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An Inorganic Iodine-Catalyzed Oxidative System for the Synthesis of Benzimidazoles Using Hydrogen Peroxide under Ambient Conditions

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Benzimidazoles are very useful building blocks for the development of molecules of pharmaceutical or biological interest.[1] Benzimidazole derivatives exhibit significant activity against several viruses, such as HIV,[2] herpes (HSV-1),[3] DNA,[4] RNA,[5] influenza,[6] and human cytomegalovirus (HCMV).[2a] Bis-benzimidazoles are being developed as DNA minor-groove binding agents with antitumor activity[7] and can act as ligands with transition metals for modeling biological systems.[8] In addition, benzimidazoles are very important intermediates in organic reactions.[9] The widespread interest in benzimidazole-containing structures has promoted extensive studies on their synthesis.[10] There are two general methods for the synthesis of benzimidazoles. One is the coupling of a carboxylic acid or derivative (nitrile, imidate, or orthoester) with phenylenediamine, which is usually performed under strongly acidic conditions,[11] harsh dehydrating conditions that often require high temperatures,[12] or via the use of agents such as phosphorus anhydrides,[13] sometimes in combination with microwave irradiation.[14] The other method is oxidative cyclo-dehydrogenation of aniline Schiff base, which is often generated in situ from the condensation of phenylenediamine and aldehyde. Various oxidative reagents, such as MnO_2,[15] $Pb(OAc)_4$,[16] $PhI(OAc)_2$,[17] Oxone,[18] DDQ,[19] I_2,[20] 1,4-benzo-quinone,[21] tetracyanoethylene,[22] benzofuroxan,[23] $NaHSO_3$,[24] $Na_2S_2O_5$,[25] $(NH_4)_2S_2O_8$,[26] and nitrobenzene or DMF (high-boiling oxidant/solvent)[27] have been employed to effect the dehydrogenation step. Although many of these methods are practical, some have problems such as the use of dangerous or toxic reagents, or the formation of N-benzylbenzimidazole side products resulting from further reaction of the aldehyde with benzimidazoline prior to oxidation.

In view of the drawbacks of existing routes and the importance of green chemistry, a few green syntheses of benzimidazoles have recently been reported, employing air,[28] HClO (generated in situ from H_2O_2 and HCl),[29] metal ions,[30] and ionic liquid.[31] However, even these methods still have several drawbacks from a practical point of view. These are: (i) the need for a high temperature (often $>100\,^{\circ}C$) and long reaction time (up to 44 h); (ii) the use of strongly acidic conditions that may be detrimental to some sensitive substrates; (iii) the use of metal ions which, in addition to environmental concerns, often requires decomplexation of the metal from the product with the help of harmful reagents such as H_2S;[13d, 30a, b] and (iv) complex routes for the synthesis of ionic liquids. From an economic and environmental perspective, the development of a new catalytic oxidation system with both a more ecofriendly oxidant and catalyst is attractive.

Recently, hypervalent iodine reagents have drawn considerable attention as mild and highly chemoselective oxidizing reagents for various organic transformations.[32] As a result of their nontoxic nature, affordability, and safety profile, hypervalent iodine reagents are nowadays popular reagents for the formation of carbon–carbon bonds, carbon–heteroatom bonds, and heteroatom–heteroatom bonds. The activation of carbon–hydrogen bonds, rearrangements, and fragmentations can also be induced by these reagents.[33] However, the use of stoichiometric amounts of hypervalent iodine reagents leads to the production of equimolar amounts of organic iodine waste, such as PhI, which is difficult to recover and reuse because of its high volatility and solubility in organic solvents. A recent significant breakthrough in the field of organoiodine chemistry was the development of catalytic systems based on hypervalent iodine.[34] In 2007, Kirihara and co-workers reported the in situ-generated hypoiodite-catalyzed oxidative coupling of thiols to disulfides with hydrogen peroxide.[35] In 2010, Ishihara and co-workers reported a mild and efficient catalytic method for oxidative cycloetherification using Bu_4NI, and its enantioselective version using chiral quaternary ammonium iodide.[36] Very recently, the method of (hypo)iodite-catalyzed α-oxyacylation of carbonyl compounds was also reported by Ishihara.[37]

In continuation of our efforts to develop new applications of hypervalent iodine reagents,[38] we report herein a simple and efficient catalytic oxidative system for the synthesis of benzimidazole derivatives using H_2O_2 as a green and economic terminal oxidant in the presence of catalytic amounts of Bu_4NI.

