ORGANIC LETTERS

2005
Vol. 7, No. 26
5801−5804

Aryl Iodide Mediated Aziridination of Alkenes

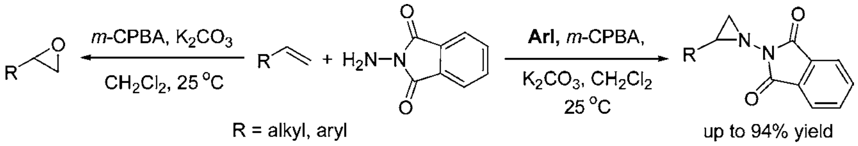
Jiayin Li,[†] Philip Wai Hong Chan,[‡] and Chi-Ming Che*,[†,‡]

Shanghai-Hong Kong Joint Laboratory on Chemical Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, P. R. China, and Department of Chemistry and Open Laboratory of Chemical Biology of the Institute of Molecular Technology for Drug Discovery and Synthesis, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China

cmche@hku.hk

Received September 22, 2005

ABSTRACT



Aryl iodide mediated aziridination of a variety of alkenes with *N*-aminophthalimide under mild conditions (*m*-CPBA, K_2CO_3, CH_2Cl_2, 25 °C) was achieved in moderate to good yields (up to 94%). By recovering the aryl iodide, a recyclable system is developed with product yield over 79% attained for the aziridination of *trans*-1,2-diphenylethylene.

Aryl-λ^3-iodane mediated organic transformations have attracted a myriad of attention in recent years due to the useful oxidative properties of hypervalent iodine(III) compounds and the benign ecological character and commercial availability of aryl-λ^3-iodane precursors.[1] Indeed, works by us[2] and others[3] have shown that polyvalent iodine(III) compounds such as $PhI{=}NSO_2R$ (usually R = Ar), PhI=O, and $PhI(OAc)_2$ have useful applications in transition metal catalyzed C−N bond forming reactions. In this regard, we[4] and Yudin et al.[5] reported that a $PhI(OAc)_2$ mediated version of the lead(IV) acetate[6] catalyzed intermolecular aziridination of alkenes using *N*-aminophthalimide ($PthNH_2$) as a nitrogen source could be accomplished in good to excellent yields. Despite these advances, the challenge remains to develop

---

[†] Shanghai Institute of Organic Chemistry.

[‡] The University of Hong Kong.

(1) (a) *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; Springer: Berlin, 2003; *Top. Curr. Chem.* issue 224. (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523.

(2) (a) Zhang, J.; Chan, P. W. H.; Che, C.-M. *Tetrahedron Lett.* **2005**, *46*, 5403. (b) He, L.; Chan, P. W. H.; Tsui, W.-M.; Yu, W.-Y.; Che, C.-M. *Org. Lett.* **2004**, *6*, 2405. (c) Liang, J.-L.; Yuan, S.-X.; Huang, J.-S.; Che, C.-M. *J. Org. Chem.* **2004**, *69*, 3610. (d) Liang, J.-L.; Yuan, S.-X.; Chan, P. W. H.; Che, C.-M. *Tetrahedron Lett.* **2003**, *44*, 5917. (e) Liang, J.-L.; Huang, J.-S.; Yu, X.-Q.; Zhu, N.; Che, C.-M. *Chem. Eur. J.* **2002**, *8*, 1563. (f) Liang, J.-L.; Yu, X.-Q.; Che, C.-M. *Chem. Commun.* **2002**, 124. (g) Zhang, J.-L.; Che, C.-M. *Org. Lett.* **2002**, *4*, 1911. (h) Liang, J.-L.; Yuan, S.-X.; Huang, J.-S.; Yu, W.-Y.; Che, C.-M. *Angew. Chem., Int. Ed.* **2002**, *41*, 3465. (i) Liang, J.-L.; Yuan, S.-X.; Chan, P. W. H.; Che, C.-M. *Org. Lett.* **2002**, *4*, 4507. (j) Yu, X.-Q.; Huang, J.-S.; Zhou, X.-G.; Che, C.-M. *Org. Lett.* **2000**, *2*, 2233. (k) Au, S.-M.; Huang, J.-S.; Yu, W.-Y.; Fung, W.-H.; Che, C.-M. *J. Am. Chem. Soc.* **1999**, *121*, 9120. (l) Au, S.-M.; Zhang, S.-B.; Fung, W.-H.; Yu, W.-Y.; Che, C.-M.; Cheung, K.-K. *Chem. Commun.* **1998**, 2677.

