Tetrahedron 70 (2014) 5884–5894

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Sodium-iodoxybenzoate mediated highly chemoselective aziridination of olefins

Ananthan Bakthavachalam, Hui-Chun Chuang, Tu-Hsin Yan *

Department of Chemistry, National Chung Hsing University, Taichung, Taiwan, ROC

ARTICLE INFO

Article history:
Received 10 March 2014
Received in revised form 7 June 2014
Accepted 8 June 2014
Available online 13 June 2014

Keywords:
N-Aminophthalimide
Aziridination
Hypervalent compounds
Sodium iodoxybenzoate
Oxidation

ABSTRACT

Herein we utilized, for the first time, sodium 2-iodoxybenzoate as a highly specific oxidant for $PhthNH_2$ to create a highly chemoselective aziridination reagent. This method efficiently effects aziridination of electron-rich, electron-deficient, allylic alcohol and alkenyl bromide C=C bonds in good to excellent yields. Inter and intramolecular chemoselectivity was demonstrated between electron-rich and electron-deficient alkenes by using this efficient and metal free protocol.

1. Introduction

Great attention is being gained by the strained and smallest three membered aziridines,[1–5] which are important building blocks for various nitrogen-containing intermediates synthesis. Keen efforts have been devoted in the improvement of various aziridination methods.[2–5] Number of synthetically useful aziridination processes are based, predominantly, on the use of metal salts or complexes as catalyst and *N*-tosyliminodanes or haloamine-T as nitrogen precursors.[6–9] In economical and eco-friendly regards, developing a non-metallic and chemoselective reaction condition with non-toxic oxidant and inexpensive amine precursor is the longstanding goal for aziridine chemistry.[10]

Various research groups have been studying aziridination of olefins with *N*-aminophthalimide ($PhthNH_2$) as the amine precursor.[10–29] Recently, Xue et al. investigated the effect of N–H bond dissociation energies of various amine source on the reactivity of the amidation reaction with (diacetoxyiodo)benzene (DIB) as an oxidant on styrene. Interestingly, $PhthNH_2$ was found as one of the most preferable choice for amidation reactions.[30] Notably, aziridination promoted by the electrochemical oxidation of $PhthNH_2$ has found to be good method.[10–13] More interestingly, DIB mediated aziridination of olefins with $PhthNH_2$ has proven to be synthetically useful transformations.[14–17] Recently, recyclable systems, such as *m*-CPBA/Ar-I[18] and *m*-CPBA/Bu_4NI derived hypoiodite[19] have been reported to effect metal-free aziridination of aromatic olefins and simple alkenes in moderate to good yields. These previously reported aziridination systems were remain limited due to the usage of excessive oxidizing reagent, poor chemoselectivity, narrow range substrate scope (e.g., not suitable for the coupling with allylic alcohol C=C bonds or electron-deficient alkenes) and incompatibility with wide range of functional groups. The significant limitation on the metal-free alkene–aziridination often arises from using less selective oxidants to mediate the coupling of alkenes with hydrazine derivatives.[10–29] Therefore, the search for new entry of metal-free aziridination reagents, which are highly chemoselective and suitable for broad range of substrates, such as electron-deficient, electron-rich and allylic alcohol C=C bonds, continues to stimulate much thought from a synthetic point of view. Among the various metal-free iodo-based oxidizing reagents, *o*-iodoxybenzoic acid (IBX)[31,32] is one of the mildest oxidizing reagents and inexpensive to prepare,[33,34] and more tolerant to moisture and generally promotes clean transformation in many new oxidation-based applications reported by Nicolaou group and others.[34–45] Most importantly, some useful transformations have been reported by utilizing IBX coupled with *N*-methyl morpholine[37] and 2-hydroxypyridine (HyP).[45] Nevertheless, the reactivity of IBX with base requires further investigation. Compared with IBX, its conjugate base should be a more selective oxidant. We envisioned the feasibility of a highly chemoselective coupling of $PhthNH_2$ with alkenes promoted by a conjugate base of IBX.[32]

* Corresponding author. E-mail address: thyan@mail.nchu.edu.tw (T.-H. Yan).
URL: http://www.nchu.edu.tw/~chem/thyan.htm

http://dx.doi.org/10.1016/j.tet.2014.06.029
0040-4020/

Herein we utilized, for the first time, sodium 2-iodoxybenzoate as a highly specific oxidant for $PhthNH_2$ to generate a highly chemoselective aziridination reagent. This novel protocol efficiently effects aziridination of electron-deficient, electron-rich, alkenyl bromide and allylic alcohol C=C bonds in good to excellent yields.

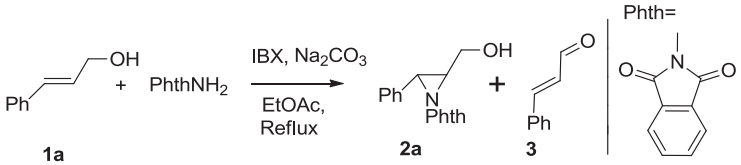
2. Results and discussion

For exploring iodine (V) reagents mediated aziridination reaction conditions, we carefully examined the reactions of **1a** and $PhthNH_2$ with broad range of oxidants (like, SIBX, DMP and IBX). Additionally, in the search to find an efficient and selective conjugate base, we examined various bases (including, TEA, Pyridine, DBU, DMAP, K_2CO_3 and Na_2CO_3). Furthermore, we also investigated the utilisation of many additives and various solvents at different temperatures to improve reaction yield (Table 1 and please see Supplementary data Table S1).

to find that, when **1a** reacts with IBX, $PhthNH_2$ and Na_2CO_3 in EA (Table 1, entry 9) the desired adduct **2a** was produced in 84% isolated yield with an additional trace (<5%) of the oxidation product **3**. Addition of additives (e.g., iodine, acetic anhydride) does not meliorate the yield in this C–N bond formation.[49] Altering the concentration of this reaction lead to diminutive yield. We also got discontented results while increasing or decreasing the equivalents of IBX, $PhthNH_2$ and Na_2CO_3.[49]

Having established this ripest novel aziridination procedure, its generality and selectivity with respect to the structure of alkenes were investigated. We were delighted to find that the chemistry was successful for a diverse range of olefins. Thus the inclusion of a ketone, an ester, an acetonide, an amide, an imide, a secondary or even a primary hydroxyl group did not hinder the desired reaction. In other words, functional group tolerance is excellent by this protocol. In general, electron-deficient alkenes were found to proceed well than electron rich alkenes.

Table 1
Optimization of reaction conditions for aziridination of olefin **1a**[a]



1a 2a 3

Entry	Oxidant	Base	Time (h)	*T* (°C)	**2a** (%)[b]	**3** (%)
1	SIBX	K_2CO_3	30	25	[13]	[12]
2	DMP	K_2CO_3	12	Reflux	[27]	[13]
3	IBX-HyP	K_2CO_3	24	25	[30]	—
4	IBX	—	30	Reflux	0	[39]
5	IBX	TEA	27	Reflux	[7]	[26]
6	IBX	Li_2CO_3	27	Reflux	22	[7]
7	IBX	K_2CO_3	30	25	21	[2]
8	IBX	K_2CO_3	27	Reflux	77	[10]
9	IBX	Na_2CO_3	27	Reflux	84	[5]
10	IBX	$NaHCO_3$	27	Reflux	[41]	[20]
11	IBX	KOAc	12	Reflux	[46]	[13]

[a] Reactions were performed in 0.25 mmol scale with $PhthNH_2$ (1.5 equiv), Oxidant (1.4 equiv), Base (2.8 equiv).
[b] Isolated yield; NMR ratio is in parenthesis.

Initial studies centred on the aziridination of alkene containing oxidation-sensitive groups, such as hydroxyl group and C=C bond. Due to the known sensitivity of the allylic primary alcohol to oxidants, such as IBX,[46] Dess-Martin periodinane (DMP),[47] and *m*-CPBA[48] at 0 °C, we intentionally chose **1a** to devise a suitable condition for the aziridination of olefin substrates bearing sensitive functional groups. On exposing $PhthNH_2$ to either SIBX (Table 1, entry 1), or DMP (entry 2), or IBX-HyP (entry 3) for the aziridination of alkene **1a** gave unsatisfactory results. Inspection of optimization entries (Table 1 and Supplementary data Table S1) unveils that under basic conditions the intermolecular aziridination of **1a** with IBX as oxidant is a better choice than the other iodine (v) reagents.[49]

We believe that the choice of a base plays a vital role in this transformation. Unlike DIB and $Pb(OAc)_4$ we did not observe the expected product in the absence of base (entry 4). The only product observed was cinnamaldehyde **3**. In general, inorganic bases were the best choice than organic bases. Specifically, carbonate bases were better than bicarbonate and acetate bases (entries 5–11).[49] Out of bases tested,[49] Na_2CO_3 is the best choice (entry 9). Previously reported aziridination methods, predominantly, used toxic halogenated solvents. We found that, among various solvents examined, ethyl acetate (EA) is the most effective.[49] We were pleased