Initial experiments were carried out with phenylenediamine and benzaldehyde as model substrates. When phenylenediamine and benzaldehyde were treated with H_2O_2/Bu_4NI in MeCN at room temperature for 4 h, the desired 2-phenylbenzimidazole was isolated in 64% yield (Table 1, entry 1). As control experiments, the same reaction was carried out in the absence of Bu_4NI and H_2O_2 (entries 2 and 3, respectively). The yield of 2-phenylbenzimidazole was either much lower, or null. Moreover, other tetrabutylammonium halogenides, such as Bu_4NBr and Bu_4NCl, were tested for this reaction. All of them were unsatisfactory except for Bu_4NI (entries 4 and 5). Encouraged by these results, we examined the effects of solvents on the reaction, which showed that EtOH was the most efficient solvent, giving the highest yield (entries 6–10). To optimize the reaction conditions, the role of H_2O_2 was studied: 2.0 equiv of H_2O_2 was the better choice for this reaction (entries 11–13).

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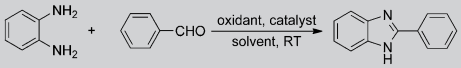
Table 1. Optimization studies for the synthesis of 2-phenylbenzimidazole.[a]



Entry	Oxidant	Equiv	Catalyst	Equiv	Solvent	Yield[b] [%]
1	H_2O_2	3.0	Bu_4NI	0.1	MeCN	64
2	H_2O_2	3.0	–	–	MeCN	16
3	–	–	Bu_4NI	0.1	MeCN	–
4	H_2O_2	3.0	Bu_4NBr	0.1	MeCN	23
5	H_2O_2	3.0	Bu_4NCl	0.1	MeCN	37
6	H_2O_2	3.0	Bu_4NI	0.1	MeOH	81
7	H_2O_2	3.0	Bu_4NI	0.1	EtOH	85
8	H_2O_2	3.0	Bu_4NI	0.1	THF	<10
9	H_2O_2	3.0	Bu_4NI	0.1	Et_2O	<10
10	H_2O_2	3.0	Bu_4NI	0.1	EtOAc	45
11	H_2O_2	2.0	Bu_4NI	0.1	EtOH	94
12	H_2O_2	1.5	Bu_4NI	0.1	EtOH	92
13	H_2O_2	1.0	Bu_4NI	0.1	EtOH	88
14	H_2O_2	1.5	Bu_4NI	0.05	EtOH	90
15	H_2O_2	1.5	–	–	EtOH	13
16	H_2O_2	1.5	$[Bu_4N]^+[OH]^-$	0.1	EtOH	21
17	H_2O_2	1.5	$[Bu_4N]^+[OH]^-$	0.1	EtOH	89[c]

[a] Reactions were performed by using phenylenediamine (1 mmol), benzaldehyde (1 mmol), H_2O_2, Bu_4NI, solvent (5 mL) at RT for 4 h. [b] Isolated yield. [c] 0.1 mmol KI was added.

With regard to the Bu_4NI dosage, it was possible to decrease the amount of Bu_4NI to as low as 0.05 equiv. without significant loss in catalytic efficiency (entry 14). However, the poor yield of a blank reaction under the best reaction conditions (EtOH, 1.5 equiv H_2O_2) indicates the importance of Bu_4NI in this reaction (entry 15). This could be further supported by the fact that replacing Bu_4NI with $[Bu_4N]^+[OH]^-$ under the same conditions gave the desired product in 21% yield, however, the oxidation with KI in the presence of $[Bu_4N]^+[OH]^-$ gave the desired product in 89% yield (entries 16 and 17), which clearly indicates Bu_4NI is essential for this reaction.

To evaluate the versatility of the catalytic system, we applied the procedure to the synthesis of a variety of substituted benzimidazoles. As can be seen in Table 2, most aldehydes underwent smooth transformation to afford the corresponding benzimidazoles in excellent yields. Benzylic aldehydes underwent smooth oxidation (entries 1–7). Excellent chemoselectivity was observed under the present oxidation. We detected no phenol oxidation products, which are well-known to form in reactions with aryl-λ^3-iodanes (entry 7).[39] Allylic aldehyde, such as cinnamyl aldehyde (entry 8), was also oxidized efficiently without any observable reaction at the double-bond functionality. The electronic properties of the substituents in the aromatic ring had a remarkable influence on the reaction rate. Strongly electron-withdrawing groups, such as $-NO_2$, improved the reaction (entry 4). Strongly electron-donating groups, such as $-OCH_3$, lowered the rate of the ring-closure step because of the decreased electrophilicity of the carbonyl carbon atom (entry 5). This is different from previously reported procedures, where the $-OCH_3$ group favored the oxidation.[30d] Heteroaryl aldehydes 2-pyridinyl, 2-furyl, and 2-thiophene carboxaldehyde also gave good yields (entries 9–11). Notably, together with the good results with benzylic, allylic, and heteroaryl aldehydes, the yields obtained from the reaction of aliphatic aldehydes under the same conditions are also high (entries 12–13). In view of the fact that the reaction of aliphatic aldehyde is much more difficult than the reaction of benzylic aldehyde,[26] the results obtained with the present procedure are very satisfactory. Next, we extended this synthetic method for the preparation of bis-benzimidazoles in a 2:1 molar ratio of phenylenediamine/terephthaldicarboxaldehyde (entry 16).

