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o-Alkoxyphenyliminoiodanes: Highly Efficient Reagents for the Catalytic Aziridination of Alkenes and the Metal-Free Amination of Organic Substrates

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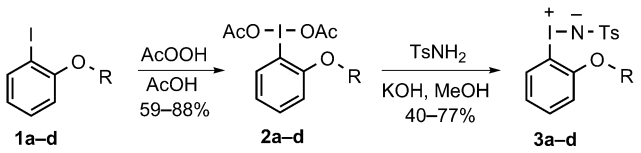
Within the rapidly growing field of hypervalent iodine chemistry,[1] iminoiodanes occupy a special and important place. *N*-Tosyliminoiodanes, ArINTs, have found a broad range of synthetic applications as useful nitrene precursors under thermal or catalytic conditions in the aziridination of alkenes and the amidation reactions of various organic substrates.[1d,e,2] Representative recent examples of the synthetic use of PhINTs include the highly efficient Ru^{II}- or Cu^{I}-catalyzed C–H-bond amidation of aldehydes,[2a,b] the gold-catalyzed nitrene transfer and C–H insertion reactions,[2c,d] the silver-catalyzed C–H insertion and aziridination reactions,[2e,f] and numerous asymmetric aziridinations of alkenes by using copper catalysts with chiral dinitrogen ligands.[2g–l] However, despite its importance, PhINTs is not a perfect reagent and has a serious drawback: it is insoluble in most organic solvents due to its strong intermolecular secondary bonding that creates a three-dimensional polymeric structure.[1d,e,3a–c] Several research groups have tried to improve the synthetic potential of iminoiodanes by developing new reagents or reagent combinations.[1e,3d–h] A particularly fruitful approach to soluble iminoiodanes is based on the placement of an *ortho-tert*-butylsulfonyl group onto the iodobenzene ring of the parent PhINTs.[3d–f] Thus, several ArINTs (Ar = 2-*t*BuSO$_2$C$_6$H$_4$, 2-*t*BuSO$_2$-5-*t*BuC$_6$H$_3$, and 2-*t*BuSO$_2$-4-CF$_3$C$_6$H$_3$) have been synthesized and utilized as soluble nitrene precursors, the reactivity of which is similar to the parent PhINTs. The solubility of these reagents is explained by the presence of intramolecular I···O secondary bonds due to the *ortho*-sulfonyl substituent, which redirects the intermolecular I···O and I···N secondary bonds responsible for the polymeric structure of PhINTs.[3d–f] These soluble nitrene precursors have proved to be useful reagents;[3d–f,4] however, their preparation requires four to seven synthetic steps and their reactivity does not show any improvement relative to PhINTs.

Herein, we report the preparation, structural investigation, and reactivity of new highly soluble and reactive nitrene precursors **3**, which are derived from *ortho*-alkoxyiodobenzenes. The choice of this structural motif is based on our previous observation that the presence of an *ortho*-alkoxy group in iodine(V) derivatives leads to the replacement of the intermolecular I···O secondary bonds with intramolecular I···O bonds and results in a significant improvement in the solubility of iodylarenes, ArIO$_2$.[5]

o-Alkoxyphenyliminoiodanes **3a–d** were synthesized in two simple steps starting from readily available 2-iodophenol ethers **1a–d** (Scheme 1). In the first step, iodides **1** were oxidized by peracetic acid to form diacetoxyiodo derivatives **2**; the structures of products **2a** and **d** were established by X-ray analysis.[6] In the second step, diacetates **2** were converted to iminoiodanes **3** by treatment with tosylamide under basic conditions, in methanol.



Scheme 1. Preparation of *o*-alkoxyphenyliminoiodanes **3a–d** (Ts = tosyl).

