JOC The Journal of Organic Chemistry

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Regioselective (Diacetoxyiodo)benzene-Promoted Halocyclization of Unfunctionalized Olefins

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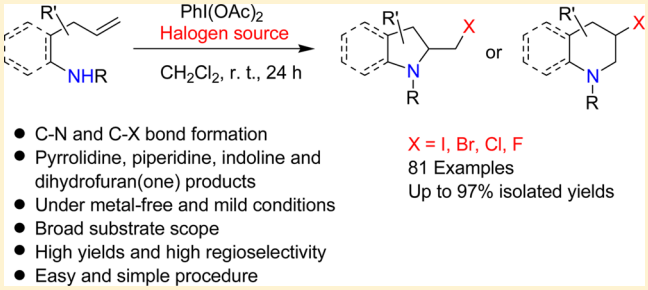
Supporting Information

ABSTRACT: A metal-free method for intramolecular halocyclization of unfunctionalized olefins was detailed. (Diacetoxyiodo)benzene (PIDA) was very effective for haloamidation, haloetherification, and halolactonization of unfunctionalized olefins. In the presence of 1.1 equiv of PIDA and suitable halogen sources, a variety of unfunctionalized olefins could be converted to the corresponding 1,2-bifunctional cyclic skeletons in good to excellent isolated yields, and key intermediates for biologically interesting compounds could be obtained in high yields under mild conditions via nucleophilic substitution of the thus obtained halocyclization products.



INTRODUCTION

Halogen containing 1,2-difunctional structures such as vicinal haloamines are important functional groups in mechanism-based anticancer/antitumor drugs (Figure 1).[1] They are key

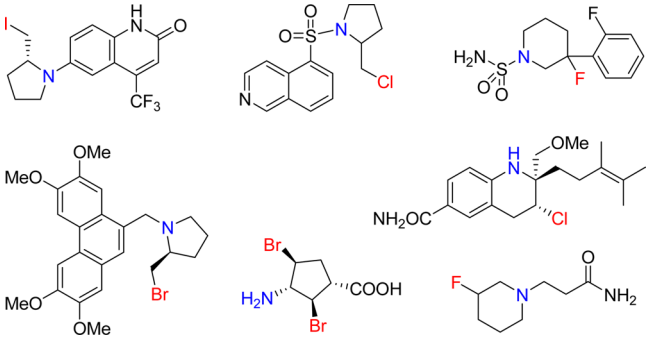


Figure 1. Examples of bioactive vicinal haloamines.

intermediates for several biologically interesting skeletons[2] and also appear as key structures in different natural products.[3] To this end, significant efforts have been made toward the construction of vicinal haloamine structures.[4]

Haloamination of activated C=C double bonds have been well studied in the past decades,[5] and the reactions can be carried out regio- and stereoselectively by fine-tuning the structures of the catalysts.[6] In contrast, only limited progress was achieved for the haloamination of unactivated C=C double bonds due to the low reactivity of the substrates. Direct formation of 1,2-haloamines could be realized via halogen-assisted haloamination,[7] but application of this method was generally limited due to the possible sensitivity of other functional groups toward dihalogens. Free radical chloroamination of C=C double bonds with N-electron rich amines could be realized by in situ generation of free radicals[8] or using catalyst systems such as Cu(I)[9] or Lewis acid-$TiCl_3$.[10] Intramolecular haloamination of amine or (sulfon)amide substrates could also be carried out using palladium compounds as catalysts in combination with a variety of additives,[11] and olefinic substrates bearing sulfonamide, carboxylic amide, or carbamate functional groups could be converted to the corresponding N-substituted heterocyclic compounds in high yields.[5b] Cu(II) was also reported to promote a variety of aminocyclization reactions such as carboamination,[12] amonooxygenation,[13] diamination,[14] and haloamination[15] of unfunctionalized olefins, and good to excellent enantioselectivities were realized in the presence of appropriate chiral ligands.[13a,15,16]