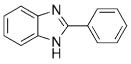
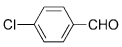
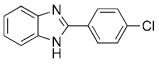
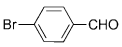
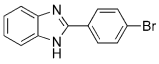
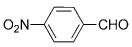
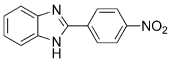
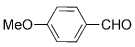
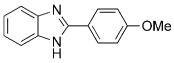
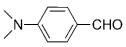
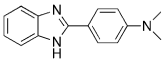
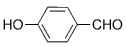
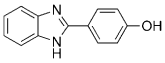
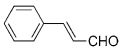
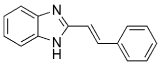
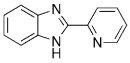
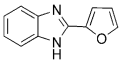
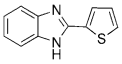
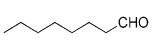
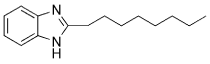
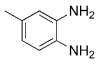
To demonstrate the scope and efficiency of the present method, the H_2O_2/Bu_4NI system was then extended for the synthesis of imidazoline, benzoxazole, and benzothiazole. 2-Aminophenol was also converted to the corresponding benzoxazole in moderate yield (Table 2, entry 18). However, the yields of imidazoline and benzthiazole under the same conditions were quite low (entries 17 and 19). Ethylenediamine exhibited a low reactivity toward this system, most probably due to the absence of electron cloud conjugation. The reaction of 2-aminobenzenethiol with aldehyde gave many side products. This poor selectivity might be attributable to the high reactivity of the –SH group.

To assess the feasibility of using this method on a preparative scale, the multigram-scale catalytic system was examined for the coupling of phenylenediamine with 4-chlorobenzaldehyde on a 100 mmol scale. As expected, the reaction proceeded smoothly, similar to the smaller-scale case, and the desired 2-(4-chlorophenyl)benzimidazole was obtained in 90% isolated yield (Table 2, entry 2).

Developing environmentally benign and economical syntheses is an area of research that is being vigorously pursued, and avoiding the use of harmful organic solvents is a fundamental strategy to achieving this goal. One of the most attractive alternatives to organic solvents is water, which has witnessed increasing popularity due to being inexpensive, readily available, and environmentally benign. The development of aqueous-phase reactions using hypervalent iodine reagents is also one of the active fields in organic synthesis due to a recent demand for realization of green chemical processes.[40] So, we attempt to run the reaction in water in our search for a more practical and clean procedure. The present catalytic system was examined for the synthesis of 2-phenylbenzimidazole in water by adjusting the feeding sequence. First, Bu_4NI was added in a mixture of phenylenediamine, benzaldehyde, and water. The solution was stirred at room temperature for 2 h. Then H_2O_2 was added. The use of water instead of EtOH in this reaction led to similar results, albeit with a small decrease in the yield of 2-phenylbenzimidazole (Table 2, entry 1).

Very recently, Bai and co-workers reported the preparation of 2-imidazolines from aldehydes and ethylenediamine by using catalytic amounts of sodium iodide and hydrogen peroxide as terminal oxidant in the presence of anhydrous magnesium sulfate. They suggested a mechanism in which in situ-generated molecular iodine is the actual oxidant.[41] To understand the reaction pathway, we conducted ESI–MS experiments directed toward identifying an active hypervalent iodine species. $[Bu_4N]^+$ and 2-phenylbenzimidazole were detected by

Table 2. Synthesis of benzimidazoles from aldehydes and diamines.[a]

Entry	Diamine	Aldehyde	Product[b]	Time [h]	Yield[c] [%]
1				6	92 (80[d])
2				4	96 (90[e])
3				4	93
4				4	95
5				8	84
6				8	87
7				6	90
8				5	83
9				6	85
10				7	82
11				7	80
12		HCHO		8	72[f]
13				10	74
14				6	91[g]
15				6	93[g]
16				7	90
17				12	37
18				7	68
19				5	15[g]

[a] Reaction conditions: diamine (1 mmol), aldehyde (1 mmol), H_2O_2 (1.5 mmol), Bu_4NI (0.1 mmol), EtOH (5 mL), RT. [b] Products were confirmed by ^1H NMR, MS, and IR. [c] Yields of isolated products unless otherwise noted. [d] Water was used as solvent. [e] Yield of large-scale synthesis on a 100 mmol scale. [f] 36% formaldehyde solution was used. [g] Yield was determined by GC-MS.

positive-ion ESI–MS (Figure 1, peaks at *m/z* 242.15 and *m/z* 195.00). IO_2^- was detected by negative-ion ESI–MS (Figure 2, peak at *m/z* 159.13). We also detected IO^- (*m/z* 143.08), but this species disappeared too fast to obtain a measurement. This result suggests that in situ-generated $[Bu_4N]^+[IO]^-$ may be an active oxidant species. However, $[Bu_4N]^+[IO]^-$ may also disproportionate to $[Bu_4N]^+[IO_2]^-$ and Bu_4NI under our reaction conditions, implying that $[Bu_4N]^+[IO_2]^-$ is another potential actual oxidant species.