(3) For recent reviews, see: (a) Davies, H. M. L.; Long, M. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 3518. (b) Müller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905. (c) Katsuki, T. *Synlett* **2003**, 281. For selected works by others, see: (d) Catino, A. J.; Nichols, J. M.; Forslund, R. E.; Doyle, M. P. *Org. Lett.* **2005**, *7*, 2787. (e) Fruit, C.; Müller, P. *Helv. Chim. Acta* **2004**, *87*, 1607. (f) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378. (g) Levites-Agababa, E.; Menhaji, E.; Perlson, L. N.; Rojas, C. M. *Org. Lett.* **2002**, *4*, 863. (h) Padwa, A.; Stengel, T. *Org. Lett.* **2002**, *4*, 2137. (i) Guthikonda, K.; Du Bois J. *J. Am. Chem. Soc.* **2002**, *124*, 13672. (j) Espino, C. G.; Wehn, P. M.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935. (k) Dauban, P.; Sanière, L.; Tarrade, A.; Dodd, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 7707. (l) Müller, P.; Baud, C.; Jacquier, Y. *Can. J. Chem.* **1998**, *76*, 738. (m) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742. (n) Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326. (o) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. *Tetrahedron Lett.* **1988**, *29*, 1927. (p) Breslow, R.; Gellman, S. H. *Chem. Commun.* **1982**, 1400.

(4) Li, J.; Liang, J.-L.; Chan, P. W. H.; Che, C.-M. *Tetrahedron Lett.* **2004**, *45*, 2685.

(5) Krasnova, L. B.; Hili, R. M.; Chernoloz, O. V.; Yudin A. K. *ARKIVOC* **2005**, *4*, 26.

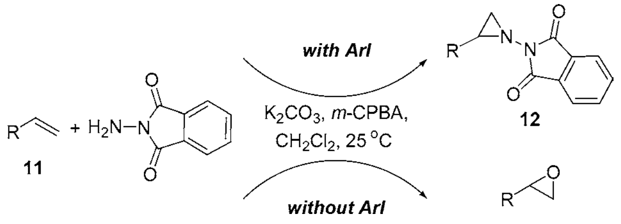
(6) (a) Yang, K.-S.; Chen, K. *Org. Lett.* **2002**, *4*, 1107. (b) Atkinson, R. S. *Tetrahedron* **1999**, *55*, 1519. (c) Kapron, J. T.; Santarsiero, B. D.; Vederas, J. C. *Chem. Commun.* **1993**, 1074. (d) Atkinson, R. S.; Jones, D. W.; Kelly, B. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1344.

10.1021/ol052293c CCC: $30.25

less toxic and inexpensive alternatives to aryl-λ^3-iodane reagents such as $PhI(OAc)_2$. Such reagents would be desirable in view of the growing interest and needs of the chemical industry to develop nontoxic and inexpensive catalysts that can mediate a wide variety of chemical processes.

As part of an ongoing program aimed at developing polyvalent iodine(III) reagents for C−N bond formation, we examined the potential applications of aryl iodides for stereoselective nitrogen atom transfer reactions such as alkene aziridination. Herein we describe the realization of a "ArI + $PthNH_2$" protocol that is useful for the construction of aziridines[7] under mild conditions (Scheme 1). Notable observations we have made for this intermolecular C−N bond formation process are: (1) in the absence of ArI, complete chemo-switching occurs and the epoxide product is furnished with quantitative recovery of $PthNH_2$, and (2) it is possible to recover and recycle the ArI systems we have employed. Since the completion of this work, the groups of Kita[8] and Ochiai[9] have reported the use of a variety of aryl iodides as recyclable catalysts for various organic oxidations that proceeded in moderate to good yield.