We have shown that Cu(II) was able to promote cyclization of unfunctionalized olefins under mild conditions, and intramolecular chloroamination and bromoamination could be realized for a variety of 4-penten-1-amine and 5-hexen-1-amine substrates without the use of palladium. The reactions were carried out using $CuCl_2$ and $CuBr_2$ as both the reaction promoters and the halogen sources, and cyclization products 2-chloromethylpyrrolidines, *N*-tosyl 2-bromomethylpyrrolidines, *N*-tosyl 2-bromomethylpiperidines, and 3-bromo/3-chloropiperidines could all be obtained in good isolated yields at

Received: July 30, 2014

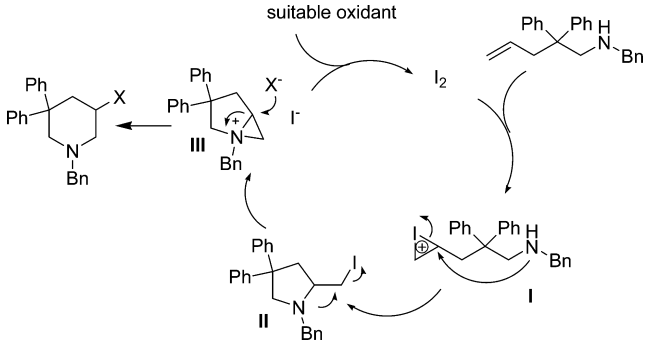
   dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

ambient temperature without special care for air and moisture.[17] In this paper, we wish to report our recent progress on (diacetoxyiodo)benzene (PIDA)-promoted intramolecular halocyclization of different unfunctionalized olefins as a continuation of our program on the functionalization of unactivated olefins.

RESULTS AND DISCUSSION

In our course of searching for new methods for intramolecular haloamination of unfunctionalized olefins, we found that zinc iodide was able to promote the intramolecular iodoamination of *N*-benzyl-2,2-diphenyl-4-penten-1-amine. Further study indicated that the reaction was promoted by molecular iodine temporally formed via oxidation of I^-. On the basis of this finding, we developed an iodine-catalyzed method for intramolecular chloro- and bromoamination of unfunctionalized olefins (Scheme 1).[18]

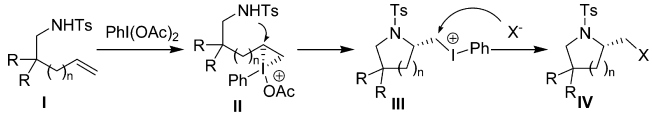
Scheme 1. Iodine-Catalyzed Haloamination of *N*-Benzyl-2,2-diphenyl-4-penten-1-amine



The substrate was first activated via traditional electrophilic addition pathway and nucleophilic opening of the iodonium three-membered ring of the intermediate **I** produced iodoamination compound **II** as a temporary product. In the presence of an excess amount of halogen source, iodine was replaced by chlorine or bromine, yielding the corresponding chloro- or bromoamination compounds as the final products. The reaction was carried out with 2 mol % of molecular iodine and appropriate amount of halogen source, a suitable oxidant was required to regenerate I_2 and to complete the catalytic cycle. The reaction proceeded readily at ambient temperature, and the products 3-chloro- or 3-bromopiperidines were obtained in good to excellent isolated yields. However, the reaction was only suitable for *N*-alkyl substrates, and no reaction was observed for *N*-(sulfon)amide substrates. We reasoned that the low reactivity was due to the low nucleophilicity of the amide nitrogen atom which limited the conversion of intermediate **II** to intermediate **III**. Without the formation of intermediate **III**, the reaction was stopped at intermediate **II**, and no chloro- or bromoamination products could be formed.

The potential application of vicinal haloamines drove us to develop a general method for intramolecular haloamination of unfunctionalized olefins, and our attention focused on hypervalent iodine compounds due to their good performance in a variety of organic reactions. In addition to the widespread application of periodinane I(V) in Dess-Martin oxidation of primary and secondary alcohols,[19] hypervalent iodine compounds were also found to have application as oxidants in palladium-catalyzed C=C double bond amination reactions[20] and as catalysts[21] in the functionalization of different C=C double bonds.[22] Encouraged by these literature results, we proposed a (diacetoxyiodo)benzene (PIDA)-mediated haloamidation of unfunctionalized olefins as shown in Scheme 2.