Based on these results, a plausible reaction pathway for the formation of benzimidazole is shown in Scheme 1. First, the condensation of phenylenediamine with aldehyde takes place to form Schiff base **1**, which then transforms to the final product through the intermediary benzimidazoline **2**. The highly reactive iodine (I) intermediate $[Bu_4N]^+[IO]^-$ or iodine (III) intermediate $[Bu_4N]^+[IO_2]^-$ are the actual oxidants for the oxidative cyclo-dehydrogenation of **2** to afford the final product benzimidazole. The role of H_2O_2 is to regenerate $[Bu_4N]^+[IO]^-$ (or $[Bu_4N]^+[IO_2]^-$) from Bu_4NI.

In conclusion, a clean and efficient method for the synthesis of benzimidazole derivatives using H_2O_2 as a green and economic terminal oxidant in the presence of catalytic amounts of

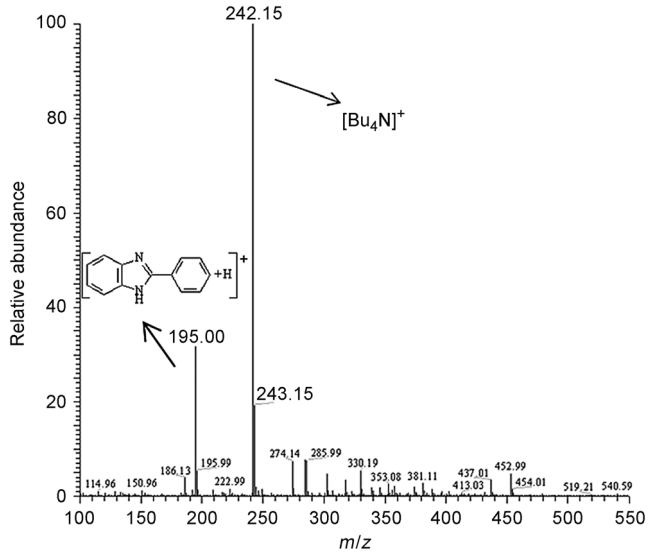


Figure 1. Positive-ion ESI mass spectrum of the reaction mixture.

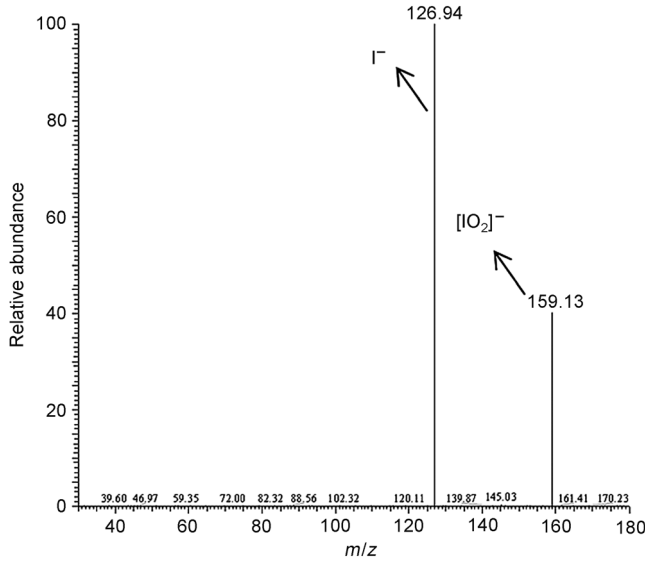
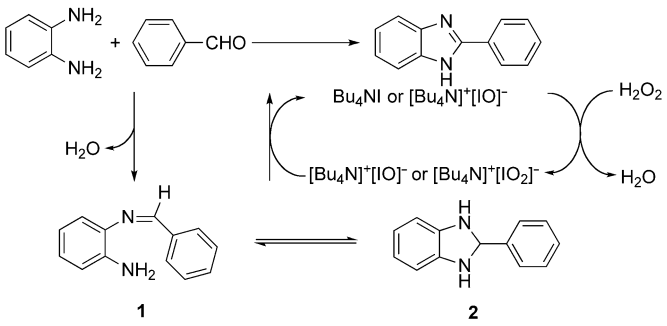


Figure 2. Negative-ion ESI mass spectrum of the reaction mixture.



Scheme 1. A possible reaction pathway for the formation of benzimidazole.

Bu_4NI is presented. The highly reactive iodine (III) intermediate $[Bu_4N]^+[IO_2]^-$ was detected by ESI–MS for the first time. The advantages of this green catalytic oxidation system are: (1) it avoids the use of acid and transition metal catalysts; (2) it has good atom economy and environmental merits; the only by-product is H_2O; (3) it employs mild reaction conditions. A key feature of this protocol is its inherent simplicity. There is no need for rigorous exclusion of air or moisture to effect a clean oxidation, and the reaction conditions and reagents are easy to handle. Moreover, the present non-transition metal catalytic system also provides an easy scale-up and separation protocol. Hence, we believe that it will find wide application in organic synthesis as well as in industry.

