \\ \begin{array}{c} \begin{array}{c} \\ p-TsON(Et)_4 (10)-KI (6) \\ NaOAc (10)-KI (6) \\ NaOAc (10)-KI (6) \\ NaOH (10)-KI (6) \\ NaOMe (10)-KI (6) \\ NaOMe (10)-KI (6) \\ NaOMe (10)-KI (6) \\ S2 \\ NaOMe (10)-KI (6) \\ S9 \\ NaOMe (10)-KI (6) \\ S2 \\ S3 \\ NaOMe (10)-KI (6) \\ S3 \\ S3 \\ S4 \\ S4 \\ S4 \\ S4 \\ S4 \\ S4$	

 Table 1. Influence of supporting electrolytes<sup>a</sup>

<sup>*a*</sup>1a, 5 mmol; MeOH, 40 mL; constant current, 0.3 A; current passed,  $13.4 \text{ Fmol}^{-1}$ ; rt ca. 20 °C.

<sup>b</sup>Yields were determined by GC analysis.

(entry 8) or KCl (entry 9) resulted in lower yields of **2a** (17% and 28%, respectively). The use of a stronger base (*t*-BuOK instead of NaOMe) did not increase the yield (entry 7). These results indicate that the relative amount of KI strongly affects the yield of **2a** (entries 4–6). Contrary to the typical role as a catalyst for indirect electrooxidations, the use of iodide ions in substantial amounts (relative to substrate **1a**) was essential in increasing the yield of **2a** was proportional to the amount of current passed—specifically, 28% after 3.0 Fmol<sup>-1</sup>, then 57% after 6.0 Fmol<sup>-1</sup>. However, as the reaction proceeded, current efficiency gradually decreased—specifically, 86% after  $12.0 \text{ Fmol}^{-1}$ , then 89% after  $15 \text{ Fmol}^{-1}$ . Accordingly, sufficient amounts of current are required to consume most of **1a**. As a note, significant differences were not observed by varying the amount of NaOMe [from 5 mmol (81%) to 25 mmol (84%)] nor by adjusting the reaction conditions were applied to the electroox-idation reaction of a wide variety of biaryl methanols (**1a–m**), as listed in Table 2.

In most cases, the reactions involve the passage of  $13.4 \text{ Fmol}^{-1}$  with a constant current of 0.3 A (6.0 h). In the cases of **1e**, **1k**, and **1m**, however, the consumption of the substrates required only about half of the electricity (7.2 Fmol<sup>-1</sup>); the reason remains unclear. Unexpectedly, substituent effects were not observed (for example, **1e** versus **1h**). The electrooxidation was also applied to a fluorene-type **1m**, in which two aromatic rings are combined via two carbon-carbon bonds. In the cases of **1e**, **1h**, and **1i**, the resulting products (**2e**, **2h**, and **2i**, respectively) precipitated from the reaction mixture during the latter half of the electrooxidation system, although the

	O⊦ I R <sup>1</sup> —CH	H electroo -R <sup>2</sup> KI-NaOM 1	xidation → R <sup>1</sup> -	0 II -C-R <sup>2</sup> 2	
Substrates	$\mathbb{R}^1$	$\mathbb{R}^2$	Current passed (Fmol <sup>-1</sup> )	Yield of <b>2</b> $(\%)^b$	Mp or bp (°C)
1a	Ph	Ph	13.4	83	47–49
1b	Ph	3,4- <i>di</i> -Me-C <sub>6</sub> H <sub>3</sub>	13.4	90	43-45
1c	Ph	4-t-Bu-C <sub>6</sub> H <sub>4</sub>	13.4	88	151–153/1 mmg
1d	Ph	4-MeO-C <sub>6</sub> H <sub>4</sub>	13.4	92	58-61
1e	4-MeO-C <sub>6</sub> H <sub>4</sub>	4-MeO-C <sub>6</sub> H <sub>4</sub>	7.2	95	141–143
lf	Ph	2-CO <sub>2</sub> Me-C <sub>6</sub> H <sub>4</sub>	13.4	82	49–52
1g	Ph	$4 - F - C_6 H_4$	13.4	95	46–48
1h	$4-Cl-C_6H_4$	$4-Cl-C_6H_4$	13.4	95	142–144
1i	Ph	$4-NO_2-C_6H_4$	13.4	77	130-132
1j	$3-F-C_6H_4$	4-MeO-C <sub>6</sub> H <sub>4</sub>	13.4	81	68–70
1k	Ph	2-Thionyl	7.2	96	56-57
11	Ph	4-Pyridil	13.4	73	69-72
1m	Flu	orenol	7.2	93	79–81

Table 2. Indirect electrooxidation of biaryl methanols<sup>a</sup>

<sup>*a*</sup>1, 5 mmol; KI, 6 mmol; NaOMe, 10 mmol; MeOH, 40 mL; constant current, 0.3 A; rt ca. 20 °C. <sup>*b*</sup>Isolated yields based on the substrates.