Products **3** precipitated from the reaction mixture and were isolated in good yields in analytically pure form as yellow microcrystalline solids by filtration followed by washing with hexane and drying in a vacuum. Compounds **3** are relatively stable at room temperature and can be stored for several weeks in a refrigerator. Products **3a–d** have good solubility in dichloromethane, chloroform, and acetonitrile (e.g., the solubility of **3b** in dichloromethane is 0.25 g mL^{-1}). All products were identified by NMR spectroscopy and elemental analysis, and the structures of **3a** and **c** were characterized by single crystal X-ray crystallography.[6]

The X-ray crystal structure of **3a**, showing intra- and intermolecular interactions with the hypervalent iodine center, is given in Figure 1a. Similar to the structure of PhINTs (Figure 1b),[3b] molecules of **3a** have a polymeric, asymmetrically bridged structure with a T-shaped geometry around the iodine centers formed by two iodine–nitrogen bonds and one iodine–carbon bond. However, in contrast to PhINTs, compound **3a** has two additional weak intra- and

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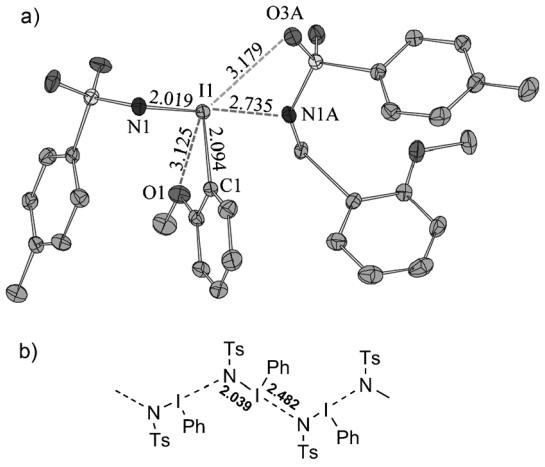


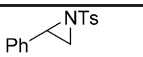
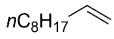
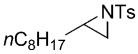
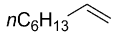
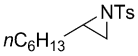
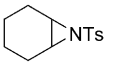
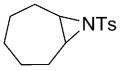
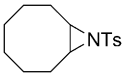
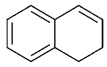
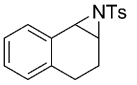
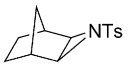
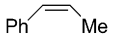
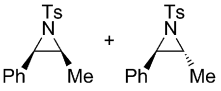
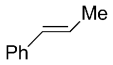
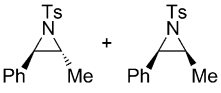
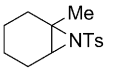
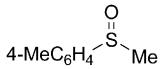
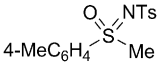
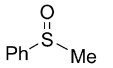
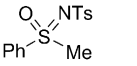
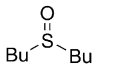
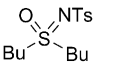
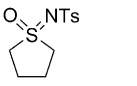
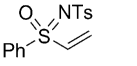
Figure 1. a) The X-ray crystal structure of **3a** showing intra- and intermolecular interactions with the hypervalent iodine center. Only two identical molecules forming close contacts are shown. b) The polymeric structure of PhINTs according to single-crystal X-ray analysis[3b] (bond lengths are in Å).

intermolecular I···O contacts between the iodine center and the oxygen atoms of the alkoxy and sulfonyl groups (Figure 1 a). These weak interactions lead to an elongation of the I···N1A intermolecular bond in **3a** (2.735 Å) compared with that observed in PhINTs (2.482 Å). As a result, the polymeric structure of **3a** is weakened and the solubility is significantly increased.

We have tested the reactivity of *o*-alkoxyphenyliminoiodane **3b** as a nitrene source in the typical Cu-catalyzed reactions—the aziridination of alkenes[2g–l] and the tosylimination of sulfoxides;[7] the results are summarized in Table 1. The yields of products for the Cu-catalyzed aziridinations of alkenes (Table 1, entries 1–11) and the *cis*/*trans* ratio for the aziridine products of the reactions of (*Z*)- and (*E*)-1-phenylpropenes (Table 1, entries 9 and 10) are in good agreement with the previously reported reactions of PhINTs,[2 g] which is indicative of the common Cu–nitrenoid intermediate in these reactions.[2g–i] Likewise, the reactivity of **3b** in the catalytic tosylimination of sulfoxides is similar to the reactivity of PhINTs[7] (Table 1, entries 12–16). Therefore, reagent **3b** can find applications as an alternative to the PhINTs nitrene precursor in useful catalytic aziridinations and iminations under homogeneous conditions. *o*-Alkoxyphenyliminoiodanes **3c** and **d** show similar reactivity to **3b** in catalytic aziridinations and iminations, whereas **3a** is less reactive because of its lower solubility.