Experimental Section

Typical procedure for the synthesis of benzimidazole with H_2O_2/Bu_4NI: To a stirred solution of diamine (1 mmol) in EtOH (5 mL) the aldehyde (1 mmol) was added, and the solution was stirred at room temperature for 2 h. Bu_4NI (36.9 mg, 0.1 mmol) and 30% H_2O_2 (51 mg, 1.5 mmol) were then added, and the mixture was stirred at room temperature for several hours while checking the reaction progress by using gas or thin-layer chromatography. After completion, the mixture was diluted with water (10 mL), and extracted with EtOAc (3×10 mL). The organic layer was dried and concentrated to provide the corresponding product in an almost pure state. If necessary, the crude product was purified by using crystallization or column chromatography (petroleum ether/ethyl acetate = 5:1) to provide the analytically pure product, which was characterized by using ^1H NMR, MS, and IR. The Supporting Information provides details of these measurements.

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Keywords: aldehydes · dehydrogenation · heterocycles · homogeneous catalysis · hypervalent compounds

[1] a) D. A. Horton, G. T. Bourne, M. L. Smythe, *Chem. Rev.* **2003**, *103*, 893–930; b) J. Velík, V. Baliharová, J. Fink-Gremmels, S. Bull, J. Lamka, L. Skálová, *Res. Vet. Sci.* **2004**, *76*, 95–108; c) M. Boiani, M. Gonzalez, *Mini-Rev. Med. Chem.* **2005**, *5*, 409–424; d) S. Bhattacharya, P. Chaudhuri, *Curr. Med. Chem.* **2008**, *15*, 1762–1777.

[2] a) M. Roth, M. L. Morningstar, P. L. Boyer, S. H. Hughes, R. W. Bukheit, C. J. Michejda, *J. Med. Chem.* **1997**, *40*, 4199–4207; b) A. R. Porcari, R. V. Devivar, L. S. Kucera, J. C. Drach, L. B. Townsend, *J. Med. Chem.* **1998**, *41*, 1252–1262.

[3] M. T. Migawa, J. L. Giradet, J. A. Walker, G. W. Koszalka, S. D. Chamberlain, J. C. Drach, L. B. Townsend, *J. Med. Chem.* **1998**, *41*, 1242–1251.

[4] a) J. M. Woynarowski, M. M. McHugh, R. D. Sigmud, T. A. Beerman, *Mol. Pharmacol.* **1989**, *35*, 177–182; b) A. Y. Chen, C. Yu, B. Gatto, L. F. Liu, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 8131–8135; c) J. S. Kim, B. Gatto, C. Yu, A. Liu, L. F. Liu, E. J. LaVoie, *J. Med. Chem.* **1996**, *39*, 992–998.

[5] I. Tamm, P. B. Seghal, *Adv. Virus Res.* **1978**, *22*, 187–258.

[6] T. Hisano, M. Ichikawa, K. Tsumoto, M. Tasaki, *Chem. Pharm. Bull.* **1982**, *30*, 2996–3004.

[7] J. Mann, A. Baron, Y. Opoku-Boahen, E. Johansson, G. Parkinson, L. R. Kelland, S. Neidle, *J. Med. Chem.* **2001**, *44*, 138–144.

[8] a) M. A. Pujar, T. D. Bharamgoudar, *Transition Met. Chem.* **1988**, *13*, 423–425; b) E. Bouwman, W. L. Driessen, J. Reedijk, *Coord. Chem. Rev.* **1990**, *104*, 143–172.

[9] a) E. Hasegawa, A. Yoneoka, K. Suzuki, T. Kato, T. Kitazume, K. Yangi, *Tetrahedron* **1999**, *55*, 12957–12968; b) Y. Bai, J. Lu, Z. Shi, B. Yang, *Synlett* **2001**, 544–546.

[10] a) P. N. Preston, *Chem. Rev.* **1974**, *74*, 279 – 314; b) M. R. Grimmett, *Imidazole and Benzimidazole Synthesis*, Academic Press, London, **1997**.

[11] a) W. Huang, R. M. Scarborough, *Tetrahedron Lett.* **1999**, *40*, 2665 – 2668; b) Y.-C. Chi, C.-M. Sun, *Synlett* **2000**, 591 – 594; c) D. Kumar, M. R. Jacob, M. B. Reynolds, S. M. Kerwin, *Bioorg. Med. Chem.* **2002**, *10*, 3997 – 4004; d) B. Gong, F. Hong, C. Kohm, L. Bonham, P. Klein, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1455 – 1459; e) S.-T. Huang, I.-J. Hsei, C. Chen, *Bioorg. Med. Chem.* **2006**, *14*, 6106 – 6119.