Fortunately, exposing **1b** and **1c** to the IBX/Na_2CO_3/$PhthNH_2$ system gave 79% and 81% yield of **2b** and **2c**, respectively (Table 2, entries 1 and 2). Notably, the ability to effect monoaziridination of the double bond of allylic alcohol in geraniol **1b** highlights the chemoselectivity of this aziridination regent. Even though oxidation of geraniol **1b** and cinnamyl alcohol **1a** were reported by using IBX in EA,[46] we predominantly got the desired aziridine. Interestingly, this aziridination reagent is also suitable for the aziridination of phenyl vinyl carbinol **1d** (entry 3), which is sensitive to benzylic oxidation. On the other hand, aziridination onto cyclic allylic alcohol **1e** was also effective (entry 4). Changing alkene to **1f** in which the hydroxyl group was further removed from the double bond also gave satisfactory results with IBX/Na_2CO_3/$PhthNH_2$ with exclusive formation of the *cis*-aziridine **2f** (entry 5), which could serve as an important building block for Amarylidaceae alkaloids synthesis, which is an ongoing research in our lab. The *cis* relationship between aziridine and hydroxyl group indicates the *syn* directing effect of the hydroxyl group. The *cis*-aziridine structure of **2f**, studied with the single crystal X-ray analysis (Fig. 1) confirms the stereochemistry. Similarly varying alkene to **1g**, the structural analogue of **1e**, in which the hydroxyl group was protected with benzyl group, also gave good yield (entry 6). To further demonstrate the scope of this aziridine-forming methodology, the utility of this

Table 2
Sodium 2-iodoxybenzoate mediated aziridination of electron rich alkenes with $PhthNH_2$[a]

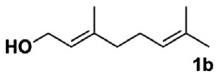
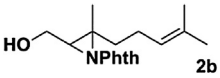
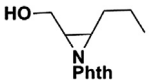
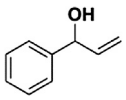
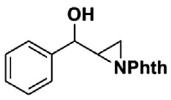
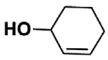
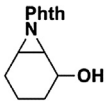
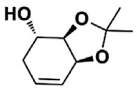
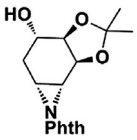
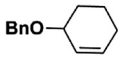
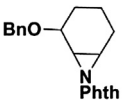
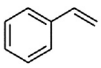
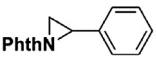
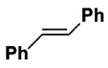
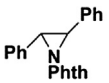
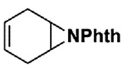
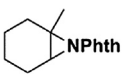
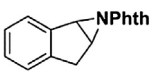
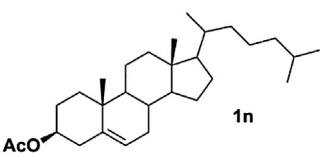
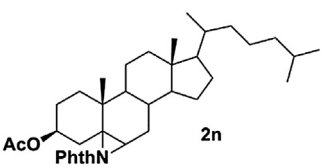
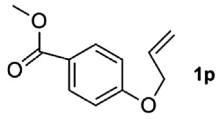
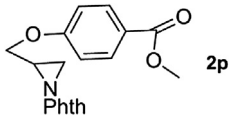
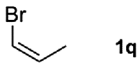
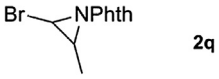
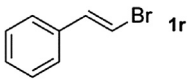
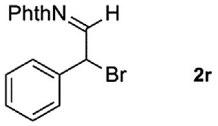
Entry	Substrate	Product	Yield[b]
1	 1b	 2b	79
2	 1c	 2c	81
3	 1d	 2d	75
4	 1e	 2e	61
5	 1f	 2f	70
6	 1g	 2g	67
7	 1h	 2h	82
8	 1i	 2i	84
9	 1j	 2j	55
10	 1k	 2k	53
11	 1l	 2l	51
12	 1m	 2m	71
13	 1n	 2n	31[c]
14	 1o	 2o	88

Table 2 (*continued*)

Entry	Substrate	Product	Yield[b]
15	 **1p**	 **2p**	74
16	 **1q**	 **2q**	62
17	 **1r**	 **2r**	85

[a] Reaction was performed in refluxing EA for 27 h by using alkene (1 equiv), $PhthNH_2$ (1.5 equiv), IBX (1.4 equiv) and Na_2CO_3 (2.8 equiv).
[b] Isolated yield.
[c] Reaction was performed over 39 h.

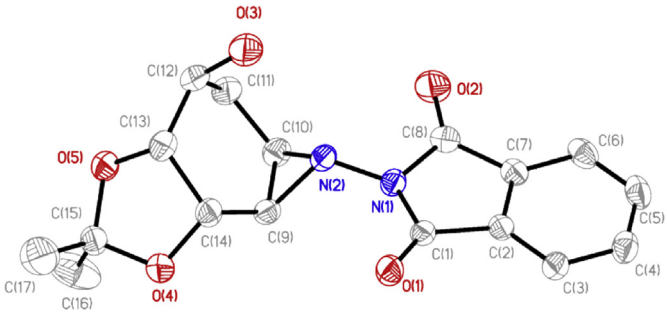


Fig. 1. X-ray crystal structure of **2f** (hydrogen atoms omitted).

protocol was examined in the aziridination of alkenes without directing functional group. Gratifyingly, aziridination of various alkenes **1h**, **1i**, **1j**, **1k** and **1l** under the standard conditions was equally effective in the formation of aziridines **2h**, **2i**, **2j**, **2k** and **2l** (entries 7–11). We achieved complete conservation of stereochemistry in the case of *trans*-stilbene **1i** (see mechanism part for detailed discussion). Conformationally restricted olefin *1H*-indene **1m** (Table 2, entry 12) was also found to undergo aziridination by this protocol to give aziridine in 71% yield. Biologically important molecule cholesteryl acetate **1n** (Table 1, entry 13) was tested with this present aziridination method, corresponding aziridine product **2n** was obtained.[14] Aziridination of norbornene **1o** was found to be effective (entry 14). The aziridination product **2o** was obtained in 88% yield. To further ascertain the viability of this system, terminal alkene **1p** was studied under optimum conditions gave desired product **2p** (entry 15), in good yield.

α-Halogenated hydrazones and imines have acquired significant attraction due to their usage in the preparation of pyrrolidines,[50] pyrroles,[51,52] cyclopropylamines,[53] diimines[51,54] and epoxyimines.[55] The synthesis of α-haloimine and α-halohydrazone commonly involves α-halogenation of imines or hydrazones and condensation of primary amine hydrazine with α-halogenated carbonyl compounds.[29] Unfortunately, either halogenation of imines and hydrazones or aforementioned condensation reaction suffers with poor chemoselectivity.[56] To avoid these issues Yudin et al. proposed DIB based protocol to prepare α-bromoaziridines and α-bromohydrazones.[29]

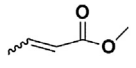
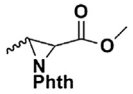
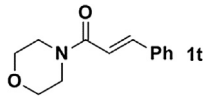
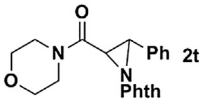
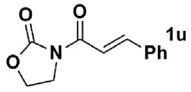
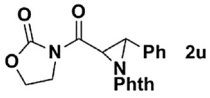
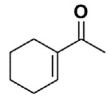
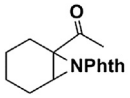
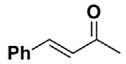
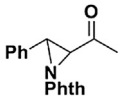
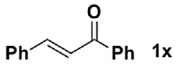
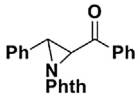
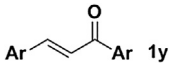
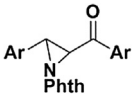
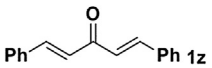
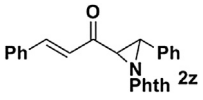
In the light of our versatile aziridination protocol, we extend the substrate scope to alkenyl bromides. However, the previous report used non basic condition.[29] Our optimized condition has applied directly in this reaction and the required product was obtained. Thus 1-bromo-propene (**1q**) was subjected to this aziridination reaction condition to give α-bromoaziridine **2q**[29] in 62% isolated yield (Table 2, entry 16). The column purification was performed by using cold water circulation to achieve better yield.

The α-bromoaziridines are known to be thermally labile. Hence this will yield corresponding hydrazones through an electrocyclic rearrangement, which allows a highly regioselective product. In addition to this, stability of carbocation is an important phenomenon for this rearrangement.[29] β-bromostyrene, which is a progenitor of stable carbocation prepared by our in-house Ti–Mg method,[57] was tested with the optimized condition and smoothly yielded **2r**[29] in 85% as the only product (Table 2, entry 17).

