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2017

Tejo, C., Tirtorahardjo, D., Day, D. P., Ma, D.-L., Leung, C.-H., & Chan, P. W. H. (2017).
Brønsted Base-Mediated Aziridination of 2-Alkyl-Substituted-1,3-Dicarbonyl Compounds
and 2-Acyl-Substituted-1,4-Dicarbonyl Compounds by Iminoiodanes. *Australian Journal of
Chemistry*, 70(4), 430-435.

<https://hdl.handle.net/10356/86641>

<https://doi.org/10.1071/CH16580>

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The published version is available at: [<http://dx.doi.org/10.1071/CH16580>].

Brønsted Base-Mediated Aziridination of 2-Alkyl-Substituted-1,3-Dicarbonyl Compounds and 2-Acyl-Substituted-1,4-Dicarbonyl Compounds by Iminoiodanes

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The synthesis α,α -diacylaziridines and α,α,β -triacylaziridines from reaction of 2-alkyl-substituted-1,3-dicarbonyl compounds and 2-acyl-substituted-1,4-dicarbonyl compounds with arylsulfonyliminoiodanes ($\text{PhI}=\text{NSO}_2\text{Ar}$) under Brønsted base-mediated atmospheric conditions is described. The reaction mechanism was thought to involve the formal oxidation of the substrate followed by aziridination of the ensuing α,β -unsaturated intermediate by the hypervalent iodine(III) reagent.

Manuscript received: 2016.

Manuscript accepted: 2016.

Published online: 2016.

Aziridines are versatile building blocks in organic synthesis as well as a structural motif found in many bioactive natural products and compounds of pharmaceutical interest.^[1–23] As a consequence, this has prompted a significant amount of effort toward the development of a myriad of synthetic methods to efficiently and selectively prepare the three-membered nitrogen-containing heterocycle.^[24–38] As part of an ongoing program exploring the reaction chemistry of iminoiodanes,^[39–70] we recently reported a facile synthetic approach to α,α -diacylaziridines involving Cu(II)-catalyzed aziridination of 2-alkyl-substituted 1,3-dicarbonyl compounds with p -TsN=IPh (Scheme 1a).^[38] Building on this initial work, we queried whether the construction of the aziridine motif in this manner could be achieved in the analogous reactions under transition metal-free mediated conditions (Scheme 1b).^[64–66,71–81] In doing so, we report herein the aziridination of 2-alkyl-substituted-diethyl malonates and β -ketoesters in the presence of a Brønsted base

and o -NsN=IPh under atmospheric conditions to give the corresponding α,α -diacylaziridine products in moderate to excellent yields. Under similar reaction conditions, the aziridination of 2-acyl-substituted-succinates and dimethyl 2-(2-oxo-substituted)malonates by o -NsN=IPh to produce α,α,β -triacylaziridines in good yields is also presented.

Our studies commenced began by examining the Brønsted base-mediated aziridination of diethyl ethylmalonate **1a** by p -NsN=IPh to establish the optimum conditions for this reaction (Table 1). This initially revealed that treating the substrate with 2.2 equiv of p -NsN=IPh and 1.1 equiv of K_2CO_3 in acetonitrile at room temperature under atmospheric conditions gave the 1,1-diacylaziridine **2a** and α,β -unsaturated 1,3-dicarbonyl compound **3a** in 70 and 23% yield, respectively (Table 1, entry 1). Changing the base to other inorganic bases such as Na_2CO_3 or t -BuOK led to the recovery of the starting material (Table 1, entries 2 and 3). On the other hand, replacing K_2CO_3 with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) as the base in reactions with 3.3 or 2.2 equiv of p -NsN=IPh was found to lead to the aziridine adduct being the only product obtained in yields 71 and 72% (Table 1, entries 4 and 5). Lower product yields of 29 and 21% were observed when the amount of DBU was reduced from 2.2 equiv to 20 and 10 mol % (Table 1, entries 6 and 7). On the other hand, increasing the concentration of the reaction mixture from 0.1 M to 0.2 M at a catalyst loading of 20 mol % was found to give a product yield of 71% (Table 1, entry 8). Replacing the Brønsted base catalyst with other organic bases such as MTBD

