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IBS-Catalyzed Oxidative Rearrangement of Tertiary Allylic Alcohols to Enones with Oxone

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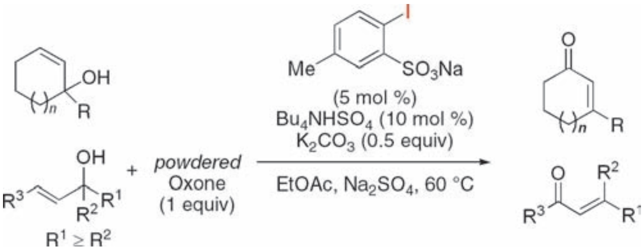
ABSTRACT



A 2-iodoxybenzenesulfonic acid (IBS)-catalyzed oxidative rearrangement of tertiary allylic alcohols to enones with powdered Oxone in the presence of potassium carbonate and tetrabutylammonium hydrogen sulfate has been developed.

The oxidative rearrangement of tertiary allylic alcohols to β-disubstituted α,β-unsaturated ketones or aldehydes using oxochromium(VI)-based reagents (Collins reagent, PCC, PDC) has been widely used in synthetic organic chemistry.[1,2]

In 2004, Iwabuchi and co-workers reported that 2-iodoxybenzoic acid (IBX, **1**) could be used instead of hazardous Cr(VI) for the oxidative rearrangement of tertiary allylic alcohols.[3] Several 5- and 6-membered cyclic tertiary allylic alcohols were effectively converted to the corresponding enones with a stoichiometric amount of **1** in DMSO. In 2008, the same research group reported that TEMPO-derived oxoammonium salts (TEMPO$^+$ BF_4^- and TEMPO$^+$ SbF_6^-) were more effective as stoichiometric reagents for this transformation of acyclic tertiary allylic alcohols in acetonitrile.[4] Very recently, Iwabuchi[5] and Vatèle[6] independently reported the first catalytic oxidative rearrangement of tertiary allylic alcohols. Iwabuchi's group used catalytic amounts of TEMPO with $NaIO_4-SiO_2$ as a co-oxidant in dichloromethane, and several cyclic and acyclic tertiary allylic alcohols were converted to the corresponding enones in good yield.[5] In contrast, Vatèle developed a Lewis acid-promoted

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(1) (a) Büchi, E.; Egger, B. *J. Org. Chem.* **1971**, *36*, 2021. (b) Grieco, P. A. *J. Org. Chem.* **1972**, *37*, 2363. (c) Babler, J. H.; Coghlan, M. J. *Synth. Commun.* **1976**, *6*, 469. (d) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682. (e) Sundararabhan, P.; Herz, W. *J. Org. Chem.* **1977**, *42*, 813. (f) Takano, S.; Inomata, K.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1989**, 271. (g) Brown, P. S.; McElroy, A. B.; Warren, S. *Tetrahedron Lett.* **1985**, *26*, 249. (h) Majetich, G.; Lowery, D.; Khetani, V. *Tetrahedron Lett.* **1990**, *31*, 51. (i) Luzzio, F. A.; Moore, W. J. *J. Org. Chem.* **1993**, *58*, 2966. (j) Majetich, G.; Song, J.-S.; Leigh, A. J.; Condon, S. M. *J. Org. Chem.* **1993**, *58*, 1030. (k) Guevel, A.-J.; Hart, D. J. *J. Org. Chem.* **1996**, *61*, 465. (l) Trost, B. M.; Pinkerton, A. B. *Org. Lett.* **2000**, *2*, 1601. (m) Nagata, H.; Miyazawa, N.; Ogasawara, K. *Chem. Commun.* **2001**, 1094. (n) Hanada, K.; Miyazawa, N.; Ogasawara, K. *Org. Lett.* **2002**, *4*, 4515. (o) Muratake, H.; Natsume, M. *Tetrahedron Lett.* **2002**, *43*, 2913. (p) Mohr, P. J.; Halcomb, R. L. *J. Am. Chem. Soc.* **2003**, *125*, 1712. (q) Bohno, M.; Imase, H.; Chida, N. *Chem. Commun.* **2004**, 1086. (r) Mandal, M.; Yun, H.; Dudley, G. B.; Lin, S.; Tan, D. S.; Danishefsky, S. J. *J. Org. Chem.* **2005**, *70*, 10619. (s) Chavan, S. P.; Thakkar, M.; Jogdand, G. F.; Kalkote, U. R. *J. Org. Chem.* **2006**, *71*, 8986. (t) Tanimoto, H.; Kato, T.; Chida, N. *Tetrahedron Lett.* **2007**, *48*, 6267. (u) Majetich, G.; Nishide, H.; Phillips, R. M.; Yu, J. *Heterocycles* **2007**, *74*, 225.