With an eye to extend these observations to other electron-deficient alkenes, we explored the aziridination of alkenes bearing electron-withdrawing groups. Thus, either unsaturated ester **1s** or amide **1t** reacted efficiently with $IBX/Na_2CO_3/PhthNH_2$ derived aziridination reagent to give 86% and 65% yield of the desired aziridination adducts **2s** and **2t**, respectively (Table 3, entries 1 and 2). Interestingly, imide **1u** also proved to be a satisfactory trap (entry 3). On the other hand, this aziridination reagent reacted efficiently with unsaturated ketone **1v** to give the desired aziridinyl ketone **2v** in a remarkable 90% yield (entry 4). Moreover, the reaction directly scales up; thus, aziridinyl ketone **2v** was obtained in 68% yield on a 10-mmol scale. Changing the ketone to benzylidene ketone **1w**, **1x** and **1y** have also been yielded satisfactory results (entries 5–7). Most delightfully, aziridination with dibenzylideneacetone **1z** led to smooth aziridination with formation of monoaziridination adduct **2z** in 92% yield (entry 8). Many of the products (Table 2, entries 1–17 and Table 3, entries 1–8) were found to form in higher yield than the previously reported procedures.

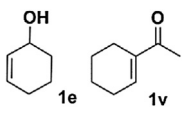
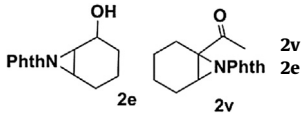
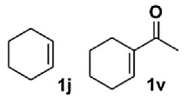
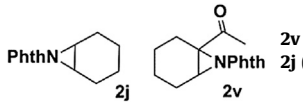
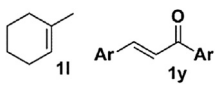
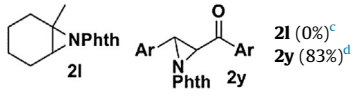
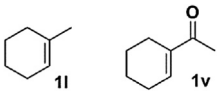
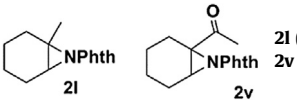
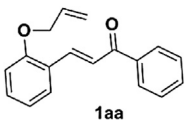
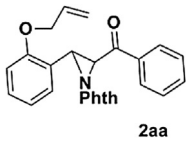
To evaluate further the chemoselectivity of this $IBX/Na_2CO_3/PhthNH_2$ system mediated transformation, it becomes necessary to ascertain whether this aziridination proceeds with preference over electronically different types of double bond. Therefore, a series of inter- and intramolecular competition reactions were, therefore, undertaken. Gratifyingly, exposure of a mixture of 1-acetyl-1-cyclohexene **1v** and 2-cyclohexene-1-ol **1e** at optimized condition

Table 3
Sodium 2-iodoxybenzoate mediated aziridination of electron-deficient alkenes with $PhthNH_2$[a]

Entry	Substrate	Product	Yield[b]
1	 1s	 2s	86
2	 1t	 2t	65
3	 1u	 2u	67
4	 1v	 2v	90 68[c]
5	 1w	 2w	80
6	 1x	 2x	91
7[d]	 1y	 2y	90
8	 1z	 2z	92

[a] Reaction was performed in refluxing EA for 27 h by using alkene (1 equiv), $PhthNH_2$ (1.5 equiv), IBX (1.4 equiv) and Na_2CO_3 (2.8 equiv).
[b] Isolated yield.
[c] Reaction was performed on 10 mmol scale.
[d] Ar=4-Methoxyphenyl.

Table 4
Chemoselectivity in sodium 2-iodoxybenzoate/$PhthNH_2$ mediated aziridination of olefins

Entry	Alkene mixture[a]	Products	Yield (%)[b]
1	 1e 1v	 2e 2v	**2v** (80%) **2e** (0%)[c]
2	 1j 1v	 2j 2v	**2v** (86%) **2j** (0%)[c]
3	 1l 1y	 2l 2y	**2l** (0%)[c] **2y** (83%)[d]
4	 1l 1v	 2l 2v	**2l** (0%)[c] **2v** (84%)
5	 1aa	 2aa	**2aa** (79%)

[a] 0.25 mmol of each substrate was used.
[b] Isolated yield.
[c] Determined by ^1H NMR on the crude mixture.
[d] Ar=4-Methoxyphenyl.

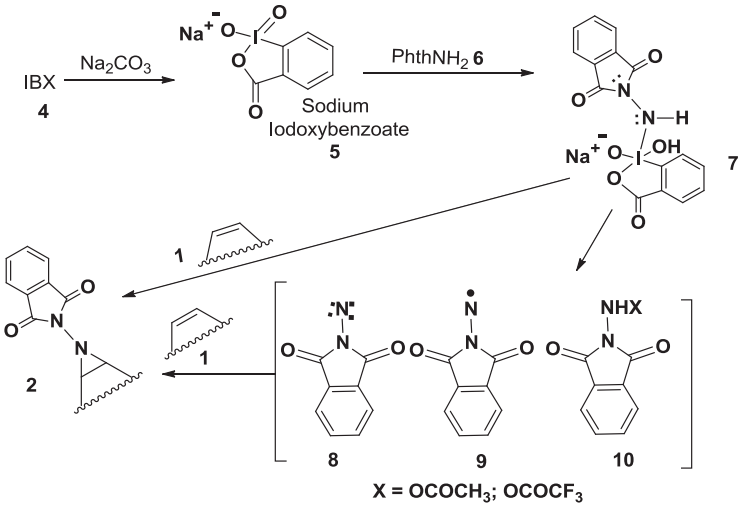
has produced exclusively **2v** (Table 4, entry 1). Highly selective aziridination onto a mixture of 1-acetyl-1-cyclohexene **1v** and cyclohexene **1j** was equally effective (entry 2). As expected, exposing a mixture of benzylidene ketone **1y** and 1-methyl-1-cyclohexene **1l** to the IBX/Na_2CO_3/$PhthNH_2$ system also led to highly selective aziridination (entry 3). Intramolecular competition reaction was demonstrated already in **1b**, (Table 2, entry 1). However, another example **1aa** manifests the chemoselectivity of this method (Table 4, entry 5).

In order to understand the mechanism of this chemoselective aziridination reaction, we also proposed the possible mechanisms[20] and examined each in turn (Scheme 1). However, Yudin[15] and Che[14] proposed that the alkene aziridination mechanism proceeds via PhthNHOCOR using hypervalent iodine species and $PhthNH_2$. This reaction is proceeding well in the absence of acetic anhydride or trifluoroacetic anhydride. Therefore, we rejected the possibility of involvement of acyloxyamine **10** (Scheme 1) in this reaction.

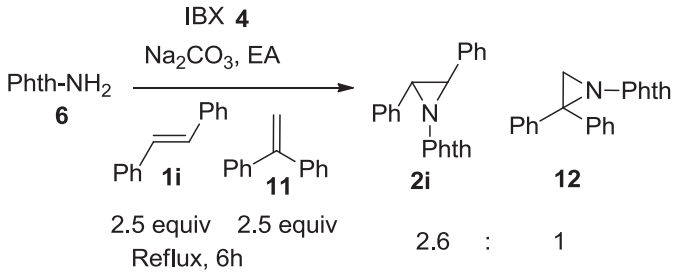
We examined the possibility of radical mechanism by accounting the reactivity of *trans*-stilbene and *cis*-2-hexene-1-ol. We observed complete conservation of stereochemistry in the case of **2c** and **2i** (Table 2, entries 2 and 7). It revealed the concerted formation of aziridine ring. Therefore the reaction may not proceed through radical mechanism. In addition to this, we performed a competitive reaction to get further evidence against radical intermediate **9** (Scheme 1). 1,1-Diphenylethene **11** is a known and preferential trap for radical intermediate.[20] Preferential reaction over *trans*-stilbene was observed while $PhthNH_2$ was oxidized with IBX/Na_2CO_3 in the presence of 1:1 mixture of *trans*-stilbene and 1,1 diphenylethene (Scheme 2). Based on the experimental results, we conclude the proposed radical intermediate **9** is not involved in this aziridination reaction.

Focus was next turned to the phthalimidonitrene **8**, which was thought to be involved in $Pb(OAc)_4$ mediated aziridination of alkenes.[21] Nevertheless, there are some questions to be answered, before claiming phthalimidonitrene **8** as the intermediate for IBX/Na_2CO_3 mediated aziridine reaction, such as how this nitrene controls its rapid inter-conversion between singlet and triplet states to yield the product stereo-selectively.

Atkinson et al. investigated the possibility of nitrene intermediate by selectivity trials.[22b] He generated phthalimidonitrene **8** from **13** (Scheme 3) by thermolysis in refluxing benzene, which undergoes irreversible reaction with 1:1 mixture of styrene **1h** and methyl acrylate **14** yielded preferential reaction over methyl acrylate in 3:1 product ratio (Scheme 3, Eq. 1).[22b] In contrast, preferential reaction over styrene **1h** was observed (1:1.5) while the reaction was performed by using $PhthNH_2$ and $Pb(OAc)_4$ in refluxing benzene (Eq. 2).[22b] Interestingly, when the reaction was performed by using $PhthNH_2$ and DIB, preferential reaction was detected with methyl acrylate in 1.2:1 product ratio (Eq. 3).[20] We did an identical reaction employing $PhthNH_2$ and IBX in the presence of Na_2CO_3 and found preferential reaction with methyl



Scheme 1. Possible intermediates for this aziridination reaction.