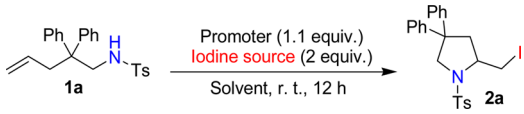
Scheme 2. Proposed Reaction Sequence for I(III)-Mediated Intramolecular Haloamidations



The C=C double bond in substrate **I** was first activated by PIDA, and intramolecular nucleophilic attack of nitrogen atom on the three-membered ring in **II** produced the intermediate **III**, which was converted to product **IV** by the action of the halogen source.

To test the feasibility of this proposed reaction sequence, iodoamidation of an unfunctionalized C=C double bond was investigated using **1a** as model substrate, and the preliminary results were summarized in Table 1.

Table 1. Intramolecular Iodoamidation of 1a with Different Promoters[a]



entry	promoter	iodine source	solvent	isolated yield (%)[b]
1	PIDA	NaI	CH_2Cl_2	78
2	PIDA	ZnI_2	CH_2Cl_2	72
3	PIDA	LiI	CH_2Cl_2	83
4	PIDA	KI	CH_2Cl_2	91
5	PIDA	KI	MeOH	61
6	PIDA	KI	benzene	33
7	PIDA	KI	acetone	23
8	PIDA	KI	DMF	ND[c]
9	PIDA	KI	DMSO	ND[c]
10	PIDA		CH_2Cl_2	NR[c]
11		KI	CH_2Cl_2	NR[c]
12		I_2	CH_2Cl_2	80
13		NIS	CH_2Cl_2	78
14	$(n\text{Bu})_4\text{NI}$	KI	CH_2Cl_2	NR
15	PhI	KI	CH_2Cl_2	NR
16	IBX	KI	CH_2Cl_2	61
17[d]	DMP	KI	CH_2Cl_2	73

[a]The reaction was carried out with 0.5 mmol of **1a**, 0.55 mmol of promoter, 1 mmol of iodine source, and 20 mL of solvent. [b]Isolated yields based on **1a**. [c]ND = not detectable, NR = no reaction. [d]DMP = Dess-Martin periodinane.

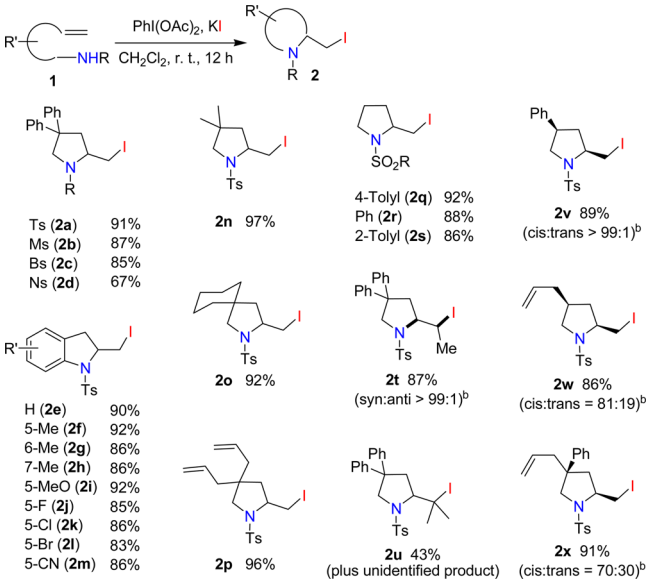
We were delighted to find that exo cyclization of substrate **1a** proceeded readily in the presence of PIDA, giving the kinetically favored product **2a** in 78% yield in CH_2Cl_2 without the formation of the endo cyclization product (entry 1). The sole formation of exo product may be attributed to the use of sulfonamide which suppressed the rearrangement of the exo product to the thermodynamically stable endo product.[17c] Iodine source investigation showed that KI gave the best result (entries 1–4). The effect of the solvents on the course of the

dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX–XXX

reaction was also noteworthy (entries 4–9), and CH_2Cl_2 was the most suitable solvent for the reaction. Reaction in solvents such as DMF or DMSO failed to occur, possibly due to the solvation of PIDA which caused the decrease of the electrophilicity of the latter (entries 8 and 9). No product was obtained in the absence of iodine source, indicating that the iodine atom in the product came from KI rather than from PIDA (entry 10). No reaction occurred in the absence of PIDA, indicating the important role that PIDA played in the reaction (entry 11). Mocular iodine could promote the reaction (entry 12), but the workup was generally troublesome, and it was difficult to completely remove the deep color from the reaction mixture. NIS was also able to promote the reaction but to a lesser extent (entry 13). $(n\text{Bu})_4\text{NI}$ or PhI was unable to promote the reaction, and no product was observed when the reaction was carried out with $(n\text{Bu})_4\text{NI}$ or PhI under otherwise identical conditions (entries 14 and 15). IBX or Dess-Martin periodinane in combination with KI could also be used for iodoamination of **1a**, but the yields were generally lower than PIDA-induced reactions (entries 16 and 17).

After optimization of the reaction conditions, different substrates were tested to study the scope of the reaction. The reactions were carried out using 1.1 equiv of PIDA as reaction promoter and 2 equiv of KI as iodine source, and the results are summarized in Scheme 3.

Scheme 3. PIDA-Promoted Intramolecular Iodoamidation of Different Unfunctionalized Olefins[a]



[a]The reaction was carried out with 0.5 mmol of substrate, 0.55 mmol of PIDA, 1 mmol of KI, and 20 mL of CH_2Cl_2. For **2d**, reaction time = 48 h; for **2e**–**2m**, reaction time = 24 h. [b]Diastereoisomeric ratios were determined by ^{1}H NMR.

As shown in Scheme 3, 2-iodomethylpyrrolidines and 2-iodomethylindoles could be obtained in good to excellent isolated yields. Electronic effect of the sulfonamides had some impact on the course of the reaction (**2a**–**2c** vs **2d**), and *p*-nitrobenzenesulfonamide gave product **2d** in moderate isolated yield. This was possibly due to the low nucleophilicity of sulfonamide caused by the strong electron withdrawing nitro group at the para position of the benzene ring. Cyclization of *N*-tosyl *o*-allyl aniline substrates could be realized in high isolated yields (**2e** to **2m**), and methyl, methoxy, halogen, and cyano groups on benzene ring could all be tolerated during the reactions. Comparing with I_2-mediated chloro- and bromoamination of unfunctionalized olefins in which strong Thorpe-Ingold effect was observed,[18] the current reaction system was less dependent on the substituents on the main chain (**2n** to **2p**), and substrates without substituents on the main chain could also be converted to 2-iodomethylpyrrolidines in good to excellent isolated yields (**2q** to **2s**). Substituents on C=C double bonds showed some impact on the reaction, and slightly lower yields were obtained for such substrates (**2t** and **2u**). When chiral substrates were used, cis products were isolated as the major products (**2v** to **2x**). The diastereomeric ratios depended on the substituents on the main chain, and substrates bearing larger substituent gave high regioselectivity. The cis configuration of **2v** was further confirmed by X-ray diffraction experiment. The ORTEP drawing of compound **2v** showed an envelope conformation of the five-membered ring, the phenyl and iodomethyl groups stayed at the equatorial positions and were away from each other (Figure 2).

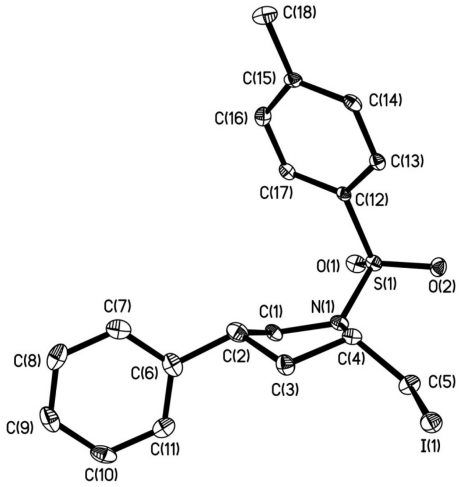
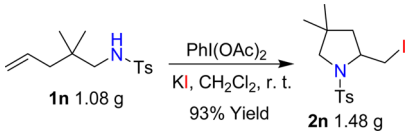


Figure 2. ORTEP drawing of **2v**. Hydrogen atoms were omitted for clarity.