Scheme 1



At the outset of this study, we examined the effect of several substituted aryl iodides **1**−**10** (Figure 1) on the outcome of various intermolecular alkene aziridination reactions. The aryl iodide reagents **1**−**10** were prepared following literature methods[8] or purchased from commercial sources.[10] With styrene **11a** as our initial probe substrate, a survey of different reaction conditions revealed that aziridination of **11a** was best performed in the presence of $PthNH_2$ (1.4 equiv), *m*-CPBA (2 equiv), and K_2CO_3 (3 equiv) in CH_2Cl_2 at 25 °C for 12 h with 1.4 equiv of *p*-$MeOC_6H_4I$ (**1**) as aryl iodide source (Table 1, entry 1). Under these conditions, 2-(2-phenyl-aziridin-1-yl)-isoindole-1,3-dione **12a** was obtained in 81% yield. Slightly lower product yields (66−70%) were obtained upon lowering the loading of **1** from 1.4 to 1 equiv or in the absence of K_2CO_3. A markedly lower product yield (31%) was found when the reaction was conducted with 0.6 equiv of **1** (entries 2−4). In contrast, on changing the oxidant from *m*-CPBA to either Na_2O_2, $NaBO_3$, ${}^tBuO_2H$, or oxone no reaction was found on the basis of ${}^1H$ NMR analysis.

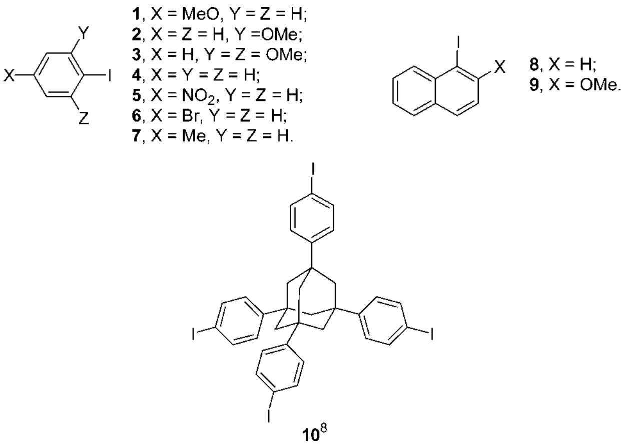
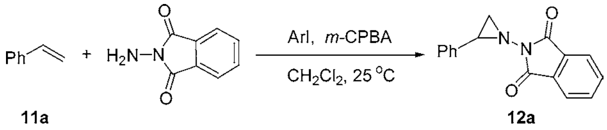


Figure 1. Aryl iodides used in this work.

Inspection of entries 5−7, 9−11, and 13 in Table 1 reveals that the intermolecular aziridinations of **11a** with other aryl iodides are slightly less effective. Under the conditions of 1 equiv of **11a**, $PthNH_2$ (1.4 equiv), and *m*-CPBA (2 equiv) in CH_2Cl_2 at 25 °C for 12 h, aziridination with 1 equiv of **2**−**4**, **6**−**8**, or **10** as the ArI source gave **12a** in 49−65%

Table 1. Optimization of Reaction Conditions[a]



entry	ArI	yield (%)[b]
1[c]	**1**	81
2[d]	**1**	70
3	**1**	66
4[e]	**1**	31
5	**2**	64
6	**3**	65
7	**4**	49
8	**5**	26
9	**6**	51
10	**7**	55
11	**8**	60
12	**9**	27
13	**10**	65

[a] All reactions were performed in CH_2Cl_2 at 25 °C for 12 h with styrene/ArI/$PthNH_2$/*m*-CPBA ratio of 1:1:1.4:2. [b] Isolated yield. [c] Conducted with 1.4 equiv of **1** and 3 equiv of K_2CO_3. [d] Conducted with 1 equiv of **1** and 3 equiv of K_2CO_3. [e] Conducted with 0.6 equiv of **1**.