Scheme 2. Investigating possible radical intermediate.

acrylate but in 2.4:1 product ratio (Eq. 4), whereas when the same reaction performed in refluxing EA we noticed insignificant difference in product ratio. This was an interesting result because we got a similar trend in preferential reactivity like the case of Eqs. 1 and 3 (Scheme 3), however, product ratio was found to be different. Based on these experimental results, we tentatively propose the non-involvement of phthalimidonitrene **8** in the transition state of this sodium-iodoxybenzoate mediated aziridination reaction.

In an attempt to understand the mechanism, we investigated the role aminoiodane **7** in transition state of this reaction. Since $PhthNH_2$ does not possess α-amino hydrogen atom and it would form a complex with IBX.[40] Recently, Wirth et al. proposed the possible involvement of aminoiodane (from DIB and $PhthNH_2$, Fig. 2) by the experimental insights.[20] Nicolaou et al. illustrated the change in reactivity of IBX by modifying the ligand.[37] In the same way, we envisioned that the change in base would show the difference in selectivity if IBX conjugate base participates in the transition state.

As anticipated, we observed a difference in selectivity while changing the base (Scheme 3, Eqs. 5–9). This is also serves as further evidence for the non-involvement of phthalimidonitrene **8** in the transition state. The preferential ratio in Scheme 3 also reveals the importance of base for this C–N bond formation reaction. When the reaction was performed in the presence of Na_2CO_3, Imidazole, Li_2CO_3 preferential reaction over methyl acrylate was observed (Eqs. 5–7). On the contrary, an identical reaction employed with HyP as base and detected that preferential reaction over styrene but in 1.4:1 (**2g**/**15**) product ratio (Eq. 8). The preferential reaction over electron rich substrate in the case of HyP/IBX/$PhthNH_2$ reveals the involvement of different type of intermediate than others (Scheme 3, Eq. 8). On the other hand, non preferential result was observed while TEA was used as base in the same reaction. At this juncture we would like to highlight that employment of base for the aziridination reaction is indispensible. Based on these experimental insights, we observed different selectivity trend while changing the base. So we presume that the involvement of aminoiodane along with base in transition state of this aziridine reaction.

The above results[58] strongly implicates a tentative reaction mechanism as shown in Scheme 4, wherein the less electrophilic sodium iodoxybenzoate acts as a highly specific oxidant for the amino group of $PhthNH_2$ to provide aminoiodane **7.** The aminoiodane, presumably, exist in equilibrium between electrophilic (**7a**) and nucleophilic (**7b**) equivalents and the role of base is crucial here to move the equilibrium towards the nucleophilic side. Reduction at the iodine centre most likely proceeds through ionic pathway[40] to render sodium *o*-iodosobenzoate[59,60] along with required aziridine. Left unanswered by this proposal are the specific oxidizing properties of sodium iodoxybenzoate, the novel nucleophilic character of aminoiodane under basic conditions and the unique electrophilic behaviour of HyP/IBX/$PhthNH_2$. Further mechanistic insights are required before any definite conclusions can be reached.

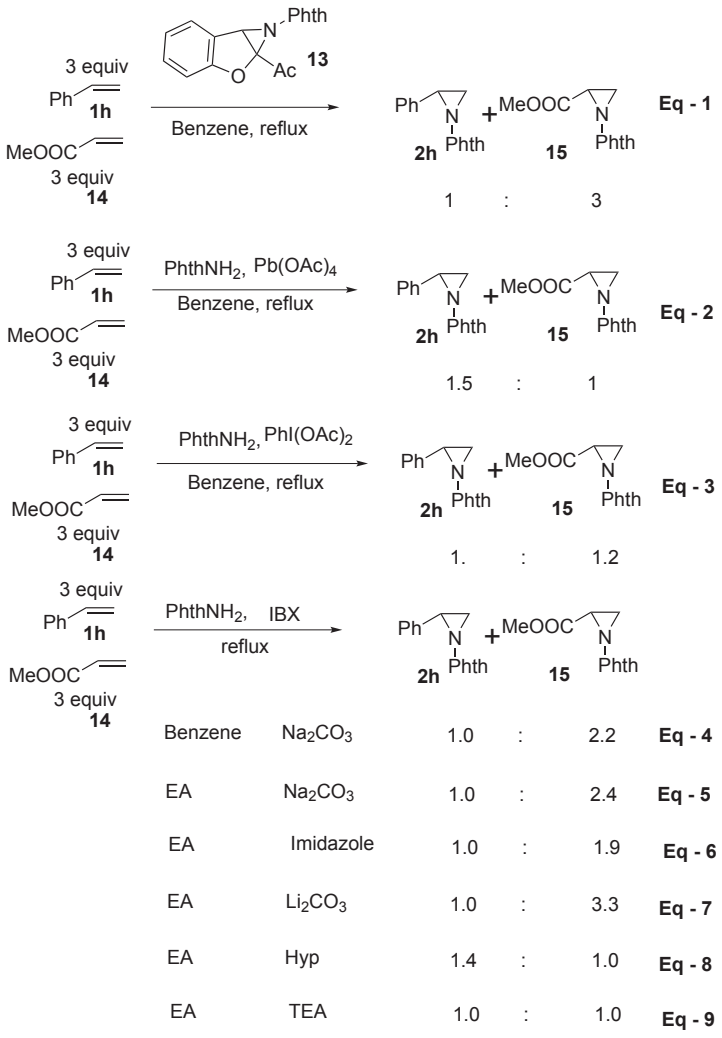
3. Conclusions

The successful application of the sodium 2-iodoxybenzoate promoted aziridination of $PhthNH_2$ with a variety of alkenes illustrates the extraordinary reactivity of this new aminoiodane species. Not only is this IBX/Na_2CO_3/$PhthNH_2$ system highly reactive, it also seems highly chemoselective and might become a practical aziridination reagent applicable to large scale synthesis. Our work exemplifies the chemoselective rational aziridination without hazardous metal catalyst and super-stoichiometric oxidant. The operational simplicity of this novel procedure provides access to aziridines, those are difficult to prepare but utile. The highly specific oxidizing properties of sodium iodoxybenzoate suggested several intriguing directions, which are currently under active investigation.

4. Experimental section

4.1. General information

All reactions were conducted in flame-dried glassware under nitrogen atmosphere. Ethyl acetate (EA) was distilled from CaH_2



Scheme 3. Investigation of possible intermediates in IBX mediated aziridination of alkenes. (a) 3 equiv of each starting materials and 2.8 equiv of base with respect to IBX were used. (b) All the reactions were performed in 210 min at reflux temperature. (c) Ratios were determined by ^{1}H NMR on the crude mixture.

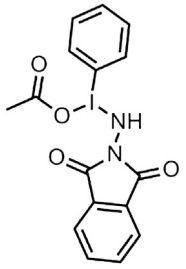
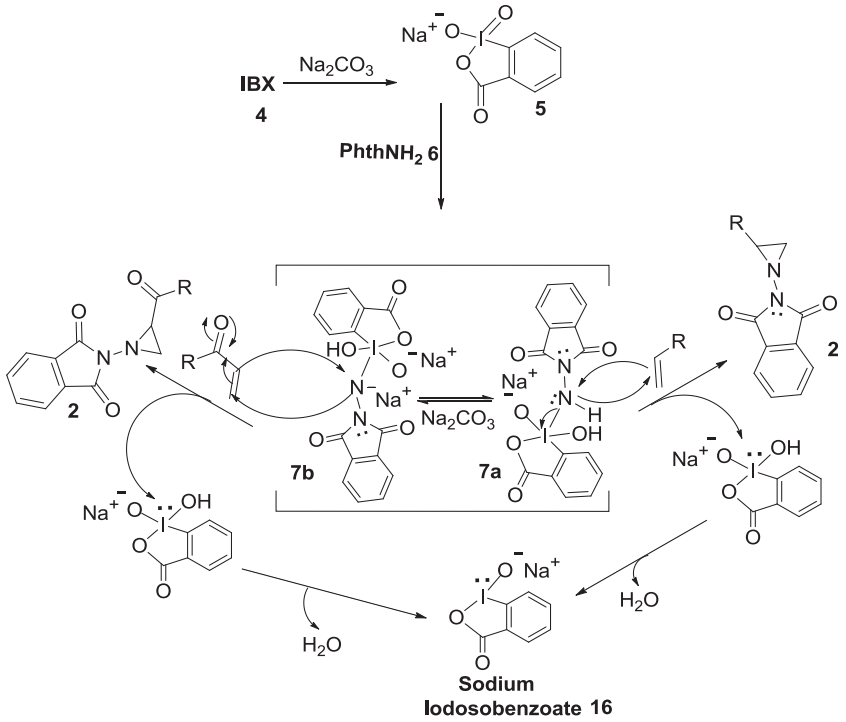


Fig. 2. Aminoiodane intermediate proposed by Wirth et al.

and CH_2Cl_2 was distilled from P_2O_5. IBX and $PhthNH_2$ were dried to constant weight under vacuum. Na_2CO_3 was dried to constant weight at 150 °C under vacuum prior to use. Flash chromatography was performed over silica gel 60 (230–400 mesh). All commercially available reagents were purchased and used as received. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded using indicated solvent at ambient temperature. Chemical shifts have been reported in parts per million and coupling constants (*J*) (H,H) are given in Hertz, spectral splitting patterns have been assigned as singlet (s), doublet (d), triplet (t), quadruplet (q), broad (br), broad band (br b), multiplet or more overlapping signals (m), etc. Mass spectra were obtained using orbitrap apparatus from high resolution ESI mass spectrometer. Mass spectra were obtained using double focussing apparatus from high resolution EI and FAB mass spectrometer. IR spectra were recorded as a thin film and expressed in cm^{-1}.