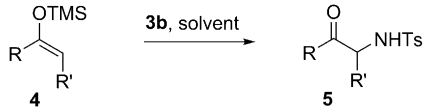
Next, we investigated the metal-free tosylamination reactions by using reagent **3b**. It has previously been reported that, in the absence of copper catalysts, PhINTs does not react with the silyl enol ether of cyclohexanone,[2g,8] but does react with the silyl enol ethers of acetophenones under reflux conditions in acetonitrile.[8] We were pleased to find that reagent **3b** readily reacts with silyl enol ethers of acetophenone under these conditions giving the product of α-tosylamination (Table 2, entry 1). Further optimization of the reaction conditions (Table 2, entries 2–6) has shown that the best yields are achieved in the presence of BF_3–etherate (1 equiv) in dichloromethane at 0 °C in 10 min (Table 2, entry 6). Several other silyl enol ethers **4** can be readily aminated under these conditions (Table 2, entries 7–13). Nota-

Table 1. The Cu^{II}-catalyzed aziridination of alkenes[a] and the tosylimination of sulfoxides[b] by using *o*-alkoxyphenyliminoiodane **3b**.

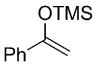
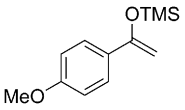
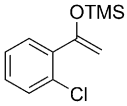
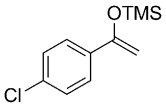
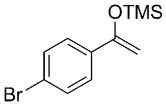
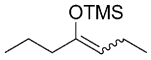
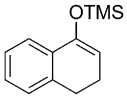
Entry	Substrate	Product	Yield [%][c]
1			92 (92)
2			81[d] (62)
3			51
4			63 (60)
5			86
6			73
7			61 (73)
8			81 (95)
9		 87 : 13	83[e]
10		 98 : 2	71[e]
11			22
12			96
13			94 (84)
14			89
15			73 (91)
16			68[f] (53)

[a] The aziridination of alkenes was conducted in MeCN at room temperature for 1 h by using **3**b (1 equiv), alkene (5 equiv), and $Cu(OTf)_2$ (0.1 equiv, Tf = triflate), unless otherwise noted. [b] The tosylimination of sulfoxides was conducted in MeCN at room temperature for 0.5 h by using **3**b (1.2 equiv), sulfoxide (1 equiv), and $Cu(OTf)_2$ (0.05 equiv). [c] The yields of products isolated by silica gel column chromatography are given; the yields shown in parentheses correspond to the literature data[2g,7] for the reactions of PhINTs under similar conditions. [d] $Cu(acac)_2$ (acac = acetylacetate) was used instead of $Cu(OTf)_2$. [e] The product ratio was determined by ^{1}H NMR spectroscopy. [f] No product of aziridination of the double bond was observed.

Table 2. The α-tosylamination of silyl enol ethers **4** by using *o*-alkoxyphenyliminoiodane **3b** (TMS = trimethylsilyl).



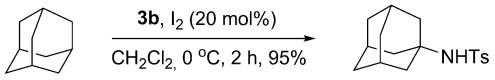
4 5

Entry	Substrate **4** ([equiv])[a]	Solvent (additive, [equiv])	*T* [°C]	*t* [h]	Yield of **5** [%][b]
1	(1.5)	MeCN (none)	81[c]	0.5	80
2	(0.83)	MeCN (none)	25	8	62
3	(0.83)	MeCN (BF_3·Et_2O, 1.2)	25	0.2	21
4	 (0.83)	CH_2Cl_2 (none)	25	24	55
5	(1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	25	0.2	48
6	(1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	0	0.2	83
7	 (1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	0	0.2	96
8	 (1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	0	0.2	94
9	 (1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	0	0.2	94
10	 (1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	0	0.2	64
11	 (1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	0	0.2	63
12	 (1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	0	0.2	60
13	 (1.2)	CH_2Cl_2 (BF_3·Et_2O, 1)	0	0.2	46