Scheme 1. Aziridination of 2-alkyl substituted-1,3-dicarbonyl compounds with arylsulfonyliminoiodanes

(7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene) and DABCO (1,4-diazabicyclo[2.2.2]octane) gave either a lower product yield of 58% or no product formation, respectively (Table 1, entries 9 and 10). An examination of the solvent effect on the aziridination reaction revealed that with THF or toluene in place of MeCN as the solvent resulted in no reaction based on TLC analysis and ^1H NMR measurements of the crude mixtures but a product yield of 74% when CH_2Cl_2 was used as solvent (Table 1, entries 11–13). At a catalyst loading of 20 mol %, our subsequent studies found that changing the arylsulfonyl-substituted iminoiodane source from $p\text{-NsN=IPh}$ to $o\text{-NsN=IPh}$ ($o\text{-Ns}$ = o -nitrobenzenesulfonyl) gave the best result, affording **2b** in 97% yield (Table 1, entry 14). In a final control experiment, repeating the DBU-mediated reaction with $p\text{-TsN=IPh}$ instead of $p\text{-NsN=IPh}$ to give **2c** in a yield of 12% (Table 1, entry 15). In comparison, the analogous reaction catalyzed by $\text{Cu}(\text{OTf})_2/1,10\text{-phenanthroline}$ was reported to give a product yield of 81%.^[38]

Table 1. Optimization of the reaction conditions^a

				2a , Ar = $p\text{-NO}_2\text{C}_6\text{H}_4$ 2b , Ar = $o\text{-NO}_2\text{C}_6\text{H}_4$ 2c , Ar = $p\text{-MeC}_6\text{H}_4$
Entry	Brønsted Base (equiv)	$\text{ArSO}_2\text{N=IPh}$ (equiv)	Solvent	Yield (%) ^b
1	K_2CO_3 (1.1)	$p\text{-NsN=IPh}$ (3)	MeCN	70 ^c
2	$t\text{-BuOK}$ (1.1)	$p\text{-NsN=IPh}$ (3)	MeCN	-
3	Na_2CO_3 (1.1)	$p\text{-NsN=IPh}$ (3)	MeCN	-
4	DBU (1.1)	$p\text{-NsN=IPh}$ (2.2)	MeCN	71
5	DBU (1.1)	$p\text{-NsN=IPh}$ (2.2)	MeCN	72
6 ^d	DBU (0.2)	$p\text{-NsN=IPh}$ (2.2)	MeCN	29
7 ^d	DBU (0.2)	$p\text{-NsN=IPh}$ (2.2)	MeCN	71
8 ^d	DBU (0.1)	$p\text{-NsN=IPh}$ (2.2)	MeCN	21
9 ^d	MTBD (0.2)	$p\text{-NsN=IPh}$ (2.2)	MeCN	58
10 ^d	DABCO (0.2)	$p\text{-NsN=IPh}$ (2.2)	MeCN	-
11 ^d	DBU (0.2)	$p\text{-NsN=IPh}$ (2.2)	THF	-
12 ^d	DBU (0.2)	$p\text{-NsN=IPh}$ (2.2)	toluene	-
13 ^d	DBU (0.2)	$p\text{-NsN=IPh}$ (2.2)	CH_2Cl_2	74
14 ^d	DBU (0.2)	$o\text{-NsN=IPh}$ (2.2)	MeCN	97 ^c
15 ^d	DBU (0.2)	$p\text{-TsN=IPh}$ (2.2)	MeCN	12[81] ^e

^aAll reactions were performed with **1a** (1 equiv) at a concentration of 0.1 M at room temperature under atmospheric conditions for 18 h. ^bProduct yield was determined by ^1H NMR analysis of the crude mixture with CH_2Br_2 as the internal standard. ^cIsolated product yield. ^dReaction performed with **1a** at a concentration of 0.2 M. ^eValue in square brackets denotes the yield of **2c** obtained from the analogous reaction catalyzed by $\text{Cu}(\text{OTf})_2/1,10\text{-phenanthroline}$ under the conditions described in ref [44].