---

(7) For some applications of aziridines in organic and natural product synthesis, see: (a) Hale, K. J.; Domostoj, M. M.; Tocher, D. A.; Irving, E.; Scheinmann, F. *Org. Lett.* **2003**, *5*, 2927. (b) Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247. (c) McCoull, W.; Davis, F. A. *Synthesis* **2000**, *10*, 1347. (d) Roth. P.; Andersson, P. G.; Somfai, P. *Chem. Commun.* **2002**, 1752. (e) Dodd, R. H. *Molecules* **2000**, *5*, 293. (f) Atkinson, R. S. *Tetrahedron* **1999**, *55*, 1519. (g) Stamm, H. *J. Prakt. Chem.* **1999**, *341*, 319. (h) Cantrill, A. A.; Osborn, H. M. I.; Sweeney, J. *Tetrahedron* **1998**, *54*, 2181. (i) Tanner, D. *Angew. Chem., Int. Ed.* **1994**, *33*, 599. (j) Tanner, D.; He, H. M. *Tetrahedron* **1992**, *48*, 6079. (k) Tanner, D.; He, H. M.; Somfai. P. *Tetrahedron* **1992**, *48*, 6069.

(8) Tohma, H.; Maruyama, A.; Maeda, A.; Maegawa, T.; Dohi, T.; Shiro, M.; Morita, T.; Kita, Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 3595.

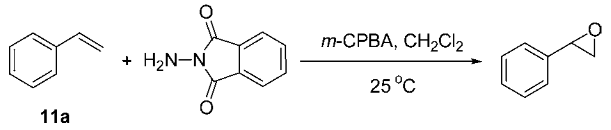
(9) Ochiai, M.; Takeuchi, Y.; Katayama, T.; Sueda, T.; Miyamoto, K. *J. Am. Chem. Soc.* **2005**, *127*, 12244.

(10) ArI **1**−**9** are commercially available from Sigma-Aldrich.

yield. Reactions of **11a** with either **5** or **9** as ArI source are the only instances where markedly lower yields of 26% and 27%, respectively, were obtained (entries 8 and 12).

At this juncture, we would like to highlight that employment of aryl iodide for the aziridination reaction is essential. As depicted in Scheme 2, under our experimental conditions, the reaction of 1 equiv of **11a**, 1.4 equiv of $PthNH_2$, and 3 equiv of *m*-CPBA in CH_2Cl_2 at 25 °C for 12 h gave styrene oxide in 40% yield; the absence of ArI seemed to act as a trigger for chemo-switching from C−N to C−O bond formation (see later section).

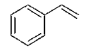
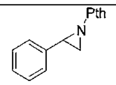
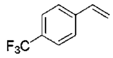
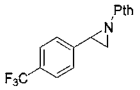
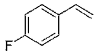
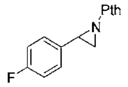
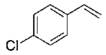
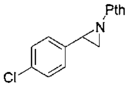
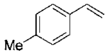
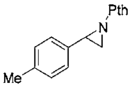
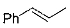
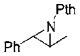
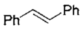
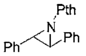
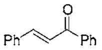
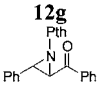
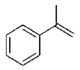
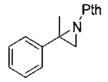
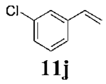
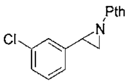
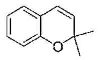
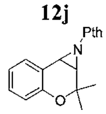
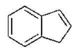
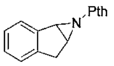
Scheme 2