4.2. (*E*)-1-(2-(Allyloxy)phenyl)-3-phenylprop-2-en-1-one (1aa)

To a stirred solution of 2-hydroxychalcone (1.12 g, 5 mmol) in DMF (2.5 mL), allyl bromide (0.91 g, 7.5 mmol) and K_2CO_3 (1.04 g, 7.5 mmol) were added successively. The reaction mixture was stirred 1 h at 25 °C then diluted with water (10 mL) and hexane (10 mL). The aqueous phase was extracted with hexane. The combined organic extracts was washed with brine and dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/EA=3.5:1) to afford 1.28 g (97%) of **1aa**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J*=16 Hz, 1H), 8.0 (d, *J*=7.2 Hz, 2H), 7.67–7.62 (m, 2H), 7.56 (t, *J*=7.2 Hz, 1H), 7.48 (t, *J*=7.6 Hz, 2H), 7.34 (t, *J*=7.8 Hz, 1H), 6.99 (t, *J*=7.4 Hz, 1H), 6.92 (d, *J*=8 Hz, 1H), 6.09 (dtd, *J*=16, 10.6, 5.2 Hz, 1H), 5.44 (dd, *J*=17.4, 1.4 Hz, 1H), 5.31 (dd, *J*=10.4, 1.2 Hz, 1H), 4.63 (d, *J*=5.2 Hz, 2H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.87, 157.67, 140.28, 138.36, 132.69, 132.39, 131.50, 129.29, 128.38, 124.04, 122.86, 120.82, 117.77, 112.44, 60.03; IR (neat) cm^{-1} 3065, 1660, 1598, 1486, 1016, 752; HRMS (ESI [M+H]): 265.1224 (calcd for $C_{18}H_{17}O_2$: 265.1223).



Scheme 4. Proposed mechanism for IBX/Na_2CO_3/$PhthNH_2$ mediated aziridination.

4.3. General procedure of aziridination of alkene

Anhydrous Na_2CO_3 (0.7 mmol) was added to the suspension of IBX (0.35 mmol) and $PhthNH_2$ (0.375 mmol) in EA (2 mL) under nitrogen. After stirring 10 min at room temperature, alkene **1** (0.25 mmol) was added to the reaction mixture and then refluxed for 27 h. The reaction mixture was quenched with water. The separated organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexane/ EA (3.5:1 for **2a**–**f**; 4.5:1 for **2g**–**aa**) to afford aziridine **2**.

4.4. Aziridination of alkene 1v in 10 mmol scale

Anhydrous Na_2CO_3 (2.97 g, 28 mmol) was added to the suspension of IBX (3.92 g, 14 mmol) and $PhthNH_2$ (2.43 g, 15 mmol) in EA (12 mL) under nitrogen atmosphere. After stirring 10 min at room temperature, alkene **1v** (1.24 g, 10 mmol) was added to the reaction mixture and then refluxed for 33 h. The reaction mixture was quenched with water. The separated organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using hexane/EA (4:1) over silica gel gave aziridine **2v** (1.86 g, 68%).

4.5. Representative procedure for chemoselectivity trials

Anhydrous Na_2CO_3 (68.89 mg, 0.65 mmol) was added to the suspension of IBX (91.0 mg, 0.325 mmol) and $PhthNH_2$ (54.80 mg, 0.338 mmol) in EA (2 mL) under nitrogen. After stirring 10 min at room temperature, alkene mixture [0.25 mmol of substrate **1e** (24.54 mg) and **1v** (31 mg)] was added to the reaction mixture and then refluxed for 27 h. The reaction mixture was quenched with water. The separated organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using hexane/EA (4.5:1) over silica gel gave aziridine **2v** (54.8 mg, 80%).

4.6. Procedure for aziridination of α-Bromo substituted alkenes and their rearrangement

Anhydrous Na_2CO_3 (0.7 mmol) was added to the suspension of IBX (0.35 mmol) and $PhthNH_2$ (0.375 mmol) in EA (2 mL) under nitrogen. After stirring 10 min at room temperature, alkene **1q** or **1r** (0.25 mmol) was added to the reaction mixture and then refluxed for 20 h. The reaction mixture was quenched with water. The separated organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexane/EA (8:1) to afford product **2q** or **2r**.

*4.6.1. 1-Phthalimido-2-hydroxymethyl-3-phenylaziridine (**2a**).*[11] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82–7.71 (m, 3H), 7.61 (d, J=4 Hz, 1H), 7.43–7.21 (m, 5H), 4.26–4.16 (m, 1H), 4.02 (d, J=4 Hz, 0.3H), 3.83–3.79 (m, 0.6H), 3.35–3.48 (m, 2H), 3.21–3.18 (m, 0.7H), 2.44 (t, J=6 Hz, 0.29H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.62, 135.76, 134.53, 133.98, 130.45, 129.45, 128.8, 128.6, 128.22, 128.19, 127.22, 123.43, 122.96, 59.13, 52.24, 46.10; IR (neat) cm^{-1} 2360, 1712, 1376, 1145; HRMS (ESI [M+Na]): 317.0889 (calcd for $C_{17}H_{14}N_2O_3Na$: 317.0897).

*4.6.2. 2-(3-(Hydroxymethyl)-2-methyl-2-(4-methylpent-3-en-1-yl) aziridine-1-yl)-isoindoline-1,3-dione (**2b**).*[23] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75–7.73 (m, 2H), 7.67–7.64 (m, 2H), 4.98 (m, 1H), 3.94 (d, J=10.8 Hz, 1H), 3.65 (dd, J=11.6, 8.8 Hz, 1H), 3.32 (br s, 1H), 2.70 (dd, J=8.8, 3.6 Hz, 1H), 2.17 (br s, 1H), 2.0–1.97 (m, 3H), 1.61 (s, 3H), 1.54 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.21, 134.12, 132.53, 130.63, 123.08, 122.86, 61.45, 54.41, 51.25, 34.94, 25.60, 25.32, 17.62, 17.58; IR (neat) cm^{-1} 2925, 1715, 1375, 1051, 711,

647; HRMS (ESI [M+Na]): 337.1526 (calcd for $C_{18}H_{22}N_2O_3Na$: 337.1523).

*4.6.3. 2-(2-(Hydroxymethyl)-3-propylaziridin-1-yl)-isoindoline-1,3-dione (**2c**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 2H), 7.66 (dd, J=4.8, 3.2 Hz, 2H), 3.93 (br s, 1H), 3.63–3.58 (m, 1H), 3.44 (br s, 1H), 2.88 (t, J=7.2 Hz, 1H), 2.57–2.55 (m, 1H), 1.75–1.47 (m, 4H), 0.98 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.37, 134.17, 130.27, 123.11, 60.50, 50.92, 47.78, 29.93, 20.35, 13.92; IR (neat) cm^{-1} 1708, 1373, 1176, 1041, 898, 782; HRMS (EI): 260.1151 (calcd for $C_{14}H_{16}N_2O_3$: 260.1161).

*4.6.4. 2-(2-(Hydroxyl(phenyl)methyl)aziridine-1-yl)-isoindoline-1,3-dione (**2d**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (dd, J=5.6, 3.2 Hz, 2H), 7.70 (dd, J=5.6, 3.2 Hz, 2H), 7.45–7.43 (m, 2H), 7.38–7.34 (m, 2H), 7.32–7.28 (m, 1H), 4.45 (br s, 1H), 4.33 (d, J=8 Hz, 1H), 2.82–2.77 (m, 1H), 2.64–2.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.44, 139.90, 134.35, 130.18, 128.56, 128.11, 126.18, 123.33, 75.77, 50.55, 35.83; IR (neat) cm^{-1} 2992, 1711, 1378, 1049, 708; HRMS (ESI [M+Na]): 317.0899 (calcd for $C_{17}H_{14}N_2O_3Na$: 317.0897).

*4.6.5. 2-(2-Hydroxy-7-azabicyclo[4.1.0]heptan-7-yl)-isoindoline-1,2-dione (**2e**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (dd, J=5.6, 3.2 Hz, 2H), 7.67–7.65 (m, 2H), 4.09–4.06 (m, 1H), 3.56 (d, J=7.2, 1H), 3.19 (ddd, J=7.4, 4.8, 2.4 Hz, 1H), 2.78 (dd, 7.6, 4 Hz, 1H), 2.02–1.98 (m, 2H), 1.70–1.67 (m, 1H), 1.57–1.54 (m, 1H), 1.41–1.32 (m, 1H), 1.22–1.17 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.42, 134.17, 130.23, 123.11, 66.69, 49.17, 45.89, 29.05, 21.72, 19.18; IR (neat) cm^{-1} 2938, 1704, 1373, 1153, 790; HRMS (ESI [M+H]): 259.1074 (calcd for $C_{14}H_{15}N_2O_3$: 259.1077).