[a] All reactions were performed by using **3**b (1 equiv). [b] Yields of products isolated by silica gel column chromatography. [c] Under reflux conditions.

bly, the silyl enol ether of cyclohexanone reacts with reagent **3b** to afford the product of α-tosylamination in good yield (Table 2, entry 12), although no reaction occurs with PhINTs.[8]

The direct amination of saturated hydrocarbons is a challenging synthetic goal that has previously been achieved by using various transition-metal catalysts.[9a] It has recently been demonstrated that the amino functionalization of a range of benzylic and aliphatic saturated and unsaturated hydrocarbons can be performed by reaction with PhINTs in the presence of I_2 as a catalyst.[9b] In particular, adamantane reacts with PhINTs and I_2 (0.2 equiv) in dichloromethane in 2 h at room temperature to afford 1-tosylaminoadamantane in 63% yield.[9b] We have found that a similar reaction of



6 7

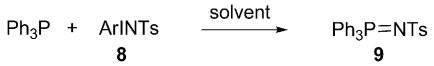
Scheme 2. Tosylamination of adamantane by using *o*-alkoxyphenyliminoiodane **3b**.

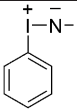
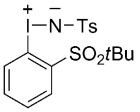
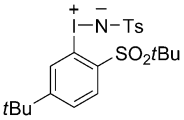
adamantane **6** with reagent **3b** readily occurs at 0 °C to give product **7** in 95% yield (Scheme 2).

The results summarized in Table 2 and Scheme 2 demonstrate that reagent **3b** is generally more reactive than PhINTs in the absence of Cu catalysts. A comparison of the reactivity of **3b** with other aryliminoiodanes, ArINTs, in the transylidation reaction with Ph_3P provides further support for this observation (Table 3). The reaction of **3b** with Ph_3P is complete in 10 min at room temperature (Table 3, entry 5), whereas a similar transylidation with PhINTs requires heating to 81–100 °C (Table 3, entries 1 and 2). The reactivity of soluble *ortho-tert*-butylsulfonyl-substituted aryliminoiodanes is also noticeably lower (Table 3, entries 3 and 4). The higher reactivity of **3b** can be explained by its excellent solubility; however, the electronic effect of an *ortho*-substituent can also have a significant influence on the reactivity of ArINTs. It is generally assumed that reactions of ArINTs proceed through the formation of nitrene intermediates, although, several alternative pathways have been considered in the literature.[3h]

In summary, we have reported the preparation, X-ray structure, and reactivity of new, highly reactive nitrene precursors that are based on the *ortho*-alkoxyiodobenzene structural fragment. Owing to the presence of the *ortho* substituent on the phenyl ring, these new iminoiodanes have ex-

Table 3. Comparison of the reactivity of *o*-alkoxyphenyliminoiodane **3b** with other aryliminoiodanes ArINTs in the tosylimination reaction with Ph_3P.



Entry[ref.]	ArINTs	Solvent	*T* [°C]	*t* [h]	Yield of **9** [%]
1[10a]		none	100	–[a]	68
2[10b]		MeCN	81	1	69
3[3d]		$CDCl_3$	25	–[b]	83
4[3e]		$CDCl_3$	25	–[b]	60
5	**3b**	MeCN	25	0.2	90

[a] Reaction time is not provided in the reference.[10a] [b] According to NMR spectroscopic monitoring this reaction required several hours to complete at RT.[3d,e]

cellent solubility in organic solvents and are efficient reagents for the catalytic aziridination of alkenes or the metal-free tosylamination of silyl enol ethers and adamantane. These new reagents could find applications as useful alternatives to PhINTs nitrene precursors for the Cu-catalyzed aziridination of alkenes and the metal-free amination of organic substrates under homogeneous conditions.

Experimental Section

General procedure for the synthesis of *N*-(4-methylphenylsulfonyl)imino-2-alkoxyphenyl-λ^3-iodanes 3: 1-Diacetoxy-2-alkoxyphenyl-λ^3-iodane **2** (1.1 mmol) was added to a stirring mixture of potassium hydroxide (2.8 mmol) and *p*-toluene sulfonamide (1.1 mmol) in methanol (4.3 mL). The resulting clear yellow solution was stirred for 2.5 h at 0 °C, followed by 0.5 h at room temperature and then poured into distilled water (27 mL). Over a period of 12 h a yellow precipitate of product **3** formed, which was then filtered, washed several times with hexane and dried in a vacuum.