To define the scope of **1**-mediated aziridination reactions, we applied this process on a series of terminal and internal alkenes **11b−l** (Table 2). These reactions afforded the corresponding aziridines **12b−l** in moderate to good yields (up to 94%) (entries 2−12). The highest product yield of 94% attained in this work was for the intermolecular aziridination of 1,3-diphenyl-propen-3-one **11h** (entry 8). To our knowledge, this represents the highest product yield so far achieved for **1**-mediated aziridination of alkenes using $PthNH_2$ as the nitrogen source under mild oxidizing conditions. Notably, the electron-rich or -deficient nature of C=C bond was found to have a marked effect on reaction yield. In general, electron-deficient alkenes were found to proceed in ≥11% higher product yields than those with electron-donating substituents (cf. entries 2−4 and 8 vs 5, 6, and 9). Conformationally restricted alkenes, such as 2,2-dimethyl-2*H*-chromene **11k** and 1*H*-indene **11l**, were also found to undergo intermolecular aziridination, to give aziridines **12k** and **12l** in 60 and 50% yield, respectively (entries 11 and 12).

As shown in Table 2, a comparison of the **1**-mediated aziridinations of **11a−l** with the analogous reactions using $PhI(OAc)_2$ as aryl iodide source revealed that in the latter, comparable product yields of 84−93% were obtained for reactions of **11a** and **11g−h** (entries 1, 7, and 8), but ≥9% lower product yields were found for reactions of **11b−d**, **11f**, and **11l** (entries 2−4, 6, and 12). In addition, $PhI(OAc)_2$ was found in this work to be unable to mediate the aziridination of **11i** and **11j**; in both instances, the alkene starting material was recovered in quantitative yield (entries 9 and 10). $PhI(OAc)_2$-mediated aziridinations of **11e** and **11k** are the only examples where higher product yields of 70% were obtained (entries 5 and 11).

Table 2. Intermolecular **1**-Mediated Aziridination with $PthNH_2$ as Nitrogen Source and Comparison with the Analogous $PhI(OAc)_2$-Mediated Reactions

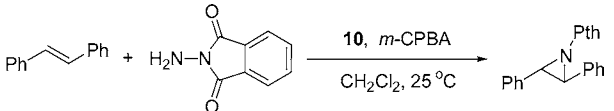
entry	substrate	product	yield (%)[a]	
			1[b]	$PhI(OAc)_2$[c]
1	 **11a**	 **12a**	81	84
2	 **11b**	 **12b**	79	62
3	 **11c**	 **12c**	82	56
4	 **11d**	 **12d**	82	73
5	 **11e**	 **12e**	49	70
6	 **11f**	 **12f**	68	35
7	 **11g**	 **12g**	84	89
8	 **11h**	 **12h**	94	93
9	 **11i**	 **12i**	57	-[d]
10	 **11j**	 **12j**	80	-[d]
11	 **11k**	 **12k**	60	70
12	 **11l**	 **12l**	50	41

[a] Isolated yield. [b] All reactions were performed in CH_2Cl_2 at 25 °C for 12 h with alkene/**1**/$PthNH_2$/*m*-CPBA/K_2CO_3 ratio of 1:1.4:1.4:2:3. [c] All reactions were performed in CH_2Cl_2 at 25 °C for 12 h with alkene/$PhI(OAc)_2$/$PthNH_2$/K_2CO_3 ratio of 1:1.5:1.4:2.8. [d] No reaction.

In this work, a recyclable aryl iodide system for aziridination of alkenes was developed. Addition of **11g** (1 equiv) to a CH_2Cl_2 solution containing **10** (1.4 equiv), $PthNH_2$ (1.4 equiv), and *m*-CPBA (2 equiv) at 25 °C followed by subsequent stirring for 12 h gave **12g** in 87% yield (Table 3, entry 1). The aryl iodide **10** was recovered and subjected to another five consecutive reactions under the same conditions mentioned above (see Supporting Information for details). As shown in entries 2−6 in Table 3, product yields of 80%, 82%, 89%, 84%, and 79% were achieved for each consecutive reaction and no apparent loss of activity was observed.