[12] a) D. W. Dunwell, D. Evans, C. E. Smith, W. R. N. Williamson, *J. Med. Chem.* **1975**, *18*, 692 – 694; b) I. B. Dzvinchuk, A. V. Vypirailenko, M. O. Lozinskii, *Russian. J. Org. Chem.* **1998**, *34*, 685 – 687.

[13] a) E. Barni, P. J. Savarino, *J. Heterocycl. Chem.* **1979**, *16*, 1583 – 1587; b) J. B. Hendrickson, M. S. Hussoin, *J. Org. Chem.* **1987**, *52*, 4137 – 4139; c) T. Gungor, A. Fouquet, J.-M. Teulon, D. Provost, M. Cazes, A. Cloarec, *J. Med. Chem.* **1992**, *35*, 4455 – 4463; d) A. W. White, R. Almassy, A. H. Calvert, N. J. Curtin, R. J. Griffin, Z. Hostomsky, K. Maegley, D. R. Newell, S. Srinivasan, B. T. Golding, *J. Med. Chem.* **2000**, *43*, 4084 – 4097; e) B. Biasotti, S. Dallavalle, L. Merlini, C. Farina, S. Gagliardi, C. Parini, P. Belfiore, *Bioorg. Med. Chem.* **2003**, *11*, 2247 – 2254.

[14] a) K. Bougrin, A. Loupy, M. Soufiaoui, *Tetrahedron* **1998**, *54*, 8055 – 8064; b) A. Ben-Alloum, S. Bakkas, M. Soufiaoui, *Tetrahedron Lett.* **1998**, *39*, 4481 – 4484; c) G. V. Reddy, V. V. V. N. S. R. Rao, B. Narsaiah, P. S. Rao, *Synth. Commun.* **2002**, *32*, 2467 – 2476; d) Z. Mao, Z. Wang, J. Li, X. Song, Y. Luo, *Synth. Commun.* **2010**, *40*, 1963 – 1977.

[15] I. Bhatnagar, M. V. George, *Tetrahedron* **1968**, *24*, 1293 – 1298.

[16] F. F. Stephens, J. D. Bower, *J. Chem. Soc.* **1949**, 2971 – 2972.

[17] L.-H. Du, Y.-G. Wang, *Synthesis* **2007**, 675 – 678.

[18] P. L. Beaulieu, B. Haché, E. von Moos, *Synthesis* **2003**, 1683 – 1692.

[19] a) J. J. Vanden Eynde, F. Delfosse, P. Lor, Y. Van Haverbeke, *Tetrahedron* **1995**, *51*, 5813 – 5818; b) K. J. Lee, K. D. Janda, *Can. J. Chem.* **2001**, *79*, 1556 – 1561.

[20] a) H. Yukawa, T. Nagatani, Y. Torisawa, Y. Okaichi, N. Tada, T. Furuta, J.-I. Minamikawa, T. Nishi, *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1267 – 1268; b) P. Gogoi, D. Konwar, *Tetrahedron Lett.* **2006**, *47*, 79 – 82.

[21] a) S. Kumar, V. Kansal, A. Bhaduri, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1991**, *20*, 254 – 256; b) E. Verner, B. A. Katz, J. R. Spencer, D. Allen, J. Hataye, W. Hruzewicz, H. C. Hui, A. Kolesnikov, Y. Li, C. Luong, A. Martelli, K. Radika, R. Rai, M. She, W. Shrader, P. A. Sprengeler, S. Trapp, J. Wang, W. B. Young, R. L. Mackman, *J. Med. Chem.* **2001**, *44*, 2753 – 2771.

[22] H. Chikashita, S. Nishida, M. Miyazaki, Y. Morita, K. Itoh, *Bull. Chem. Soc. Jpn.* **1987**, *60*, 737 – 746.

[23] F. Patzold, F. Zeuner, T. H. Heyer, H. J. Niclas, *Synth. Commun.* **1992**, *22*, 281 – 288.

[24] a) M. A. Weidner-Wells, K. A. Ohemeng, V. N. Nguyen, S. Fraga-Spano, M. J. Macielag, H. M. Werblood, B. D. Foleno, G. C. Webb, J. F. Barrett, D. J. Hlasta, *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1545 – 1548; b) S. C. Austen, J. M. J. Kane, *J. Heterocycl. Chem.* **2001**, *38*, 979 – 980.

[25] R. L. Lombardy, F. A. Tanious, K. Ramachandran, R. R. Tidwell, W. D. Wilson, *J. Med. Chem.* **1996**, *39*, 1452 – 1462.

[26] K. Bahrami, M. M. Khodaei, A. Nejati, *Green Chem.* **2010**, *12*, 1237 – 1241.