*4.6.6. 2-((3aR,4S,5aR,6aR,6bS)-4-Hydroxy-2,2-dimethyldihydro-3aH-[1,3]dioxolo[4′,5′:3,4]benzo[1,2-b]azirin-6(4H,6aH,6bH)-yl)isoindoline-1,3-dione (**2f**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J=5.6, 3.2 Hz, 2H), 7.67 (dd, J=5.6, 3.2 Hz, 2H), 4.9 (d, J=6 Hz, 1H), 4.29 (dd, J=5.8, 3.4 Hz, 1H), 3.94 (d, J=3.2 Hz, 1H), 3.75 (d, J=11.2 Hz, 1H), 3.10 (d, J=7.2 Hz, 1H), 2.96 (d, J=7.6 Hz, 1H), 2.51–2.47 (m, 1H), 2.29 (dd, J=4, 2.4 Hz, 1H), 1.41 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.48, 134.22, 130.21, 123.22, 109.51, 74.78, 70.07, 64.7, 44.66, 43.34, 27.42, 25.23, 23.75; IR (neat) cm^{-1} 2913, 1778, 1723, 1467, 1376, 1265, 708; HRMS (ESI [M+H]): 331.12882 (calcd for $C_{17}H_{19}N_2O_5$: 331.12885). Single crystals of product **2f** suitable for X-ray crystallographic analysis were obtained by slow crystallization from dichloromethane/hexane solution. CCDC number for **2f** is 994392. Crystal data for **2f**; empirical formula=$C_{17}H_{18}N_2O_5$, formula weight=330.33, temperature=296 (2) K, wavelength=1.54178 Å, Crystal system=orthorhombic, space group=*P 21 21 21*, unit cell dimensions a=6.8269 (2) Å, b=10.9827 (4) Å, c=21.5999 (7) Å, α=90°, β=90°, γ=90°, volume=1619.51 (9) Å^3, Z=4, density (calculated)=1.351 Mg/m^3, absorption coefficient=0.841 mm^{-1}, F(000)=692, crystal size=0.48×0.12×0.04 mm^3, theta range for data collection=4.09–67.35°, index ranges=$-8\leq h\leq 4$, $-13\leq k\leq 12$, $-25\leq l\leq 25$, reflections collected=24,722, Independent reflections=2890 [R(int)=0.0351], completeness to theta (67.35°)=99.6%, absorption correction=semi-empirical from equivalents, max. and min. transmission=0.9671 and 0.6883, refinement method=full-matrix least-squares on F^2, data=2890, restraints=0, parameters=222, goodness-of-fit on F^2=0.997, Final R indices [I>2sigma(I)] R1=0.0384, wR2=0.1131, R indices (all data) R1=0.0398, wR2=0.1150, absolute structure parameter=0.0(3), extinction coefficient=0.0028(5), largest diff. peak and hole=0.395 and −0.177 e Å^{-3}.

*4.6.7. 2-(2-(Benzyloxy)-7-azabicyclo[4.1.0]heptan-7-yl)isoindoline-1,3-dione (**2g**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J=5.4, 3.0 Hz, 2H), 7.66 (dd, J=5.6, 3.2 Hz, 2H), 7.48–7.44 (m, 2H), 7.35 (t, J=7.4 Hz, 2H), 7.30–7.25 (m, 1H), 4.86 (q, J=12.0 Hz, 2H), 4.00 (dd, J=9.0, 5.4 Hz, 1H), 2.90 (d, J=7.6 Hz, 1H), 2.87–2.81 (m, 1H), 2.33 (dt, J=9.6, 4.9 Hz, 1H), 1.89–1.74 (m, 2H), 1.51 (d, J=6.8 Hz, 1H), 1.35–1.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.08, 138.57, 133.97, 130.56, 128.36, 127.91, 127.54, 122.94, 72.89, 70.89, 46.57, 44.63, 27.74, 23.02, 15.88; IR (neat) cm^{-1} 3032, 2942, 2870, 1767, 1715, 1376, 1154, 889, 706; HRMS (EI) : 348.1480 (calcd for $C_{21}H_{20}N_2O_3$: 348.1474).

*4.6.8. trans-N-(2,3-Diphenylaziridin-1-yl)-phthalimide (**2i**).*[20] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.54 (m, 6H), 7.42–7.31 (m, 5H), 7.24–7.23 (m, 3H), 4.93 (d, J=4 Hz, 1H), 3.96 (d, J=4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.51, 136.58, 133.86, 131.29, 130.16, 129.37, 128.71, 128.60, 128.22, 128.13, 127.23, 122.86, 53.59, 46.52; IR (neat) cm^{-1} 2923, 1716, 1372, 896, 749, 698; HRMS (ESI [M+H]): 341.1275 (calcd for $C_{22}H_{17}N_2O_2$: 341.1285).

*4.6.9. 2-(7-Azabicyclo[4.1.0]heptan-7-yl)isoindoline-1,3-dione (**2j**).*[14,19] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71–7.68 (m, 2H), 7.63–7.60 (m, 2H), 2.70 (d, J=4 Hz, 2H), 2.21–2.18 (m, 2H), 1.93 (br s, 2H), 1.39–1.34 (m, 2H), 1.28–1.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.15, 133.76, 130.62, 122.74, 43.81, 23.09, 20.04; IR (neat) cm^{-1} 2937, 1715, 1458, 178, 712; HRMS (EI): 242.1053 (calcd for $C_{14}H_{14}N_2O_2$: 242.1055).

*4.6.10. 2-(7-Azabicyclo[4.1.0]hept-3-en-7-yl)isoindoline-1,3-dione (**2k**).*[24] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71–7.70 (m, 2H), 7.63–7.62 (m, 2H), 6.20–6.18 (m, 1H), 5.91–5.88 (m, 1H), 3.13 (d, J=6.8 Hz, 1H), 2.84 (br s, 1H), 2.53–2.48 (m, 1H), 2.17–2.11 (m, 1H), 2.07–1.99 (m, 1H), 1.68–1.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.97, 133.86, 132.13, 130.34, 122.82, 121.34, 46.23, 40.23, 20.89, 18.17; IR (neat) cm^{-1} 3034, 2922, 1711, 1463, 1380, 1151, 787; HRMS (EI): 240.0905 (calcd for $C_{14}H_{12}N_2O_2$: 240.0899).

*4.6.11. 2-(1-Methyl-7-azabicyclo[4.1.0]heptan-7-yl)isoindoline-1,3-dione (**2l**).*[19] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66–7.58 (m, 4H), 2.82 (d, J=5.2 Hz, 1H), 2.15–2.06 (m, 2H), 1.95–1.94 (m, 1H), 1.65–1.58 (m, 1H), 1.37–1.34 (m, 2H), 1.25–1.17 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 133.64, 130.72, 122.54, 48.19, 47.10, 30.29, 23.53, 20.23, 20.07, 19.91; IR (neat) cm^{-1} 2934, 1726, 1370, 1147, 711; HRMS (EI): 256.1206 (calcd for $C_{15}H_{16}N_2O_2$: 256.1212).

*4.6.12. 1-Aminophthalimide-2-6,6a-dihydroindeno[1,2-b]aziridine (**2m**).*[19] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, J=5.2, 3.2 Hz, 2H), 7.68 (dd, J=5.4, 3.0 Hz, 3H), 7.24 (br s, 3H), 4.15 (d, J=5.2 Hz, 1H), 3.77 (dd, J=5.0 Hz, 1H), 3.49 (d, J=18 Hz, 1H), 3.27 (dd, J=17.8, 4.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.11, 143.13, 138.88, 134.05, 130.52, 128.62, 126.79, 125.54, 125.33, 123.05, 53.32, 48.79, 35.1; IR (neat) cm^{-1} 2920, 1714, 1374, 1140, 707; HRMS (ESI [M+H]): 277.0976 (calcd for $C_{17}H_{13}N_2O_2$: 277.0972).

*4.6.13. 3-Phthalimido-3-azatricyclo[3.2.1.0^{2,4}]-octane (**2o**).*[25] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.71 (m, 2H), 7.64–7.62 (m, 2H), 2.77 (br s, 2H), 2.73 (br s, 2H), 1.59–1.55 (m, 1H), 1.47 (d, J=8.8 Hz, 2H), 1.26–1.24 (m, 2H), 0.78 (d, J=10 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.33, 133.83, 130.47, 122.78, 45.15, 36.21, 27.69, 26.11; IR (neat) cm^{-1} 2959, 1711, 1376, 1135, 704; HRMS (EI): 254.1051 (calcd for $C_{15}H_{14}N_2O_2$: 254.1055).