A survey of the present DBU-catalyzed procedure with other 2-alkyl substituted-1,3-dicarbonyl compounds showed reaction of the diethyl malonate **1d**, containing a $n\text{-Pr}$ group at the C-2 position, was found to provide **2d** in 80% yield (Table 2). Under similar reaction conditions, the aziridination of the 2-methyl-substituted β -keto ester **1e** was found to furnish the corresponding

Table 2. Brønsted base-mediated aziridination of 1d–l

^aMethod (a): reaction performed in MeCN at a concentration of 0.2 M in a ratio of $o\text{-NsN=IPh}:\mathbf{1}:\text{DBU} = 11:5:1$ at room temperature under atmospheric conditions for 18 h and values in parentheses denote isolated product yields. ^bValues in square brackets denote the product yield obtained from the analogous reactions of **1d**, **1e** and **1g** with $p\text{-TsN=IPh}$ catalyzed by $\text{Cu}(\text{OTf})_2/1,10\text{-phenanthroline}$ under the conditions described in ref [44]. ^cUnidentifiable decomposition products obtained. ^dMethod (b): reaction carried out in CH_2Cl_2 at a concentration of 0.2 M in a ratio of $o\text{-NsN=IPh}:\text{K}_2\text{CO}_3:\mathbf{1} = 3:1.1:1$ at 40 °C under atmospheric conditions for 18 h and values in parentheses denote isolated product yields.

product **2e** in 25% yield. However, the analogous experiment with the cyclopentanone derivative **1f** led to a complex concoction of unidentifiable byproducts based on ^1H NMR analysis of the crude reaction mixture. In our hands, the reactions of the 2-acyl-substituted-1,4-dicarbonyl compounds **1g–l** were observed to provide higher product yields with the K_2CO_3 -mediated conditions described in Table 1, entry 1 at 40 °C. The application of these second set of conditions to the reactions of diethyl succinates with a pendant methyl ketone (**1g**) or ethyl ester (**1h**) group gave the corresponding aziridines **2g** and **2h** in respective yields of 61 and 45% yield. Likewise, methyl and ethyl 4-oxo-4-arylbutanoates containing a methyl ester (**1i,k,l**) or ethyl ester (**1j**) moiety were found to proceed well. In these experiments, the corresponding α,α,β -triacylaziridine adducts **2i–l** were obtained in 37–58% yield with the structure of **2i** being confirmed by X-ray crystallography (Figure 1).^[82] The reactions of **1d** and **1g** were also found to give product yields that were either comparable or slightly lower than those obtained from the analogous experiments with these substrates with $p\text{-TsN=IPh}$ catalyzed by $\text{Cu}(\text{OTf})_2/1,10\text{-phenanthroline}$.^[38] The only exception was the reaction of **1e**, which was found to give a low product yield of 25% under the present Brønsted base-mediated conditions.

While fortuitous, the isolation of the α,β -unsaturated 1,3-dicarbonyl compound **3a** led us to speculate of its possible involvement in the reaction mechanism of the present

Figure 1. ORTEP drawing of **2i** with thermal ellipsoids at 50% probability levels.^[51]

transformation. A consequence of this would be the decomposition of *o*-NsN=IPh to *o*-NsNH₂ and PhI with the *in situ* formed sulfonamide subsequently initiating a iminoiodane-mediated Michael-initiated ring closure (MIRC) reaction and product formation.^[83–88] To verify this hypothesis as well as gain a better understanding of how the present aziridination process might proceed, we next conducted a series of control reactions with **3a** (Scheme 2). In an initial control reaction, subjecting **3a** to 20 mol% of DBU and 1.1 equiv of *o*-NsN=IPh in acetonitrile at room temperature for 18 h was found to afford **2b** in 20% yield (Scheme 2a). Conducting this control experiment again with *o*-NsNH₂ in place of *o*-NsN=IPh was found to provide the sulfonamide compound **4b** in 27% yield (Scheme 2b). In a third control reaction, the *N*-heterocyclic product was then furnished in 79% yield when the α,β -unsaturated 1,3-dicarbonyl compound was treated to the DBU-catalyzed conditions in the presence of an

Scheme 2. Control experiments with **3a**. [a] ¹H NMR yield with CH₂Br₂ as the internal standard.

equimolar amount of both the iminoiodane and sulfonamide (Scheme 2c). The possibility of a pathway involving compound **4b** was further supported by treating **3a** to 20 mol% of DBU and 1.1 equiv of *o*-NsNH₂ in toluene at room temperature for 6 h (Scheme 2d). Subsequent addition of 1.1 equiv of *o*-NsN=IPh to the ensuing reaction mixture containing the sulfonamide in 49% yield, as determined by ¹H NMR analysis with CH₂Br₂ as the internal standard, in acetonitrile at room temperature for 18 h was then shown to give the aziridine **2b** in 40% yield. In a final set of control experiments with **3a**, only the recovery of the substrate was detected when each of the above control reactions were repeated under the conditions described in Scheme 2 but in the absence of the Brønsted base.