[27] a) D. S. C. Black, N. Kumar, L. C. H. Wong, *Synthesis* **1986**, 474 – 476; b) B. Yadagiri, J. W. Lown, *Synth. Commun.* **1990**, *20*, 955 – 963; c) Y. Bathini, K. E. Rao, R. G. Shea, J. W. Lown, *Chem. Res. Toxicol.* **1990**, *3*, 268 – 280; d) M. P. Singh, T. Joseph, S. Kumar, Y. Bathini, J. W. Lown, *Chem. Res. Toxicol.* **1992**, *5*, 597 – 607; e) Q. Sun, B. Gatto, C. Yu, A. Liu, L. F. Liu, E. J. LaVoie, *J. Med. Chem.* **1995**, *38*, 3638 – 3644; f) R. S. Harapanhalli, L. W. McLaughlin, R. W. Howell, D. V. Rao, S. J. Adelstein, A. I. Kassis, *J. Med. Chem.* **1996**, *39*, 4804 – 4809; g) A. L. Satz, T. C. Bruice, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 3261 – 3266; h) C. G. Blettner, W. A. König, G. Rühter, W. Stenzel, T. Schotten, *Synlett* **1999**, 307 – 310; i) M. Rangarajan, J. S. Kim, S.-P. Sim, A. Liu, L. R. Liu, E. J. LaVoie, *Bioorg. Med. Chem.* **2000**, *8*, 2591 – 2600.

[28] a) S. Lin, L. Yang, *Tetrahedron Lett.* **2005**, *46*, 4315 – 4319; b) G. M. Coppola, *Synth. Commun.* **2008**, *38*, 3500 – 3507.

[29] a) K. Bahrami, M. M. Khodaei, I. Kavianinia, *J. Chem. Res.* **2006**, *12*, 783 – 784; b) K. Bahrami, M. M. Khodaei, I. Kavianinia, *Synthesis* **2007**, 547 – 550.

[30] a) W. A. Denny, G. W. Rewcastle, B. C. Baguley, *J. Med. Chem.* **1990**, *33*, 814 – 819; b) G. L. Gravatt, B. C. Baguley, W. R. Wilson, W. A. Denny, *J. Med. Chem.* **1994**, *37*, 4338 – 4345; c) Q. Dang, B. S. Brown, M. D. Erion, *Tetrahedron Lett.* **2000**, *41*, 6559 – 65652; d) M. P. Singh, S. Sasmal, W. Lu, M. N. Chatterjee, *Synthesis* **2000**, 1380 – 1390; e) K. Nagata, T. Itoh, H. Ishikawa, A. Ohsawa, *Heterocycles* **2003**, *61*, 93 – 96; f) M. Curini, F. Epifano, F. Montanari, O. Rosati, S. Taccone, *Synlett* **2004**, 1832 – 1834; g) K. Bahrami, M. M. Khodaei, F. Naali, *J. Org. Chem.* **2008**, *73*, 6835 – 6837; h) H. Sharghi, M. H. Beyzavi, M. M. Doroodmand, *Eur. J. Org. Chem.* **2008**, 4126 – 4138; i) H. Sharghi, M. Aberi, M. M. Doroodmand, *Adv. Synth. Catal.* **2008**, *350*, 2380 – 2390; j) K. Bahrami, M. M. Khodaei, F. Naali, *Synlett* **2009**, 569 – 557; k) A. T. Khan, T. Parvin, L. H. Choudhury, *Synth. Commun.* **2009**, *39*, 2339 – 2346; l) R. V. Shingalapur, K. M. Hosamani, *Catal. Lett.* **2010**, *137*, 63 – 68; m) K. D. Parghi, R. V. Jayaram, *Catal. Commun.* **2010**, *11*, 1205 – 1210.

[31] R. N. Nadaf, S. A. Siddiqui, T. Daniel, R. J. Lahoti, K. V. Srinivasan, *J. Mol. Catal. A: Chem.* **2004**, *214*, 155 – 160.

[32] a) A. Varvoglis, *Hypervalent Iodine in Organic Synthesis*, Academic Press, London, **1997**; b) T. Wirth, *Topics in Current Chemistry: Hypervalent Iodine Chemistry-Modern Developments in Organic Synthesis*, Springer, Berlin, **2003**; c) G. F. Koser, *Adv. Heterocycl. Chem.* **2004**, *86*, 225 – 292; d) H. Tohma, Y. Kita, *Adv. Synth. Catal.* **2004**, *346*, 111 – 124; e) R. M. Moriarty, *J. Org. Chem.* **2005**, *70*, 2893 – 2903; f) A. P. Thottumkara, M. S. Bowsher, T. K. Vinod, *Org. Lett.* **2005**, *7*, 2933 – 2936; g) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2008**, *108*, 5299 – 5358; h) V. V. Zhdankin, *ARKIVOC* **2009**, 1, 1 – 62; i) M. Uyanik, M. Akakura, K. Ishihara, *J. Am. Chem. Soc.* **2009**, *131*, 251 – 262; j) M. Uyanik, K. Ishihara, *Chem. Commun.* **2009**, 2086 – 2099.