To prove the scalability of the current protocol, compound **2n** was prepared on gram scale under the optimized reaction conditions. The iodoamidation of **1n** took place readily, affording the expected product **2n** in 93% isolated yield (Scheme 4). The iodine atom in **2n** could be replaced by a variety of nucleophiles such as azide (**3a**), phthalimide (**3b**), acetate (**3c**), or benzenethiol (**3d**) under mild condition (Scheme 5), and the current method therefore opened up a new route to a variety of biologically interesting compounds.[23]

Scheme 4. Gram-Scale Iodoamidation of Substrate 1n



After successful intramolecular iodoamidation of different unfunctionalized olefins, the bromine variant of the reaction was also tested using **1a** as a model substrate. The reaction conditions for iodoamidation were adopted, and different

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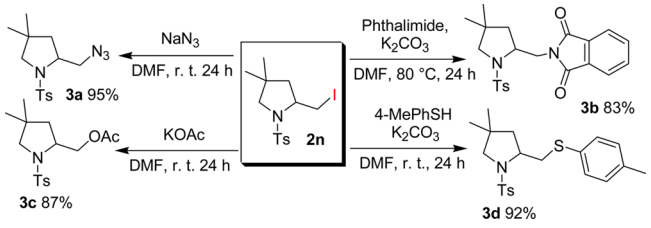
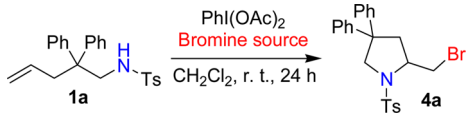
Scheme 5. Derivatization of 2-Iodomethypyrrolidine 2n to Different Bioactive Structures



commercially available bromine sources were screened to find the most suitable reaction condition. As indicated in Table 2, lithium bromide was the most suitable bromine source, and product **4a** was obtained in 87% isolated yield after 24 h.

Table 2. Bromoamidation of 1a with Different Bromine Sources[a]



entry	bromine source	isolated yield (%)
1	LiBr	87
2	$ZnBr_2$	73
3	NaBr	81
4	$MgBr_2$	70
5	Py·HBr	63

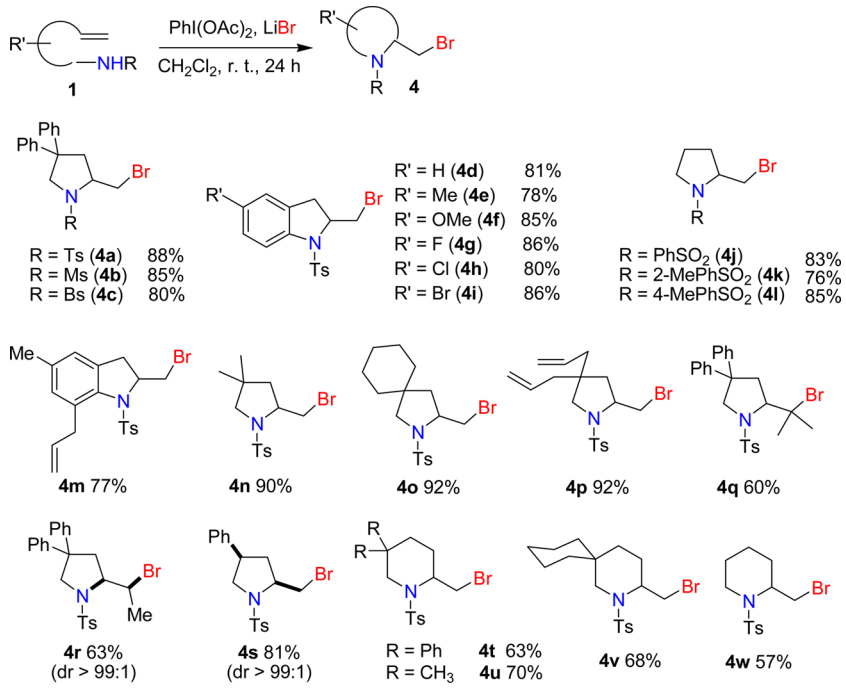
[a]The reactions were carried out with 0.5 mmol of **1a**, 0.55 mmol of PIDA, 1 mmol of bromides, and 20 mL of CH_2Cl_2.