On the basis of the above results, a tentative mechanism for the present Brønsted base-mediated aziridination reactions is illustrated in Scheme 3. This could initially involve the Brønsted base-promoted tautomerization of the substrate **1** to give the enol isomer **I**. Nucleophilic attack of this tautomer onto the iodine centre in *o*-NsN=IPh might then produce the putative iodinated species **II**.^[89–100] Intramolecular deprotonation of the β -methylene centre by the sulfonamide motif and diiodination in this newly formed adduct would afford intermediate **3** along with the release of *o*-NsNH₂ and PhI. At this juncture, an iminoiodane-mediated MIRC may now come into play with the 1,4-conjugate addition of *o*-NsNH₂ to the Michael acceptor site of **3** to furnish the posited 1,3-amino enol **III**.^[83–88] A second nucleophilic addition step involving this adduct and another molecule of *o*-NsN=IPh could occur to give the iodinated 1,3-dicarbonyl compound **IV**. Subsequent diiodination of this hypervalent iodine(III) adduct followed by deaminative cyclization of the ensuing disulfonamide adduct **V** might then deliver the aziridine product **2**.^[89–100]

Scheme 3. Proposed mechanism for the Brønsted base-mediated aziridination reaction

In summary, we have developed a transition metal-free synthetic strategy to access α,α -diacylaziridines and α,α,β -triacylaziridines that relies on the aziridination of the respective 2-alkyl-substituted-1,3-dicarbonyl compounds and 2-acyl-substituted-1,4-dicarbonyl compounds. While the substrate scope of the present methodology was found to be less broad than the analogous Cu(II)-catalyzed approach,^[44] it was shown to be more practical as it did not require the need for inert reaction

conditions. Efforts to explore the synthetic applications of the present reactions are currently underway and will be reported in due course.

Supplementary Material

Detailed experiment procedures, characterization data and ^1H and ^{13}C NMR spectra for compounds **2**, **3a** and **4a** are available on the Journal's website.

Acknowledgements

This work was supported by start-up grants from the School of Chemistry, Monash University and the Department of Chemistry, University of Warwick.