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Keywords: amination · aziridination · hypervalent compounds · iodine · oxidation

[1] Reviews: a) *Hypervalent Iodine Chemistry* (Ed.: T. Wirth), Springer, Berlin, **2003**; b) G. F. Koser, *Adv. Heterocycl. Chem.* **2004**, *86*, 225–292; c) R. M. Moriarty, *J. Org. Chem.* **2005**, *70*, 2893–2903; d) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2008**, *108*, 5299–5358; e) P. Dauban, R. H. Dodd, *Synlett* **2003**, 1571–1586; f) M. A. Ciufolini, N. A. Braun, S. Canesi, M. Ousmer, J. Chang, D. Chai, *Synthesis* **2007**, 3759–3772; g) V. V. Zhdankin, *Sci. Synth.* **2007**, *31a*, 161–233; h) M. Ochiai, K. Miyamoto, *Eur. J. Org. Chem.* **2008**, 4229–4239; i) T. Dohi, Y. Kita, *Chem. Commun.* **2009**, 2073–2085; j) S. Quideau, L. Pouysegu, D. Deffieux, *Synlett* **2008**, 467–495; k) V. V. Zhdankin, *ARKIVOC* **2009**, *I*, 1–62; l) M. Uyanik, K. Ishihara, *Chem. Commun.* **2009**, 2086–2099; m) M. Uyanik, K. Ishihara, *Aldrichimica Acta* **2010**, *43*, 83–91; n) E. A. Merritt, B. Olofsson, *Synthesis* **2011**, 517–538; o) J. P. Brand, D. F. Gonzalez, S. Nicolai, J. Waser, *Chem. Commun.* **2011**, *47*, 102–115; p) V. V. Zhdankin, *J. Org. Chem.* **2011**, *76*, 1185–1197; q) A. Duschek, S. F. Kirsch, *Angew. Chem.* **2011**, *123*, 1562–1590; *Angew. Chem. Int. Ed.* **2011**, *50*, 1524–1552; r) S. Quideau, T. Wirth, *Tetrahedron* **2010**, *66*, 5737–5738.

[2] a) J. W. W. Chang, P. W. H. Chan, *Angew. Chem.* **2008**, *120*, 1154–1156; *Angew. Chem. Int. Ed.* **2008**, *47*, 1138–1140; b) J. W. W. Chang, T. M. U. Ton, S. Tania, P. C. Taylor, P. W. H. Chan, *Chem. Commun.* **2010**, *46*, 922–924; c) Z. Li, D. A. Capretto, R. O. Rahaman, C. He, *J. Am. Chem. Soc.* **2007**, *129*, 12058–12059; d) C. Li, L. Zhang, *Org. Lett.* **2011**, *13*, 1738–1741; e) Z. Li, D. A. Capretto, R. Rahaman, C. He, *Angew. Chem.* **2007**, *119*, 5276–5278; *Angew. Chem. Int. Ed.* **2007**, *46*, 5184–5186; f) J. Llaveria, A. Beltran, M. M. Diaz-Requejo, M. I. Matheu, S. Castillon, P. J. Perez, *Angew. Chem.* **2010**, *122*, 7246–7249; *Angew. Chem. Int. Ed.* **2010**, *49*, 7092–7095; g) D. A. Evans, M. T. Bilodeau, M. M. Faul, *J. Am. Chem. Soc.* **1994**, *116*, 2742–2753; h) Z. Li, R. W. Quan, E. N. Jacobsen, *J. Am. Chem. Soc.* **1995**, *117*, 5889–5890; i) Z. Li, K. R. Conser, E. N. Jacobsen, *J. Am. Chem. Soc.* **1993**, *115*, 5326–5327; j) L. Ma, D.-M. Du, J. Xu, *Chirality* **2006**, *18*, 575–580; k) X. Wang, K. Ding, *Chem. Eur. J.* **2006**, *12*, 4568–4575; l) K. M. Gillespie, C. J. Sanders, P. O'Shaughnessy, I. Westmoreland, C. P. Thickitt, P. Scott, *J. Org. Chem.* **2002**, *67*, 3450–3458.