The proposed mechanism for the **1**-mediated aziridination of alkenes is depicted in Scheme 3.[11] We postulate that $PthNH_2$ is oxidized by $Ar^1I(OCOAr^2)_2$ (Ar^1 = *p*-$MeOC_6H_4$, Ar^2 = *m*-ClC_6H_4), the latter is produced in situ from

Table 3. Recyclable Aryl Iodide **10** for Alkene Aziridination Reaction[a]



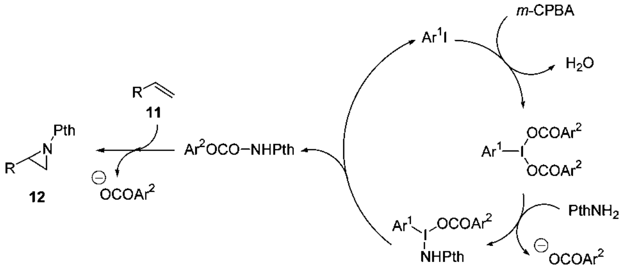
11g **12g**

entry	yield (%)[b]
1	87
2	80
3	82
4	89
5	84
6	79

[a] All reactions were performed in CH_2Cl_2 at 25 °C for 12 h with **11g**/**10**/$PthNH_2$/*m*-CPBA/K_2CO_3 ratio of 1:1.4:1.4:2:3. [b] Isolated yield.

oxidation of **1** by *m*-CPBA. Dissociation of Ar^1I from the newly formed $Ar^1I(OCOAr^2)(NHPth)$ intermediate results in the generation of *N*-benzoyloxyaminophthalimide, the active species that undergoes C═C bond addition and cyclization to give the aziridine **12**.[12] The role of **1** seems to facilitate formation of the aryl-λ^3-iodane species. As mentioned in an earlier section, this is supported by the reaction of **11a** in the absence of **1**, which gave styrene oxide (without competitive formation of **12a**) and quantitative recovery of $PthNH_2$. The involvement of such polyvalent iodine(III) intermediates is further supported by the systematic decrease in product yields from 81% to 31% with a decrease in aryl iodide loading from 1.4 to 0.6 equiv and detection of no aziridine product for reactions conducted with oxidants other than *m*-CPBA.

Scheme 3



In summary, we have developed an efficient and recyclable method for mediating alkene aziridination that is practical, nontoxic, and inexpensive. The method probably involves in situ generation of an aryl-λ^3-iodane species from oxidation of the aryl iodide with *m*-CPBA. Reaction of this intermediate with $PthNH_2$ produces the active species of the alkene aziridination step. Efforts are currently underway to develop an asymmetric aryl iodide mediated version of the present reaction and its application to the total synthesis of natural products.

Acknowledgment. This work is supported by the Area of Excellence Scheme (AoE/P-10-01) established under the University Grants Committee (HKSAR), the Hong Kong Research Grants Council (HKU7011/04P), CAS-Croucher Foundation and the University Development Fund of The University of Hong Kong. P.W.H.C. wishes to thank The University of Hong Kong (Small Project Funding Programme) for funding.

Supporting Information Available: Detailed experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL052293C

---

(11) A similar mechanism has been proposed for the analogous $PhI(OAc)_2$- and $Pb(OAc)_4$-mediated aziridinations. For $PhI(OAc)_2$-mediated reaction; see ref 5. For $Pb(OAc)_4$-mediated reactions, see ref 6c,d and (a) Atkinson, R. S.; Grimshire, M. J.; Kelly, B. J. *Tetrahedron* **1989**, *45*, 2875. (b) Atkinson, R. S.; Malpass, J. R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2242.

(12) It is possible that the *N*-benzoyloxyaminophthalimide intermediate may eliminate Ar^2CO_2H to give a nitrene species.