References

- [1] Recent reviews on the synthetic utility of aziridines, see refs [2–6]
- [2] Z. He, A. Zajdlík, A. K. Yudin, *Acc. Chem. Res.* **2014**, *47*, 1029. DOI: 10.1021/ar400210c
- [3] E. A. Ilardi, J. T. Njardarson, *J. Org. Chem.* **2013**, *78*, 9533. DOI: 10.1021/jo401776s
- [4] R. Chawla, A. K. Singh, L. D. S. Yadav, *RSC Adv.* **2013**, *3*, 11385. DOI: 10.1039/C3RA00175J
- [5] S. Stankovic, M. D'Hooghe, S. Catak, H. Eum, M. Waroquier, V. Van Speybroeck, N. De Kimpe, H.-J. Ha, *Chem. Soc. Rev.* **2012**, *41*, 643. DOI: 10.1039/C1CS15140A
- [6] D. M. Hodgson, P. G. Humphreys, S. P. Hughes, *Pure Appl. Chem.* **2007**, *79*, 269. DOI: 10.1351/pac200779020269
- [7] Recent examples on the synthetic utility of aziridines, see refs [8–14]
- [8] S. P. Chavan, L. B. Khairnar, K. P. Pawar, P. N. Chavan, S. A. Kawale, *RSC Adv.* **2015**, *5*, 50580. DOI: 10.1039/C5RA06429E
- [9] C.-Y. Huang, A. G. Doyle, *J. Am. Chem. Soc.* **2015**, *137*, 5638. DOI: 10.1021/jacs.5b02503
- [10] A. P. Treder, J. L. Hickey, M.-C. J. Tremblay, S. Zaretsky, C. C. G. Scully, J. Mancuso, A. Doucet, A. K. Yudin, E. Marsault, *Chem. Eur. J.* **2015**, *21*, 9249. DOI: 10.1002/chem.201403083
- [11] G. Wang, J. Franke, C. Q. Ngo, M. J. Krische, *J. Am. Chem. Soc.* **2015**, *137*, 7915. DOI: 10.1021/jacs.5b04404
- [12] S. Nakamura, M. Ohara, M. Koyari, M. Hayashi, K. Hyodo, N. R. Nabisaheb, Y. Funahashi, *Org. Lett.* **2014**, *16*, 4452. DOI: 10.1021/ol501990t
- [13] Y. Xu, K. Kaneko, M. Kanai, M. Shibasaki, S. Matsunaga, *J. Am. Chem. Soc.* **2014**, *136*, 9190. DOI: 10.1021/ja5039165
- [14] G. Arena, C. C. Chen, D. Leonori, V. K. Aggarwal, *Org. Lett.* **2013**, *15*, 4250. DOI: 10.1021/ol4020333
- [15] Recent reviews on the biological activity and natural product constructed from aziridines, see refs [16–18]
- [16] H.-Y. Lee, S.-B. Song, T. Kang, Y. J. Kim, S. J. Geum, *Pure Appl. Chem.* **2013**, *85*, 741. DOI: 10.1351/PAC-CON-12-10-01
- [17] F. M. D. Ismail, D. O. Levitsky, V. M. Dembitsky, *Eur. J. Med. Chem.* **2009**, *44*, 3373. DOI: 10.1016/j.ejmech.2009.05.013
- [18] P. A. S. Lowden, In *Aziridines and Epoxides in Organic Synthesis*; Wiley-VCH Verlag GmbH & Co. KGaA: 2006, p 399.
- [19] Recent examples on the biological activity and natural product constructed from aziridines, see refs [20–23]
- [20] B. T. Adams, S. Niccoli, M. A. Chowdhury, A. N. K. Esarik, S. J. Lees, B. P. Rempel, C. P. Phenix, *Chem. Commun.* **2015**, *51*, 11390. DOI: 10.1039/C5CC03828F
- [21] X. Pan, X. Li, Q. Lu, W. Yu, W. Li, Q. Zhang, F. Deng, F. Liu, *Tetrahedron Lett.* **2013**, *54*, 6807. DOI: 10.1016/j.tetlet.2013.09.136
- [22] J. M. Vega-Pérez, C. Palo-Nieto, M. Vega-Holm, P. Góngora-Vargas, J. M. Calderón-Montaño, E. Burgos-Morón, M. López-Lázaro, F. Iglesias-Guerra, *Eur. J. Med. Chem.* **2013**, *70*, 380. DOI: 10.1016/j.ejmech.2013.10.020
- [23] I. Kreituss, E. Rozenberga, J. Zemītis, P. Trapencieris, N. Romanchikova, M. Turks, *Chem. Heterocycl. Compd.* **2013**, *49*, 1108. DOI: 10.1007/s10593-013-1248-7
- [24] Recent reviews on the synthesis of aziridines, see refs [23–27]
- [25] A. Fingerhut, O. V. Serdyuk, S. B. Tsogoeva, *Green Chem.* **2015**, *17*, 2042. DOI: 10.1039/C4GC02413C
- [26] L. Degennaro, P. Trinchera, R. Luisi, *Chem. Rev.* **2014**, *114*, 7881. DOI: 10.1021/cr400553c