(2) For reviews on oxochromium(VI)-based reagents, see:(a) Luzzio, F. A. *Org. React.* **1998**, *53*, 1. (b) Wietzerbin, K.; Bernadou, J.; Meunier, B. *Eur. J. Inorg. Chem.* **2000**, 1391.

(3) Shibuya, M.; Ito, S.; Takahashi, M.; Iwabuchi, Y. *Org. Lett.* **2004**, *6*, 4303.

(4) Shibuya, M.; Tomizawa, M.; Iwabuchi, Y. *J. Org. Chem.* **2008**, *73*, 4750.

(5) Shibuya, M.; Tomizawa, M.; Iwabuchi, Y. *Org. Lett.* **2008**, *10*, 4750.

(6) Vatèle, J.-M. *Synlett* **2008**, 1785.

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oxidative rearrangement using catalytic amounts of TEMPO with iodosylbenzene (PhIO) as a co-oxidant in the presence of molecular sieves 4 Å.[6] Bi(OTf)$_3$ promoted the oxidative rearrangement of cyclic tertiary allylic alcohols, while Re$_2$O$_7$ was a more effective promoter for the oxidative rearrangement of tertiary vinyl carbinols.

We recently reported a highly efficient and chemoselective oxidation of various alcohols to carbonyl compounds such as aldehydes, carboxylic acids, and ketones with powdered Oxone (2KHSO$_5$•KHSO$_4$•K$_2$SO$_4$) in the presence of catalytic amounts (0.05−5 mol %) of 2-iodobenzenesulfonic acid or its sodium salt (**4a**) under nonaqueous conditions.[7,8] Cycloalkanones can be further oxidized to cycloalkenones and lactones by controlling the amount of Oxone under the same conditions. 2-Iodoxybenzenesulfonic acid (IBS, **3a**),[7,9] which is an analogue of IBX **1**, is generated in situ from **4a** and Oxone (eqs 1 and 2). IBS **3a** serves as the actual catalyst for the oxidations. As part of our continuing interest in the use of cat. IBS with co-oxidant Oxone systems in organic synthesis, we report here the *in situ*-generated IBS-catalyzed oxidative rearrangement of tertiary allylic alcohols to β-disubstituted α,β-unsaturated ketones with Oxone.

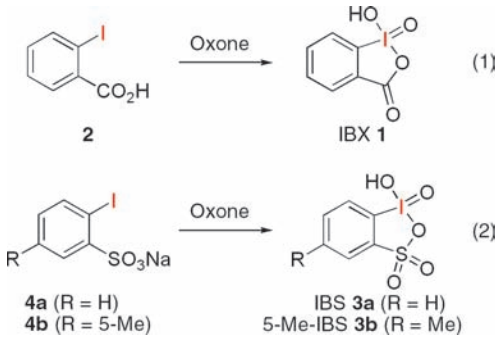
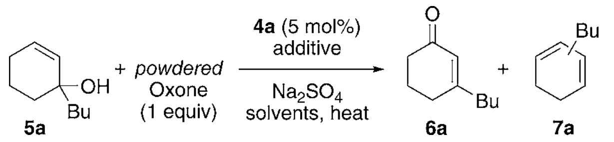