To explore the scope and limitation of PIDA-promoted bromoamidation reactions, a variety of substrates were tested, and the results are listed in Scheme 6. Bromoamidation of unfunctionalized olefins generally gave results similar to iodoamidations, and most products were isolated in good yields. The reactions of *N*-alkenyl sulfonamides bearing different sulfonyl groups such as 4-toluenesulfonyl, methanesulfonyl, and benzenesulfonyl groups gave the corresponding products in good yields (**4a** to **4c**). A variety of substituted 2-bromomethyl indolines were prepared using the optimized reaction conditions, and the para substituents on the aromatic rings showed little effect on the course of the reaction (**4d** to **4i** and **4m**). Again, Thorpe-Ingold effect showed less impact on the reaction, and substrates without gem disubstituents also gave acceptable isolated yields (**4j** to **4l**). Different substituents on the main chain did not significantly influence the reaction outcomes (**4n** to **4p**), but adding substituents on the C═C double bond led to significantly diminished yields (**4q** and **4r**). Chiral substrate also gave a product in good isolated yield and high diastereoselectivity (**4s**). Reactions of 1-sulfonamido-5-hexene substrates generally gave lower isolated yields, possibly due to the unfavorable entropy feature for cyclization reactions (**4t** to **4w**).[24]

In addition to iodo- and bromoamidation of functionalized olefins, chloroamidation could also be realized under similar conditions. After screening different chlorine sources, pyridinium chloride was found to be suitable for the reaction, and several chloromethylpyrrolidine compounds were obtained in good isolated yields for terminal olefins (Table 3). Introduction of substituents on C═C double bonds led to drops of isolated yields (Table 3, entries 14 and 15). Normal metal chlorides failed to give good results possibly due to their poor solubility in the reaction medium (Table 3, entries 1−5).

Comparing to the successful intramolecular iodo-, bromo-, and chloroamidation reactions, intramolecular fluoroamidation reactions[20f,25] were relatively unsuccessful. Conventional metal fluorides or fluorine sources could not give the corresponding

Scheme 6. PIDA-Meadited Intramolecular Bromoamidation of Different Alkenes[a]



[a]The reaction was carried out with 0.5 mmol of substrate, 0.55 mmol of PIDA, 1 mmol of LiBr, and 20 mL of CH_2Cl_2.

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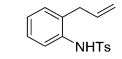
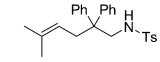
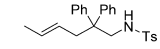
Table 3. PIDA-Mediated Intramolecular Chloroamidation of Different Unfunctionalized Olefins[a]

Entry	Substrate (R)	Chlorine source	Isolated yield (%)
1	Ph	NaCl	NR
2	Ph	KCl	NR
3	Ph	LiCl	20 (**5a**)
4	Ph	$MgCl_2$	9 (**5a**)
5	Ph	$ZnCl_2$	37 (**5a**)
6	Ph	Py·HCl	82 (**5a**)
7	Ph	Et_3N·HCl	NR
8	Ph	$(nBu)_4NCl$	NR
9	Me	Py·HCl	88 (**5b**)
10	-$(CH_2)_5$-	Py·HCl	76 (**5c**)
11	H	Py·HCl	76 (**5d**)
12	Allyl	Py·HCl	88 (**5e**)
13		Py·HCl	61 (**5f**)
14		Py·HCl	37 (**5g**)
15		Py·HCl	60 (**5h**)