- [27] H. Pellissier, *Adv. Synth. Catal.* **2014**, *356*, 1899. DOI: 10.1002/adsc.201400312
- [28] Recent examples of aziridine synthesis, see refs [29–38]
- [29] J.-H. Jung, D.-H. Yoon, K. Lee, H. Shin, W. K. Lee, C.-M. Yook, H.-J. Ha, *Org. Biomol. Chem.* **2015**, *13*, 8187. DOI: 10.1039/C5OB00375J
- [30] T. Moragas, I. Churcher, W. Lewis, R. A. Stockman, *Org. Lett.* **2014**, *16*, 6290. DOI: 10.1021/ol502967x
- [31] Y. Zhao, G. Wang, S. Zhou, Z. Li, X. Meng, *Org. Biomol. Chem.* **2014**, *12*, 3362. DOI: 10.1039/C4OB00443D
- [32] G.-H. Huang, J.-M. Li, J.-J. Huang, J.-D. Lin, G. J. Chuang, *Chem. Eur. J.* **2014**, *20*, 5240. DOI: 10.1002/chem.201304633
- [33] Y. Li, H. Huang, Z. Wang, F. Yang, D. Li, B. Qin, X. Ren, *RSC Adv.* **2014**, *4*, 969. DOI: 10.1039/C3RA44174A
- [34] X. Meng, W. Chen, Y. Zhang, Y. Chen, B. Chen, *J. Heterocycl. Chem.* **2014**, *51*, 937. DOI: 10.1002/jhet.1555
- [35] Y. Guan, M. P. López-Alberca, Z. Lu, Y. Zhang, A. A. Desai, A. P. Patwardhan, Y. Dai, M. J. Vetticatt, W. D. Wulff, *Chem. Eur. J.* **2014**, *20*, 13894. DOI: 10.1002/chem.201404587
- [36] J. Egloff, M. Ranocchiari, A. Schira, C. Schotes, A. Mezzetti, *Organometallics* **2013**, *32*, 4690. DOI: 10.1021/om400735p8
- [37] W.-J. Liu, Y.-H. Zhao, X.-W. Sun, *Tetrahedron Lett.* **2013**, *54*, 3586. DOI: 10.1016/j.tetlet.2013.04.046
- [38] T. M. U. Ton, C. Tejo, D. L. Y. Tiong, P. W. H. Chan, *J. Am. Chem. Soc.*, **2012**, *134*, 7344. DOI: 10.1021/ja301415k
- [39] Selected reviews on transition metal-mediated nitrene transfer reactions, see refs [40–33]
- [40] G. Dequierez, V. Pons, P. Dauban, *Angew. Chem. Int. Ed.* **2012**, *51*, 7384. DOI: 10.1002/anie.201201945
- [41] J. L. Roizen, M. E. Harvey, J. Du Bois, *Acc. Chem. Res.*, **2012**, *45*, 911. DOI: 10.1021/ar200318q
- [42] F. Collet, C. Lescot, P. Dauban, *Chem. Soc. Rev.*, **2011**, *40*, 1926. DOI: 10.1039/C0CS00095G
- [43] J. W. W. Chang, T. M. U. Ton, P. W. H. Chan, *Chem. Rev.*, **2011**, *11*, 331. DOI: 10.1002/tcr.201100018
- [44] F. Collet, R. H. Dodd, P. Dauban, *Chem. Commun.*, **2009**, 5061. DOI: 10.1039/B905820F
- [45] M. M. Díaz-Requejo, P. J. Pérez, *Chem. Rev.*, **2008**, *108*, 3379. DOI: 10.1021/cr078364y
- [46] H. M. L. Davies, J. R. Manning, *Nature*, **2008**, *451*, 417. DOI: 10.1038/nature06485
- [47] H. M. L. Davies, *Angew. Chem. Int. Ed.*, **2006**, *45*, 6422. DOI: 10.1002/anie.200601814
- [48] P. Müller, C. Fruit, *Chem. Rev.*, **2003**, *103*, 2905. DOI: 10.1021/cr020043t
- [49] Selected examples on transition metal-mediated nitrene transfer reactions, see refs [50–62]
- [50] J. Buendia, B. Darses, P. Dauban, *Angew. Chem. Int. Ed.* **2015**, *54*, 5697. DOI: 10.1002/anie.201412364
- [51] J. Wang, M. Frings, C. Bolm, *Angew. Chem. Int. Ed.* **2013**, *52*, 8661. DOI: 10.1002/anie.201304451
- [52] R. Gava, A. Biffis, C. Tubaro, F. Zaccheria, N. Ravasio, *Catal. Commun.* **2013**, *40*, 63. DOI: 10.1016/j.catcom.2013.06.001
- [53] L.-M. Jin, X. Xu, H. Lu, X. Cui, L. Wojtas, X. P. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 5309. DOI: 10.1002/anie.201209599
- [54] Á. Beltrán, C. Lescot, M. M. Díaz-Requejo, P. J. Pérez, P. Dauban, *Tetrahedron* **2013**, *69*, 4488. DOI: 10.1016/j.tet.2013.02.005
- [55] L. Maestre, W. M. C. Sameera, M. M. Díaz-Requejo, F. Maseras, P. J. Pérez, *J. Am. Chem. Soc.* **2013**, *135*, 1338. DOI: 10.1021/ja307229e