reaction pathway remains to be further investigated, it is clear that iodide ions play an important role as electron carriers. Because catalytic amounts of the iodide ion were not enough to fully enhance the oxidation process of biaryl methanols, our reaction mechanism may differ from that proposed by Shono's group.<sup>[17]</sup> The results of this study represent the first known examples of indirect electrooxidations of multiple biaryl methanols to the corresponding ketones in good yields. In conclusion, our method involves the use of a slight excess of iodide ions as the mediators and allows for the preparation of biaryl ketones without any effects of the construction and/or property of substituent of the substrate. Moreover, the advantages of our method include (1) very mild reaction conditions, (2) absence of harsh toxic reagents, such as metal oxidants or special reagents, and (3) a simple one-pot procedure.

#### **EXPERIMENTAL**

Preparative-scale electrooxidations were carried out in a tall 50-mL beaker equipped with a fine frit cup as the cathode compartment with a nickel coil cathode, along with a cylindrical platinum net anode. The typical procedure was as follows: A solution of diaryl methanol 1 (5 mmol) in MeOH (40 mL) containing KI (6 mmol) and NaOMe (10 mmol) was electrooxidized under a constant current (0.3 A). During the course of the electrooxidation, the anolyte was magnetically stirred at ca. 20 °C. Upon passage of the electrolytic current (7.2 or  $13.4 \,\mathrm{Fmol}^{-1}$ ), the reaction mixture was concentrated in vacuo (ca. 10 mL) at approximately 50 °C. The resulting oily residue was treated with water (ca. 30 mL), extracted with ethyl ether or chloroform  $(3 \times 40 \text{ mL})$ , and dried over magnesium sulfate. After removal of the solvent in vacuo, the desired biaryl ketones 2 were isolated by silica-gel column chromatography using ether/hexane (1:3) as the eluent. During the electrooxidation, the composition of the reaction mixture was monitored by gas chromaography (GC) or thin-layer chromatography (TLC). Electric current was passed until almost all of the substrate was consumed. Melting points and Infrared (IR) spectra of all products were in good agreement with those of authentic samples.

### ACKNOWLEDGMENT

We are thankful for the financial support of the President's Discretionary Finance Council of Kitami Institute of Technology (2008–2009).

#### REFERENCES

- 1. Shono, T.; Matsumura, Y.; Mizoguch, M.; Hayashi, J. Oxidation of alcohols by active species generated by electrochemical oxidation of organosulfur compounds. *Tetrahedron Lett.* **1979**, *40*, 3861–3864.
- Demizu, Y.; Shiigi, H.; Oda, T.; Matsumura, Y.; Onomura, O. Efficient oxidation of alcohols electrochemically mediated by azabicyco-N-oxyls. *Tetrahedron Lett.* 2008, 49, 48–52.
- Raju, T.; Manivasagan, S.; Revathy, B.; Kulangiappar, Muthukumaran, A. A mild and efficient method for the oxidation of benzylic alcohols by two-phase electrolysis. *Tetrahedron Lett.* 2007, 48, 3681–3684.