[3] a) C. J. Carmalt, J. G. Crossley, J. G. Knight, P. Lightfoot, A. Martin, M. P. Muldowney, N. C. Norman, A. G. Orpen, *J. Chem. Soc. Chem. Commun.* **1994**, 2367–2368; b) A. K. Mishra, M. M. Olmstead, J. J. Ellison, P. P. Power, *Inorg. Chem.* **1995**, *34*, 3210–3214; c) M. Boucher, D. Macikenas, T. Ren, J. D. Protasiewicz, *J. Am. Chem. Soc.* **1997**, *119*, 9366–9376; d) D. Macikenas, E. Skrzypczak-Jankun, J. D. Protasiewicz, *J. Am. Chem. Soc.* **1999**, *121*, 7164–7165; e) B. V. Meprathu, J. D. Protasiewicz, *Tetrahedron* **2010**, *66*, 5768–5774; f) B. V. Meprathu, J. D. Protasiewicz, *ARKIVOC* **2003**, *VI*, 83–90; g) A. J. Blake, A. Novak, M. Davies, R. I. Robinson, S. Woodward, *Synth. Commun.* **2009**, *39*, 1065–1075; h) R. D. Richardson, M. Desaize, T. Wirth, *Chem. Eur. J.* **2007**, *13*, 6745–6754.

[4] a) M. J. Zdilla, M. M. Abu-Omar, *Inorg. Chem.* **2008**, *47*, 10718–10722; b) M. J. Zdilla, J. L. Dexheimer, M. M. Abu-Omar, *J. Am. Chem. Soc.* **2007**, *129*, 11505–11511; c) F. Avenier, E. Goure, P. Dubourdeaux, O. Seneque, J.-L. Oddou, J. Pecaut, S. Chardon-Noblat, A. Deronzier, J.-M. Latour, *Angew. Chem.* **2008**, *120*, 727–729; *Angew. Chem. Int. Ed.* **2008**, *47*, 715–717; d) M. J. Zdilla, M. M. Abu-Omar, *J. Am. Chem. Soc.* **2006**, *128*, 16971–16979; e) F. Avenier, J.-M. Latour, *Chem. Commun.* **2004**, 1544–1545.

[5] a) A. Y. Koposov, R. R. Karimov, I. M. Geraskin, V. N. Nemykin, V. V. Zhdankin, *J. Org. Chem.* **2006**, *71*, 8452–8458; b) A. Yoshimura, C. T. Banek, M. S. Yusubov, V. N. Nemykin, V. V. Zhdankin, *J. Org. Chem.* **2011**, *76*, 3812–3819; c) V. V. Zhdankin, A. Y. Koposov, D. N. Litvinov, M. J. Ferguson, R. McDonald, T. Luu, R. R. Tykwinski, *J. Org. Chem.* **2005**, *70*, 6484–6491.

[6] CCDC-830952 (**2a**), 830953 (**2d**), 830954 (**3a**), and 830955 (**3c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[7] a) J. F. K. Müller, P. Vogt, *Tetrahedron Lett.* **1998**, *39*, 4805–4806; b) D. Leca, K. Song, M. Amatore, L. Fensterbank, E. Lacote, M. Malacria, *Chem. Eur. J.* **2004**, *10*, 906–916.

[8] B.-W. Lim, K.-H. Ahn, *Synth. Commun.* **1996**, *26*, 3407–3412.

[9] a) M. Johannsen, K. A. Jorgensen, *Chem. Rev.* **1998**, *98*, 1689–1708; b) A. A. Lamar, K. M. Nicholas, *J. Org. Chem.* **2010**, *75*, 7644–7650.

[10] a) Y. Yamada, T. Yamamoto, M. Okawara, *Chem. Lett.* **1975**, 361–362; b) W. Ou, Z.-G. Wang, Z.-C. Chen, *Synth. Commun.* **1999**, *29*, 2301–2309.

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