*4.6.14. Methyl 4-((1-(1,3-dioxoisoindolin-2-yl)aziridin-2-yl)methoxy)benzoate (**2p**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J=8.8 Hz, 2H), 7.77 (dd, J=5.8, 3.0 Hz, 2H), 7.68 (dd, J=5.2, 3.2 Hz, 2H), 6.98 (d, J=9.2 Hz, 2H), 4.47 (dd, J=10.6, 4.6 Hz, 1H), 4.21 (dd, J=11, 5 Hz, 1H), 3.86 (s, 3H), 3.07–3.03 (m, 1H), 2.68–2.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.84, 166.74, 164.96, 162.14, 134.22, 134.14, 131.6, 130.25, 123.53, 123.13, 114.29, 67.41, 51.81, 40.56, 35.69; IR

(neat) cm^{-1} 2951, 1716, 1605, 1377, 1170; HRMS (ESI [M+H]): 353.1145 (calcd for $C_{19}H_{17}N_2O_5$: 353.1132).

*4.6.15. Methyl 1-(1,3-dioxoisoindolin-2-yl)-3-methylaziridine-2-carboxylate (**2s**).*[26] According to the general procedure reaction of (*E*/*Z*) methyl crotonate (**1s**) yielded 86% of product **2s** in 5:1 ratio. ^1H NMR (400 MHz, $CDCl_3$): δ 7.72–7.69 (m, 2H), 7.62 (dd, *J*=5.6, 3.2 Hz, 2H), 3.65 (s, 3H), 3.35–3.32 (m, 1H), 3.01 (d, *J*=5.2 Hz, 1H), 1.48 (d, *J*=6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.47, 164.74, 133.87, 130.32, 122.99, 52.63, 44.93, 44.73, 16.31; IR (neat) cm^{-1}: 2954, 1717, 1441, 1137, 709; HRMS (ESI [M+H]) 261.0879 (calcd for $C_{13}H_{13}N_2O_4$: 261.0870).

*4.6.16. 2-(2-(Morpholine-4-carbonyl)-3-phenyaziridin-1-yl)-isoindoline-1,3-dione (**2t**).* ^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (dd, *J*=5.2, 3.2 Hz, 2H), 7.65 (dd, *J*=5.2, 2.8 Hz, 2H), 7.46 (d, *J*=6.4 Hz, 2H), 7.39–7.31 (m, 3H), 4.69 (d, *J*=4.8 Hz, 1H), 4.04–4.00 (m, 2H), 3.81–3.79 (m, 2H), 3.72–3.62 (m, 3H), 3.52 (d, *J*=4.8 Hz, 1H), 3.43–3.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.66, 162.59, 135.39, 134.24, 133.94, 130.41, 128.59, 128.34, 127.11, 123.46, 123.03, 66.41, 66.20, 48.31, 46.77, 45.66, 42.99; IR (neat) cm^{-1} 2964, 1774, 1718, 1464, 1377, 1144, 707; HRMS (EI): 377.1367 (calcd for $C_{21}H_{19}N_3O_4$: 377.1376).

*4.6.17. 2-(2-(2-Oxooxazolidine-3-carbonyl-3-phenylaziridin-1-yl)-isoindoline-1,3-dione (**2u**).*[27] ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (br s, 2H), 7.68 (br s, 2H), 7.49 (d, *J*=7.2 Hz, 2H), 7.37 (dd, *J*=12.8, 7.2 Hz, 3H), 5.16 (d, *J*=5.2 Hz, 1H), 4.49–4.44 (m, 3H), 4.07–3.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.89, 164.65, 153.34, 134.32, 134.06, 133.99, 128.66, 128.62, 127.47, 123.09, 62.19, 50.59, 43.99, 43.02; IR (neat) cm^{-1} 2920, 1774, 1709, 1361, 1106, 696; HRMS (EI): 377.1017 (calcd for $C_{20}H_{15}N_3O_5$: 377.1012).

*4.6.18. 2-(1-Acetyl-7-azabicyclo[4.1.0]heptan-7yl)-isoindoline-1,3-dione (**2v**).* ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (dd, *J*=5.4, 3.0 Hz, 2H), 7.60 (dd, *J*=5.2, 3.2 Hz, 2H), 3.61 (d, *J*=5.6 Hz, 1H), 2.64–2.56 (m, 1H), 2.40 (s, 3H), 2.29–2.18 (m, 2H), 2.07–1.99 (m, 1H), 1.56–1.41 (m, 3H), 1.24–1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.28, 165.07, 133.74, 130.54, 122.8, 52.5, 48.6, 28.22, 25.98, 23.04, 20.18, 19.59; IR (neat) cm^{-1} 2938, 1712, 1377, 1153, 710; HRMS (EI): 284.1160 (calcd for $C_{16}H_{16}N_2O_3$: 284.1161).

*4.6.19. 2-(2-Acetyl-3-phenylaziridin-1-yl)-isoindoline-1,3-dione (**2w**).*[28] ^1H NMR (400 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.65 (dd, *J*=5.6, 2.8 Hz, 2H), 7.44–7.34 (m, 5H), 4.35 (d, *J*=4.8 Hz, 1H), 3.69 (d, *J*=4.8 Hz, 1H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.51, 164.71, 134.97, 134.0, 130.26, 128.65, 128.56, 127.1, 123.1, 51.12, 49.97, 31.53; IR (neat) cm^{-1} 3036, 1771, 1715, 1339, 1144, 703; HRMS (ESI [M+H]): 307.1067 (calcd for $C_{18}H_{15}N_2O_3$: 307.1077).

*4.6.20. 2-(2-Benzoyl-3-phenylaziridin-1-yl)isoindoline-1,2-dione (**2x**).*[11] ^1H NMR (400 MHz, $CDCl_3$): δ 8.08–8.06 (m, 2H), 7.70–7.68 (m, 2H), 7.61–7.57 (m, 3H), 7.53–7.51 (m, 4H), 7.49–7.34 (m, 3H), 4.68 (d, *J*=4.8 Hz, 1H), 4.39 (d, *J*=4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.43, 164.48, 137.22, 135.09, 133.87, 133.49, 130.14, 128.83, 128.65, 128.57, 128.48, 127.12, 123.01, 50.51, 48.55; IR (neat) cm^{-1} 3035, 1772, 1719, 1450, 1144, 703; HRMS (ESI [M+H]): 369.1240 (calcd for $C_{23}H_{17}N_2O_3$: 369.1234).

*4.6.21. 2-(2-(4-Methoxybenzoyl)-3-(3-methoxyphenyl)aziridin-1-yl)-isoindoline-1,3-dione (**2y**).* ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J*=8.8 Hz, 2H), 7.59–7.41 (m, 4H), 7.42 (d, *J*=8.4 Hz, 2H), 6.91 (dd, *J*=16.0, 8.8 Hz, 4H), 4.62 (d, *J*=4.8 Hz, 1H), 4.33 (d, *J*=4.8 Hz, 1H), 3.82 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.6, 164.49, 163.86, 159.69, 133.77, 130.95, 130.21, 130.13, 128.35, 127.21, 122.91, 113.97, 113.88, 55.40, 55.20, 49.86, 48.17; IR (neat) cm^{-1} 2936, 1770, 1717, 1425, 1147, 707; HRMS (ESI [M+H]): 429.1449 (calcd for $C_{25}H_{21}N_2O_5$: 429.1445).

*4.6.22. (E)-2-(2-Cinnamoyl-3-phenylaziridin-1-yl)-isoindoline-1,3-dione (**2z**).*[28] ^1H NMR (400 MHz, $CDCl_3$): δ 7.74–7.71 (m, 2H), 7.65–7.63 (m, 2H), 7.58–7.56 (m, 2H), 7.50–7.48 (m, 2H), 7.41–7.33 (m, 7H), 7.09 (d, *J*=16.0 Hz, 1H), 4.58 (d, *J*=4.8 Hz, 1H), 3.97 (d, *J*=4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.23, 164.58, 144.60, 135.33, 134.23, 133.94, 131.02, 130.38, 129.0, 128.75, 128.67, 128.54, 127.20, 125.98, 123.14, 50.80, 50.22; IR (neat) cm^{-1} 2923, 1716, 1674, 1450, 1146, 703; HRMS (ESI [M+H]): 395.1383 (calcd for $C_{25}H_{19}N_2O_3$: 395.1390).

*4.6.23. 2-(2-(2-(Allyloxy)benzoyl)-3-phenylaziridin-1-yl)-isoindoline-1,3-dione (**2aa**).* ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J*=7.6 Hz, 2H), 7.71 (dd, *J*=5.2, 3.2 Hz, 2H), 7.63 (dd, *J*=5.2, 2.8 Hz, 2H), 7.57 (d, *J*=7.6 Hz, 2H), 7.48 (t, *J*=8 Hz, 2H), 7.29 (d, *J*=8 Hz, 1H), 7.0 (t, *J*=7.6 Hz, 1H), 6.86 (d, *J*=8.4 Hz, 1H), 5.87 (ddd, *J*=15.6, 10.0, 4.8 Hz, 1H), 5.26 (d, *J*=17.2 Hz, 1H), 5.10 (d, *J*=10.4 Hz, 1H), 4.81 (d, *J*=4.8 Hz, 1H), 4.56–4.48 (m, 2H), 4.19 (d, *J*=4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.04, 164.66, 156.88, 137.66, 134.30, 133.85, 133.29, 132.82, 130.44, 129.24, 128.64, 127.91, 123.59, 123.08, 121.00, 117.04, 111.69, 66.84, 48.46, 47.48; IR (neat) cm^{-1} 1771, 1718, 1666, 1451, 1379, 1178, 705; HRMS (ESI [M+H]): 425.1500 (calcd for $C_{26}H_{21}N_2O_4$: 425.1496).