Table 1. Optimizing of Reaction Conditions



entry	additive	conditions	**6a**, yield (%)
1	–	CH$_3$CN, 40 °C, 6 h	*messy*[a]
2	–	CH$_3$NO$_2$, 40 °C, 6 h	*messy*[a]
3	–	EtOAc, 40 °C, 23 h	33[b]
4	K$_2$CO$_3$ (0.5 equiv)	EtOAc, 60 °C, 13 h	67
5[c]	K$_2$CO$_3$ (0.5 equiv)	EtOAc, 60 °C, 13 h	*messy*[a]
6[d]	K$_2$CO$_3$ (0.5 equiv)	EtOAc, 60 °C, 13 h	*messy*[a,e]
7	K$_2$CO$_3$ (1.5 equiv)	EtOAc, 60 °C, 13 h	n.r.[f]
8[g]	K$_2$CO$_3$ (0.5 equiv)	EtOAc, 60 °C, 3 h	84
9[g,c]	K$_2$CO$_3$ (0.5 equiv)	EtOAc, 60 °C, 3 h	63
10[g]	NaHCO$_3$ (1.0 equiv)	EtOAc, 60 °C, 4 h	68
11[g]	K$_2$HPO$_4$ (0.5 equiv)	EtOAc, 60 °C, 4 h	67

[a] **7a** was included. [b] **7a** (both regioisomer) and unknown byproduct were also obtained. [c] **2** was used instead of **4a**. [d] PhI was used instead of **4a**. [e] Rearranged allylic alcohol 3-butylcyclohex-2-enol (**8a**) was also included, but **6a** was not obtained. [f] No reaction occurred. [g] After Oxone and inorganic base in EtOAc were vigorously stirred in the presence of Na$_2$SO$_4$ for 24 h at rt, **4a** and **5a** were added.

Initially, we optimized the reaction conditions for the IBS-catalyzed oxidative rearrangement with Oxone (Table 1). A mixture of 1-butylcyclohex-2-enol (**5a**) and powdered Oxone (1 equiv) in acetonitrile or nitromethane was heated at 40 °C in the presence of 5 mol % of **4a** and anhydrous sodium sulfate (entries 1 and 2). However, no desired 3-butylcyclohex-2-enone (**6a**) was obtained. The reaction became messy and a complex product mixture that included **7** was obtained. It is likely that the dehydration of **5a** to **7a** predominantly occurred due to the acidity of Oxone. According to our recent work, the selective oxidation of acid-sensitive alcohols can be achieved in the presence of anhydrous sodium sulfate as a dehydrating agent in ethyl acetate.[7] On the basis of these previous findings, the reaction of **5a** was carried out in ethyl acetate under the same conditions as in entries 1 and 2. After 22 h, desired **6a** was obtained in 33% yield with dehydrated products **7a** and several unidentified byproducts (entry 3). To prevent the dehydration of **5a**, we examined the effect of the addition of base to buffer the acidity of the reaction mixture and found that 0.5 equiv of potassium carbonate was effective as an additional base. Thus, the dehydration of **5a** was significantly suppressed and **6a** was obtained in 67% yield (entry 4). In contrast, the reaction became messy under these conditions in the presence of **2** or iodobenzene instead of **4a** (entries 5 and 6). The amount of base was important, and no reaction occurred when 1.5 equiv of potassium carbonate was used (entry 7). Furthermore, **6a** was obtained in 84% yield after 3 h, when Oxone and potassium carbonate were sufficiently premixed in the presence of anhydrous sodium sulfate in ethyl acetate at room temperature for 24 h before the addition of **5a** and **4a** (entry 8). Notably, *in situ*-generated IBX **1** also showed moderate catalytic activity under these modified conditions, but was inferior to IBS **3a** (entry 8 versus 9). Other inorganic bases such as sodium hydrogen carbonate and dipotassium hydrogenphosphate were inferior to potassium carbonate (entries 10 and 11).