- [56] A. Yoshimura, V. N. Nemykin, V. V. Zhdankin, *Chem. Eur. J.* **2011**, *17*, 10538. DOI: 10.1002/chem.201102265
- [57] Y. Liu, C.-M. Che, *Chem. Eur. J.* **2010**, *16*, 10494. DOI: 10.1002/chem.201000581
- [58] M. Nakanishi, A.-F. Salit, C. Bolm, *Adv. Synth. Catal.* **2008**, *350*, 1835. DOI: 10.1002/adsc.200900123
- [59] L. He, J. Yu, J. Zhang, X.-Q. Yu, *Org. Lett.*, **2007**, *9*, 2277. DOI: 10.1021/ol70537i
- [60] M. Anada, M. Tanaka, T. Washio, M. Yamawaki, T. Abe, S. Hashimoto, *Org. Lett.* **2007**, *9*, 4559. DOI: 10.1021/ol702019b
- [61] M. R. Fructos, S. Trofimenko, M. M. Díaz-Requejo, P. J. Pérez, *J. Am. Chem. Soc.* **2006**, *128*, 11784. DOI: 10.1021/ja0627850
- [62] L. He, P. W. H. Chan, W.-M. Tsui, W.-Y. Yu, C.-M.; Che, *Org. Lett.* **2004**, *6*, 2405. DOI: 10.1021/ol049232j
- [63] Recent works by us, see refs [38] and [64–70]
- [64] C. Tejo, Y. F. A. See, M. Mathiew, P. W. H. Chan, *Org. Biomol. Chem.*, **2016**, *14*, 844. DOI: 10.1039/C5OB02302E
- [65] C. Tejo, X. R. Sim, B. R. Lee, B. J.; Ayers, C.-H. Leung, D.-L. Ma, P. W. H. Chan, *Molecules*, **2015**, *20*, 13336. DOI: 10.3390/molecules200713336
- [66] C. Tejo, H. Q. Yeo, P. W. H. Chan, *Synlett*, **2014**, 201. DOI: 10.1055/s-0033-1340108
- [67] T. M. U. Ton, F. Himawan, J. W. W.; Chang, P. W. H. Chan, *Chem. Eur. J.*, **2012**, *18*, 12020. DOI: 10.1002/chem.201201219
- [68] T. M. U. Ton, C. Tejo, S. Tania, J. W. W. Chang, P. W. H. Chan, *J. Org. Chem.*, **2011**, *76*, 4894. DOI: 10.1021/jo200284a
- [69] J. W. W. Chang, T. M. U. Ton, S. Tania, P. C. Taylor, P. W. H. Chan, *Chem. Commun.*, **2010**, *46*, 922. DOI: 10.1039/B918588G
- [70] J. W. W. Chang, P. W. H. Chan, *Angew. Chem. Int. Ed.*, **2008**, *47*, 1138. DOI: 10.1002/anie.200704695
- [71] Recent examples on transition metal-free mediated aminations, see refs [64–66] and [72–81]
- [72] K. Kiyokawa, T. Kosaka, S. Minakata, *Org. Lett.* **2013**, *15*, 4858. DOI: 10.1021/ol402276f
- [73] M. Ochiai, S. Yamane, M. M. Hoque, M. Saito, K. Miyamoto, *Chem. Commun.*, **2012**, *48*, 5280. DOI: 10.1039/C2CC31523H
- [74] D.-H. Zhang, Y. Wei, M. Shi, *Eur. J. Org. Chem.* **2011**, 4940. DOI: 10.1002/ejoc.201100629
- [75] R. Kowalczyk, A. J. F. Edmunds, R. G. Hall, C. Bolm, *Org. Lett.* **2011**, *13*, 768. DOI: 10.1021/ol103030w
- [76] M. Ochiai, K. Miyamoto, T. Kaneaki, S. Hayashi, W. Nakanishi, *Science*, **2011**, *332*, 448. DOI: 10.1126/science.120168
- [77] M. Ochiai, K. Miyamoto, S. Hayashi, W. Nakanishi, *Chem. Commun.*, **2010**, *46*, 511. DOI: 10.1039/B922033J