- Leonard, J. E.; Scholl, P. C.; Steckel, T. P. Electrochemical oxidation of alcohols, part II: Preparative anodic oxidation of secondary alkanols employing lithium nitrate. *Tetrahedron Lett.* 1980, *21*, 4695–4698.
- Shono, T.; Matsumura, Y.; Hayashi, J.; Mizoguchi, M. Electrooxidation of alcohols using a new double mediatory system. *Tetrahedron Lett.* 1980, 21, 1867–1870.
- 6. Yoshida, J.; Nakai, R.; Kawabata, N. Novel method of oxidation by a polymeric reagent electrochemically generated and recycled in situ: Facile oxidation of alcohols. *J. Org. Chem.* **1980**, *45*, 5269–5273.
- Matsumura, Y.; Yamada, M. Electrochemical oxidation of secondary alcohols using thioanisole as an organic mediator in the presence of 2,2,2-trifluoroethanol. *Tetrahedron Lett.* 1995, 51, 6411–6418.
- Kashiwagi, Y.; Yanagisawa, Y.; Kurashima, F.; Anzai, J.; Osa, T.; Bobbitt, J. M. Enantioselective electrocatalytic oxidation of racemic alcohols on a TEMPO-modified graphite felt electrode by use of chiral base. *Chem. Commun.* 1996, 2745–2746.
- Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. Nitroxy-mediated electrooxidation of alcohols to aldehydes and ketones. J. Am. Chem. Soc. 1983, 105, 4492–4494.
- Tanaka, H.; Kubota, J.; Miyahara, S.; Kuroboshi, M. Electrooxidation of alcohols in an N-oxyl-immobilized poly(ethylene-co-acrylic acid)/water disperse system. *Bull. Chem.* Soc. Jpn. 2005, 78, 1677–1684.
- 11. Deronzier, A.; Limosin, D.; Moutet, J. C. Electrochemical oxidation of carbinols mediated by nitroxyl radicals in solution or bonded to polypyrrolic coatings on platinum and carbon electrodes. *Electrochim. Acta* **1987**, *32*, 1643–1647.
- Inokuchi, T.; Matsumoto, S.; Torii, S. Indirect electrooxidation of alcohols by a double mediatory system with two redox couples of [R<sub>2</sub>N<sup>+</sup>=O]/R<sub>2</sub>NO and [Br or Br<sup>+</sup>]/Br<sup>-</sup> in an organic-aqueous two-phase solution. J. Org. Chem. 1991, 56, 2416–2421.
- Inokuchi, T.; Liu, P.; Torri, S. Oxidations of dihydroxyalkanoates to vicinal tricarbonyl compounds with a 4-BzoTEMPO-sodium bromite system or by indirect electrolysis using 4-BzoTENPO and bromide ion. *Chem. Lett.* 1994, 23, 1411–1414.
- Inokuchi, T.; Matsumoto, S.; Nisiyama, T.; Torii, S. Indirect electrooxidation of alcohols by a double mediatory system with of [R<sub>2</sub>N<sup>+</sup>=O]/R<sub>2</sub>N-O. and [Br<sup>-</sup> or Br<sup>+</sup>]Br<sup>-</sup> redoxes. *Synlett.* 1990, 57–58.
- Torri, S.; Inokuchi, T.; Matsumoto, S.; Saeki, T.; Oki, T. Indirect electrooxidation of halohydrines by a double mediatory system of Ru(VIII)/Ru(IV) and [Cl<sup>+</sup>]/Cl<sup>-</sup>: Optimization for the oxidation of 1,3-dichloro-2-propanol to 1.3-dichloroacetone. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 852–855.
- Inokuchi, T.; Matsumoto, S.; Nishiyama, T.; Torii, S. A selective and efficient method for alcohol oxidations mediated by N-oxoammonum salts in combination with sodium bromite. J. Org. Chem. 1990, 55, 462–466.
- Shono, T.; Matsumura, Y.; Hayashi, J.; Mizoguchi, M. Electrochemical oxidation of alcohols using iodonium ion as an electron carrier. *Tetrahedron Lett.* 1979, 2, 165–168.
- Shono, T.; Matsumura, Y.; Inoue, K.; Iwasaki, F. Electro-organic chemistry, part 93: Electro-organic transformation of aldehydes and ketones to α-hydroxylated acetals utilizing mediators and some synthetic uses of the products. J. Chem. Soc., Perkin Trans. 1986, 1, 73–77.
- Barba, F.; Elinson, M. N.; Escudero, J.; Guirado, M.; Feducovich, S. K. Indirect electrochemical oxidation of aliphatic ketones mediated by the NaI-NaOH system: A facile way to unsaturated conjugated esters. *Electrochim. Acta* 1998, 973–976.
- Okimoto, M.; Chiba, T. Electrolytic oxidation of ketones in a methanolic solution of NaCN in the presence of catalytic amount of KI. J. Org. Chem. 1993, 58, 6194–6197.

- Okimoto, M.; Takahashi, Y. Anodic oxidation of benzil hydrazones in the presence of halide ions. *Bull. Chem. Soc. Jpn.* 2002, 75, 2059–2060.
- 22. Okimoto, M.; Takahashi, Y. Electrooxidation of malonate and acetylaetate derivatives in the presence of halide ions. *Synthesis* **2002**, 2215–2219.
- Okimoto, M.; Takahashi, Y.; Kakuchi, T. Electrooxidative formation of 1,2-diaroylcyclopropanes from 1,3-diaroylpropanes in the presence of KI. *Bull. Chem. Soc. Jpn.* 2003, 76, 207–208.
- Okimoto, M.; Takahashi, Y.; Nagata, Y.; Sasaki, G.; Numata, K. Electrochemical oxidation of benzoins into the corresponding benzils in a basic media in the presence of catalytic amount of KI. *Synthesis* 2005, 705–707.
- Okimoto, M.; Numata, K.; Tomozawa, K.; Shigemoto, T.; Hoshi, M.; Takahashi, Y. Electrooxidative conversion of dibenzoylbenzene dihydrazones into the corresponding *bis*-diazo compounds and *bis*-dimentyl acetals. *Aust. J. Chem.* 2005, *58*, 560–563.
- Okimoto, M.; Takahashi, Y.; Nagata, Y.; Numata, K.; Sasaki, G. Electrochemical oxidation of benzylic amines into the corresponding imines in the presence of catalytic amount of KI. Synth. Commun. 2005, 35, 1989–1995.