To explore the generality of the *in situ*-generated IBS-catalyzed oxidative rearrangement of tertiary allylic alcohols with Oxone, various structurally diverse cyclic and acyclic tertiary allylic alcohols **5b−n** were examined as substrates under the optimized conditions: powdered Oxone (1 equiv) and potassium carbonate (0.5 equiv) in ethyl acetate were vigorously stirred at rt for 24 h in the presence of anhydrous

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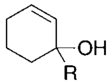
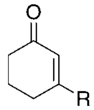
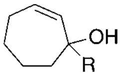
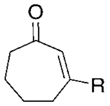
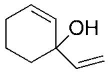
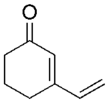
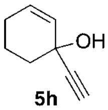
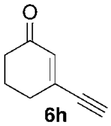
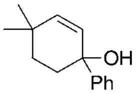
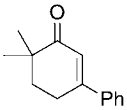
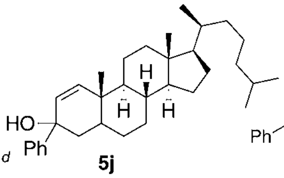
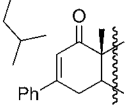
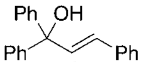
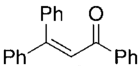
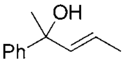
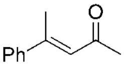
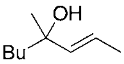
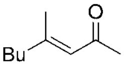
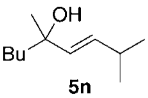
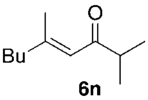
(7) Uyanik, M.; Akakura, M.; Ishihara, K. *J. Am. Chem. Soc.* **2009**, *131*, 251.

(8) For recent books and reviews focused on hypervalent iodine chemistry, see :(a) Wirth, T., Ed. Hypervalent Iodine Chemistry. In *Topics in Current Chemistry*; Springer: Berlin, 2003; p 224. (b) Wirth, T. In *Organic Synthesis Highlights V*; Wiley-VCH: Weinheim, 2003; p 144. (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (d) Tohma, H.; Kita, Y. *Adv. Synth. Catal.* **2004**, *346*, 111. (e) Richardson, R. D.; Wirth, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4402. (f) Ladziata, U.; Zhdankin, V. V. *ARKIVOC* **2006**, *ix*, 26. (g) Ochiai, M. *Chem. Rec.* **2007**, *7*, 12. (h) Ciufolini, M. A.; Braun, N. A.; Canesi, S.; Ousmer, M.; Chang, J.; Chai, D. *Synthesis* **2007**, 3759. (i) Ladziata, U.; Zhdankin, V. V. *Synlett* **2007**, 527. (j) Quideau, S.; Pouysegu, L.; Deffieux, D. *Synlett* **2008**, 467. (k) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299. (l) Ochiai, M.; Miyamoto, K. *Eur. J. Org. Chem.* **2008**, 4229. (m) Uyanik, M.; Ishihara, K. *Chem. Commun.* **2009**, 2086. (n) Dohi, T.; Kita, Y. *Chem. Commun.* **2009**, 2073.

(9) Koposov, A. Y.; Litvinov, D. N.; Zhdankin, V. V.; Ferguson, M. J.; McDonald, R.; Tykwinski, R. R. *Eur. J. Org. Chem.* **2006**, 4791.

Table 2. Scope of IBS-Catalyzed Oxidative Rearrangement of Tertiarry Allylic Alcohols **5** to Enones **6**

entry	alcohol	enone	time, yield[a]
			
1	**5b**; R = Ph	**6b**	4 h, 84%
2	**5c**; R = n-C$_6$H$_{13}$	**6c**	4 h, 81%
3[b,c]	**5d**; R = 4-(TBSOCH$_2$)C$_6$H$_4$	**6d**	2 h, 70%
			
4[b]	**5e**; R = Ph	**6e**	3 h, 85%
5	**5e**; R = Ph	**6e**	11 h, 52%
6[b]	**5f**; R = n-C$_6$H$_{13}$	**6f**	20 h, 74%
7[b,c]	 **5g**	 **6g**	10 h, 71%
8[b,c,d]	 **5h**	 **6h**	92 h, 62%
9[b,c]	 **5i**	 **6i**	26 h, 70%
10[b,c,d]	 **5j**	 **6j**	24 h, 69%
11[b,c]	 **5k**	 **6k**	7 h, 83%
12[b,c]	 **5l**	 **6l**	11 h, 75%[e]
13[b,c]	 **5m**	 **6m**	3 h, 63%[f]
14[b,c,d]	 **5n**	 **6n**	31 h, 50%[g]