- [78] C. Fang, W. Qian, W. Bao, *Synlett* **2008**, 2529. DOI: 10.1055/s-2008-1078218
- [79] M. Ochiai, T. Kaneaki, N. Tada, K. Miyamoto, H. Chuman, M. Shiro, S. Hayashi, W. Nakanishi, *J. Am. Chem. Soc.*, **2007**, *129*, 12938. DOI: 10.1021/ja075811
- [80] J. Li, P. W. H. Chan, C.-M. Che, *Org. Lett.* **2005**, *7*, 5801. DOI: 10.1021/ol052293c
- [81] B.-W. Lim, K.-H. Ahn, *Synth. Commun.* **1996**, *26*, 3407. DOI: 10.1080/00397919608003744
- [82] CCDC 1508950 (**2i**) contains 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.
- [83] Recent examples of MIRC reactions in aziridines synthesis, see refs [84–88]
- [84] C. D. Fusco, T. Fuoco, G. Croce, A. Lattanzi, *Org. Lett.*, **2012**, *14*, 4078. DOI: 10.1021/ol3017066
- [85] S. Sternativo, F. Marini, F. D. Verme, A. Calandriello, L. Testaferri, M. Tiecco, *Tetrahedron* **2010**, *66*, 6851. DOI: 10.1016/j.tet.2010.06.055
- [86] A. Cioqli, S. Fioravanti, F. Gasparrini, L. Pellacani, E. Rizzato, D. Spinelli, P. A. Tardella, *J. Org. Chem.* **2009**, *74*, 9314. DOI: 10.1021/jo902112j
- [87] S. Fioravanti, S. Morea, A. Morreale, L. Pellacani, P. A. Tardella, *Tetrahedron* **2009**, *65*, 484. DOI: 10.1016/j.tet.2008.11.017
- [88] S. Fioravanti, D. Colantoni, L. Pellacani, P. A. Tardella, *J. Org. Chem.* **2005**, *70*, 3296. DOI: 10.1021/jo050044w.
- [89] Recent reviews on hypervalent iodine(III) reagents, see refs [90–94]
- [90] A. Yoshimura, V. V. Zhdankin, *Chem. Rev.* **2016**, *116*, 3328. DOI: 10.1021/acs.chemrev.5b00547
- [91] F. V. Singh, T. Wirth, *Chem. Asian J.* **2014**, *9*, 950. DOI: 10.1002/asia.201301582
- [92] L. F. Silva, Jr, B. Olofsson, *Nat. Prod. Rep.* **2011**, *28*, 1722. DOI: 10.1039/C1NP00028D
- [93] V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2008**, *108*, 5299. DOI: 10.1021/cr800332c
- [94] R. M. Moriarty, *J. Org. Chem.* **2005**, *70*, 2893. DOI: 10.1021/jo050117b
- [95] Mechanistic studies with hypervalent iodine(III) reagents, see ref [76] and [96–100]
- [96] A. Ozanne-Beaudenon, S. Quideau, *Angew. Chem. Int. Ed.* **2005**, *44*, 7065. DOI: 10.1002/anie.200501638
- [97] M. Ochiai, T. Suefuji, K. Miyamoto, M. Shiro, *Org. Lett.* **2005**, *7*, 2893. DOI: 10.1021/ol050858z
- [98] M. Ochiai, *J. Organomet. Chem.* **2000**, *611*, 494. DOI: 10.1016/S0022-328X(00)00487-3
- [99] D. H. R. Barton, J. Cs. Jaszberenyi, K. Leßmann, T. Timár, *Tetrahedron* **1992**, *48*, 8881. DOI: 10.1016/S0040-4020(01)81987-6
- [100] S. Oae, Y. Uchida, *Acc. Chem. Res.* **1991**, *24*, 202. DOI: 10.1021/ar00007a003