[33] T. Wirth, *Angew. Chem.* **2005**, *117*, 3722 – 3731; *Angew. Chem. Int. Ed.* **2005**, *44*, 3656 – 3665.

[34] a) M. Ochiai, Y. Takeuchi, T. Katayama, T. Sueda, K. Miyamoto, *J. Am. Chem. Soc.* **2005**, *127*, 12244 – 12245; b) T. Dohi, A. Maruyama, M. Yoshimura, K. Morimoto, H. Tohma, Y. Kita, *Angew. Chem.* **2005**, *117*, 6349 – 6352; *Angew. Chem. Int. Ed.* **2005**, *44*, 6193 – 6196; c) R. D. Richardson, T. Wirth, *Angew. Chem.* **2006**, *118*, 4510 – 4512; *Angew. Chem. Int. Ed.* **2006**, *45*, 4402 – 4404; d) M. Ochiai, *Chem. Rec.* **2007**, *7*, 12 – 23; e) M. Ochiai, K. Miyamoto, *Eur. J. Org. Chem.* **2008**, 4229 – 4239; f) T. Dohi, Y. Kita, *Chem. Commun.* **2009**, 2073 – 2085; g) M. Ngatimin, D. W. Lupton, *Aust. J. Chem.* **2010**, *63*, 653 – 658; h) T. Dohi, *Chem. Pharm. Bull.* **2010**, *58*, 135 – 142.

[35] M. Kirihara, Y. Asai, S. Ogawa, T. Noguchi, A. Hatano, Y. Hirai, *Synthesis* **2007**, 3286 – 3289.

[36] a) M. Uyanik, H. Okamoto, T. Yasui, K. Ishihara, *Science* **2010**, *328*, 1376 – 1379; b) M. Uyanik, K. Ishihara, *Chim. Oggi* **2011**, *29*, 18 – 21.

[37] M. Uyanik, D. Suzuki, T. Yasui, K. Ishihara, *Angew. Chem.* **2011**, *123*, 5443 – 5446; *Angew. Chem. Int. Ed.* **2011**, *50*, 5331 – 5334.

[38] a) Q. Zhang, J. Luo, Y. Wei, *Green Chem.* **2010**, *12*, 2246 – 2254; b) C. Zhu, L. Ji, Y. Wei, *Synthesis* **2010**, 3121 – 3125; c) C. Zhu, L. Ji, Y. Wei, *Catal. Commun.* **2010**, *11*, 1017 – 1020; d) C. Zhu, C. Sun, Y. Wei, *Synthesis* **2010**, 4235 – 4241; e) C. Zhu, D. Xu, Y. Wei, *Synthesis* **2011**, 711 – 714.

[39] a) S. Quideau, L. Pouységu, D. Deffieux, *Synlett* **2008**, 467—495; b) T. Yakura, M. Omoto, *Chem. Pharm. Bull.* **2009**, *57*, 643 – 645; c) H. Fujioka, H. Komatsu, T. Nakamura, A. Miyoshi, K. Hata, J. Ganesh, K. Murai, Y. Kita, *Chem. Commun.* **2010**, *46*, 4133 – 4135; d) M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem.* **2010**, *122*, 2221 – 2223; *Angew. Chem. Int. Ed.* **2010**, *49*, 2175 – 2177; e) L. Pouységu, D. Deffieux, S. Quideau, *Tetrahedron* **2010**, *66*, 2235 – 2261.

[40] a) H. Tohma, S. Takizawa, T. Maegawa, Y. Kita, *Angew. Chem.* **2000**, *112*, 1362 – 1364; *Angew. Chem. Int. Ed.* **2000**, *39*, 1306 – 1308; b) H. Tohma, T. Maegawa, S. Takizawa, Y. Kita, *Adv. Synth. Catal.* **2002**, *344*, 328 – 337; c) B. Das, H. Holla, K. Venkateswarlu, A. Majhi, *Tetrahedron Lett.* **2005**, *46*, 8895 – 8897; d) T. Dohi, N. Takenaga, A. Goto, H. Fujioka, Y. Kita, *J. Org. Chem.* **2008**, *73*, 7365 – 7368; e) N. Takenaga, A. Goto, M. Yoshimura, H. Fujioka, T. Dohi, Y. Kita, *Tetrahedron Lett.* **2009**, *50*, 3227 – 3229; f) Y. Ye, L. Wang, R. Fan, *J. Org. Chem.* **2010**, *75*, 1760 – 1763; g) W. Panchan, S. Chiampanichayakul, D. L. Snyder, S. Yodbuntung, M. Pohmakotr, V. Reutrakul, T. Jaipetch, C. Kuhakarn, *Tetrahedron* **2010**, *66*, 2732 – 2735.

[41] G. Bai, K. Xu, G. Chen, Y. Yang, T. Li, *Synthesis* **2011**, 1599 – 1603.

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