[a] Isolated yield. [b] Bu$_4$NHSO$_4$ (10 mol %) was used. [c] Precatalyst **4b** was used instead of **4a**. [d] **4b** (10 mol %) was used. [e] E:Z = >20:1. [f] E:Z = 12:1. [g] E:Z = 2:1. For details, see Supporting Information.

sodium sulfate, and then **4a** or **4b** (5 mol %) and **5** were added and the resulting mixture was heated to 60 °C (Table 2). Since the use of **4b** gave slightly better results than **4a**, **4b** was used as a precatalyst in most cases (entries 3 and 7−14).[7] 6- and 7-Membered cyclic substrates gave the corresponding enones in moderate to high yields (entries 1−10). Oxone was almost insoluble under nonaqueous conditions. We found that the use of tetrabutylammonium hydrogen sulfate (Bu$_4$NHSO$_4$), as a solid−liquid phase transfer catalyst, further improved the reaction efficiency.[10] Thus, 7-membered cyclic substrate **5e** was effectively converted to the corresponding enone **6e** in the presence of 10 mol % Bu$_4$NHSO$_4$ (entry 4 versus 5). A *tert*-butyldimethylsilyloxy (TBSO) protecting group was tolerated under the reaction conditions, and **6d** was obtained in 70% yield (entry 3). 1-Vinylcyclohex-2-enol (**5g**) was regioselectively transformed to dienone **6g** in 71% yield (entry 7). Notably, sterically demanding steroid alcohol **5j** was converted to the desired enone **6j** in 69% yield (entry 10). In contrast, Iwabuchi reported that **5j** was rearranged to allylic alcohol **8j**,[11] which was not oxidized to **6j** under TEMPO-mediated conditions, due to considerable steric hindrance.[4,5] Various acyclic tertiary alcohols **5k**−**n** were also examined, and the corresponding enones **6k**−**n** were obtained in moderate to good yields (entries 11−14). In most cases, the starting materials **5** and their rearranged allylic alcohol intermediates **8** were fully consumed. The main byproducts were dehydrated dienes. Unfortunately, 2,3-nonsubstituted tertiary allylic alcohols were recovered under these optimized conditions due to the instability of a primary carbocation intermediate (entry 7).

To ascertain the effect of IBS on the oxidative rearrangement reaction, we conducted control experiments with cyclic and acyclic substrates in the absence of **4** under the same conditions as in Table 2 (Scheme 1). As a result, **5b** was rearranged to secondary alcohol **8b** in 30% yield together with several byproduct that included dienes **7b**. In contrast, the reaction of acyclic substrate **5l** was messy, and acetophenone was detected by ^{1}H NMR analysis as a major product along with several unknown byproducts.[1d,e] These experiments suggest that IBS promotes not only the oxidation step of **8** to **6** but also the isomerization step of **5** to **8** (Table 2, entries 1 and 12 versus Scheme 1).

A proposed reaction mechanism is depicted in Scheme 2.[3] We speculate that there are four possible pathways for the rearrangement of tertiary allylic alcohols **5** to secondary alcohol-IBS(V) complex **11**, which readily twist and disproportionate to the desired enone **6** and IBS(III) **12**.[7] In the first path (**5** → **9** → **11**), iodic ester **9** as well as chromate esters give isomeric ester **11** through concerted intramolecular