Acknowledgements

We thank the National Science Council of the Republic of China for generous financial support. B.A. thanks MOFA for Taiwan scholarship programme.

Supplementary data

Copies of ^1H and ^{13}C NMR spectra are available. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.06.029.

References and notes

1. (a) Dembitsky, V. M.; Terent'ev, A. O.; Levitsky, D. O. *Handbook of Natural Products*Vol. 1; Springer: Berlin, 2013, Vol. 1, pp 977–1006; (b) Botuha, C.; Chemia, F.; Ferreira, F.; Luna, A. P. Heterocycles in Natural Product Synthesis, Part-1 In. *Majumdar, K. C., Chattopadyay, S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2011; pp 1–39; (c) Aziridines and Epoxides in Organic Synthesis; Yudin, A. K., Ed.; Wiley-VCH: Weinheim, Germany, 2006; (d) Steuerle, U.; Feuerhake, R. Ullman's Encyclopedia of Industrial Chemistry; Wiley-VCH: Weinheim, Germany, 2006; (e) Padwa, A. In Comprehensive Heterocyclic Chemistry III; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier: Oxford, UK, 2008; p p 1.*
2. Muller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905.
3. Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247.
4. (a) McCoull, W.; Davis, F. A. *Synthesis* **2000**, 1347; (b) Chang, J. W. W.; Ton, T. M. U.; Chan, P. W. H. *Chem. Rec.* **2011**, *11*, 331; (c) Pellissier, H. *Tetrahedron* **2010**, *66*, 1509.
5. Atkinson, R. S. *Tetrahedron* **1999**, *55*, 1519.
6. Yamada, Y.; Yamamoto, T.; Okawara, M. *Chem. Lett.* **1975**, 361.
7. Evans, D. A.; Bilodeau, M. T.; Faul, M. M. *J. Am. Chem. Soc.* **1994**, *116*, 2742.
8. Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889.
9. Maestre, L.; Sameera, W. M. C.; Requejo, M. M. D.; Maseras, F.; Perez, P. J. *J. Am. Chem. Soc.* **2013**, *135*, 1338.
10. Hilt, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 3586.
11. Siu, T.; Yudin, A. K. *J. Am. Chem. Soc.* **2002**, *124*, 530.
12. Watson, I. D. G.; Yu, L.; Yudin, A. K. *Acc. Chem. Res.* **2006**, *39*, 194.
13. Siu, T.; Picard, C. J.; Yudin, A. K. *J. Org. Chem.* **2005**, *70*, 932.
14. Li, J.; Liang, J. L.; Hong Chan, P. W.; Che, C. M. *Tetrahedron Lett.* **2004**, *45*, 2685.
15. Krasnova, L. B.; Hili, R. M.; Chernoloz, O. V.; Yudn, A. K. *ARKIVOC* **2005**, *iv*, 26.
16. Schweitzer-Chaput, B.; Keita, M.; Milcent, T.; Ongeri, S.; Crousse, B. *Tetrahedron* **2012**, *68*, 7028.
17. (a) Hernández-Toribio, J.; Hussain, M. M.; Cheng, K.; Carroll, P. J.; Walsh, P. J. *Org. Lett.* **2011**, *13*, 6094; (b) Zhang, E.; Tu, Y.-Q.; Fan, C.-A.; Zhao, X.; Jiang, Y.-J.; Zhang, S.-Y. *Org. Lett.* **2008**, *10*, 4943.
18. Li, J.; Chan, P. W. H.; Che, C. M. *Org. Lett.* **2005**, *7*, 5801.
19. Yoshimura, A.; Middleton, K. R.; Zhu, C.; Nemykin, V. N.; Zhdankin, V. V. *Angew. Chem., Int. Ed.* **2012**, *51*, 8059.

20. Richardson, R. D.; Desaize, M.; Wirth, T. *Chem.—Eur. J.* **2007**, *13*, 6745.
21. Jones, D. W. *J. Chem. Soc., Perkin Trans. 1* **1972**, 225.
22. (a) Atkinson, R. S.; Malpass, J. R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2241; (b) Atkinson, R. S.; Grimshire, M. J.; Kelly, B. J. *Tetrahedron* **1989**, *45*, 2875.
23. Dickinson, J. M.; Murphy, J. A. *Tetrahedron* **1992**, *48*, 1317.
24. Hoesch, L.; Egger, N.; Dreiding, A. S. *Helv. Chim. Acta* **1978**, *61*, 795.
25. Aitken, R. A.; Gosney, I.; Farries, H.; Palmer, M. H.; Simpson, I.; Cadogan, J. I. G.; Tinley, E. J. *Tetrahedron* **1985**, *41*, 1329.
26. Anderson, D. J.; Gilchrist, T. L.; Horwell, D. C.; Rees, C. W. *J. Chem. Soc. C* **1970**, 576.
27. Yang, K. S.; Chen, K. *Org. Lett.* **2002**, *4*, 1107.
28. Kuznetsov, M. A.; Voronin, V. V. *Chem. Heterocycl. Compd.* **2011**, *47*, 173.
29. Krasnova, L. B.; Yudin, A. K. *Org. Lett.* **2006**, *8*, 2011.
30. Ma, W. B.; Li, S. N.; Zhou, Z. H.; Shen, H. S.; Li, X.; Sun, Q.; He, L.; Xue, Y. *Eur. J. Org. Chem.* **2012**, *8*, 1554.
31. Hartman, C.; Mayer, V. *Ber. Dtsch. Chem. Ges.* **1983**, *26*, 1727.
32. IBX is relatively acidic on the organic scale, for more information please see: Gallen, M. J.; Goumont, R.; Clark, T.; Terrier, F.; Williams, C. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 2929.
33. Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537.
34. Nicolaou, K. C.; Zhong, Y. L.; Baran, P. S. *J. Am. Chem. Soc.* **2000**, *122*, 7596.
35. Nicolaou, K. C.; Baran, P. S.; Zhong, Y. L. *J. Am. Chem. Soc.* **2001**, *123*, 3183.
36. Nicolaou, K. C.; Montagnon, T.; Baran, P. S.; Zhong, Y. L. *J. Am. Chem. Soc.* **2002**, *124*, 2245.
37. Nicolaou, K. C.; Montagnon, T.; Baran, P. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 993.
38. Nicolaou, K. C.; Gray, D. L. F.; Montagnon, T.; Harrison, S. T. *Angew. Chem., Int. Ed.* **2002**, *41*, 996.
39. Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 4077.
40. Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5192.
41. *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; Springer: Berlin, Germany, 2003.
42. Zhdankin, V. V. *J. Org. Chem.* **2011**, *76*, 1185.
43. Duschek, A.; Kirsch, S. T. *Angew. Chem., Int. Ed.* **2011**, *50*, 1524.
44. Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299.
45. Mazitschek, R.; Mülbaier, M.; Giannis, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 4059.
46. More, J. D.; Finney, N. S. *Org. Lett.* **2002**, *4*, 3001.
47. Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, 7277.
48. Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. *J. Am. Chem. Soc.* **1979**, 159.
49. For more information please see Supplementary data.
50. De Kimpe, N.; Palamareva, M.; Sulmon, P.; Verhe, R.; De Buyck, L.; Schamp, N.; Declercq, J. P.; Tinant, B.; Van Meerssche, M. *Tetrahedron* **1986**, *42*, 71.
51. Duhamel, P.; Duhamel, L.; Valnot, J. Y. *Tetrahedron Lett.* **1973**, *14*, 1339.
52. Duhamel, L.; Valnot, J. Y. *Tetrahedron Lett.* **1974**, *15*, 3167.
53. De Kimpe, N.; Tehrani, K. A.; Fonck, G. *J. Org. Chem.* **1996**, *61*, 6500.
54. De Kimpe, N.; Yao, Z. P.; Schamp, N. *Tetrahedron Lett.* **1986**, *27*, 1707.
55. Sulmon, P.; De Kimpe, N.; Schamp, N.; Declercq, J. P.; Tinant, B. *J. Org. Chem.* **1988**, *53*, 4457.
56. De Kimpe, N.; Schamp, N. *Org. Prep. Proced. Int.* **1979**, *11*, 115 and references therein.
57. Bhorge, Y. R.; Chang, S.-H.; Chang, C.-T.; Yan, T.-H. *Tetrahedron* **2012**, *68*, 4846.
58. In addition with experimental insights presented here, the control experimental results, presented in Supplementary data page number 5, reveal the following information (1) there is no product formation in the absence of base (2) this reaction does not proceed through 1,4 addition followed by cyclisation (3) there is no difference in selectivity trend between higher and lower temperature.
59. Moss, R. A.; Zhang, H. *J. Am. Chem. Soc.* **1994**, *116*, 4471.
60. Moss, R. A.; Scrimin, P.; Rosen, R. T. *Tetrahedron Lett.* **1987**, *28*, 251.