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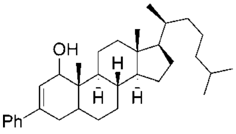
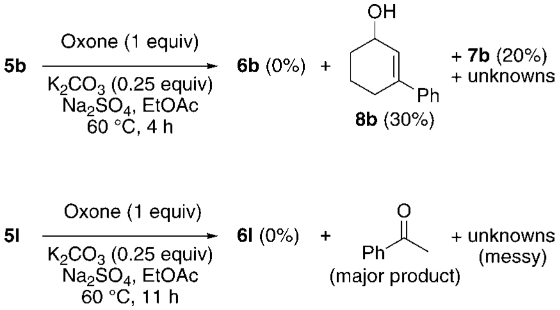
(10) For the use of phase transfer catalysis for Oxone, see:(a) Denmark, S. E.; Forbes, D. C.; Hays, D. S.; DePue, J. S.; Wilde, R. G. *J. Org. Chem.* **1995**, *60*, 1391. (b) Aggarwal, V. K.; Lopin, C.; Sandrinelli, F. *J. Am. Chem. Soc.* **2003**, *125*, 4229. (c) Schulze, A.; Giannis, A. *Synthesis* **2006**, 257 For the preparation of ammonium Oxone, see also. (d) Trost, B.; Braslau, R. *J. Org. Chem.* **1988**, *53*, 532. (e) Travis, B. R.; Ciaramitaro, B. P.; Borhan, B. *Eur. J. Org. Chem.* **2002**, 3429.

(11) For the chemical structure of **8j**, see:

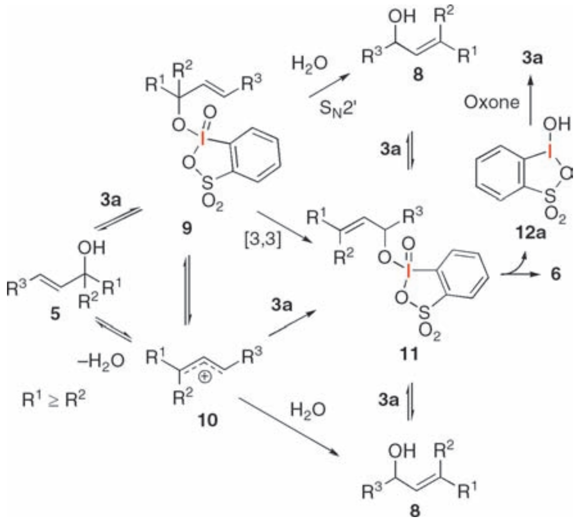


8j

Scheme 1. Control Experiments



Scheme 2. Plausible Reaction Mechanism



[3,3]-rearrangement.[1,2] In the second path (**5** → **10** → **11**), acidic solvolysis of **5** easily gives allylic cation **10**,[1e] which subsequently collapses with **3** at less-substituted termini to give **11**. In the third path (**5** → **10** → **8** → **11**), H_2O reacts with **10** to give secondary allylic alcohol **8**, which condenses with **3** to give **11**. In the fourth path (**5** → **9** → **8** → **11**), the S_N2' reaction of H_2O with **9** might also give **8**.[5] Thus, the key intermediate **11** might be generated by competitive paths 1−4. Although the use of **3** significantly accelerated the rearrangement of **5**, we could not rule out any of these paths due to some conversion from **5b** to **8b** in the absence of IBS **3a** (Scheme 1). The catalytic cycle of **3** could be accomplished by the regeneration of **3** through the oxidation of **12** with Oxone.[7] IBS **3a** and **3b** were much more effective than **1** as a catalyst for the oxidative rearrangement because of their much stronger oxidation activity and acidity[3] (Table 1). Furthermore, 5-Me-IBS **3b** gave more excellent catalytic activity than **3a**, because the regeneration of **3b** was faster than that of **3a**[7] (Table 2).

In conclusion, we have developed an oxidative rearrangement of tertiary allylic alcohols to enones with powdered Oxone promoted by the catalytic use of **4**. IBS **3**, which is generated in situ from **4** and Oxone, serves as the actual catalyst for the oxidations. Interestingly, 5-Me-IBS **3b** was more effective than IBS **3a** as a catalyst, and the addition of inorganic bases was effective to extend the substrate scope for oxidative rearrangement reactions. The precatalysis **4** are easily avaliable,[7,12] and Oxone offers several great advantages, including stability, ease of transport, simple handling, controllable addition, nontoxic nature, etc. This new protocol should be recognized as a practical method for the oxidative rearrangement of tertiary alcohols, since it does not require any toxic, dangerous, and expensive reagents.[1−6]

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Supporting Information Available: Experimental details and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Pre-catalysts **4a** and **4b** (as potassium salts) are commercially available from Junsei Chemical, Japan.