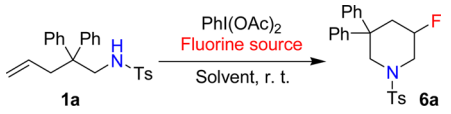
[a]The reaction was carried out with 0.5 mmol of substrates, 0.55 mmol of PIDA, 1 mmol of chlorine source, and 20 mL of CH_2Cl_2.

fluoroamidation products,[21f,h,26] and fluoroamidation products were obtained only when trifluoroborane in diethyl ether was used as fluorine source (Table 4).[27]

Fast reactions were observed for most cases, and the reactions could be completed in minutes. The corresponding 3-fluoropiperidine compounds were isolated in moderate yields with endo products as the sole isomer,[20f,21f,h,27,28] plus the formation of varied amount of 3-acetoxypiperidines (Scheme 7). The possible pathway for aminoacetoxylation is shown in Scheme 8. Intermediate **A** may be formed during the reaction, participation of sulfonamide oxygen produced the intermediate **B**[29] which could be converted to the corresponding 3-fluoro- or 3-acetoxypiperidine upon F^- or AcO^- attack. Conversion of the aminoacetoxylation product to the corresponding 3-fluoropiperidines was difficult,[21f] and searching for suitable fluorine source and suitable reaction conditions to suppress the aminoacetoxylation reaction are still underway.

Haloamidation of substrates with different functional groups on nitrogen atoms were also tested under the respective optimal conditions. No reaction occurred for N−Ac or N-Boc substrates. When *N*-benzyl substrate was subjected to different haloamination reactions, 3-iodopiperidine was obtained along with a small amount of 2-iodomethylpyrrolidine product (9:1, Table 5, entry 1). 3-Bromopiperidine was obtained as the sole product when the reaction was carried out with PIDA/LiBr (Table 5, entry 2), and 2-chloromethylpyrrolidine was obtained as the major product in the case of PIDA/Py·HCl (Table 5,

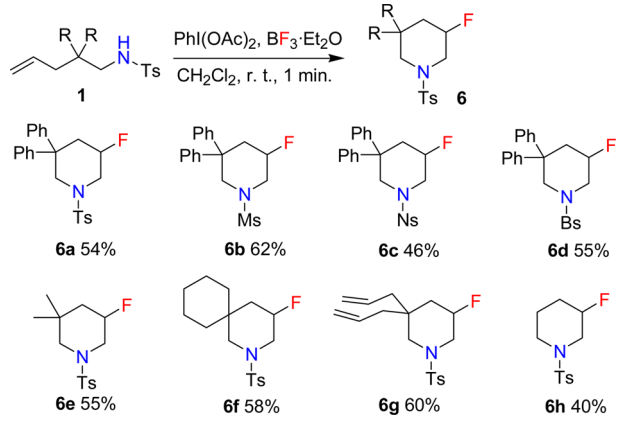
Table 4. PIDA-Mediated Intramolecular Fluoroamidation Reactions[a]



entry	[F] source	solvent	isolated yield (%)
1	MF[b]	CH_2Cl_2	NR
2	AgF	CH_2Cl_2	trace
3	fluoride salts[c]	CH_2Cl_2	NR
4	BF_3·OEt_2	CH_2Cl_2	45
5	BF_3·OEt_2	hexane	ND[d]
6	BF_3·OEt_2	benzene	33
7	BF_3·OEt_2	acetone	ND[d]
8	BF_3·OEt_2	THF	ND[d]
9	BF_3·OEt_2	DCE	40
10	HBF_4	CH_2Cl_2	38
11[e]	BF_3·OEt_2	CH_2Cl_2	54

[a]The reaction was carried out with 0.5 mmol of substrates, 0.55 mmol of PIDA, 1 mmol of fluorine source, and 20 mL of solvent. For entries 1−3, reaction time = 24 h, and for entries 4−11, reaction time = 1 min. [b]MF = CaF_2, MgF_2, ZnF_2, CuF_2, KF, CsF, LiF, and NaF. [c]Fluorine salts = HF, NH_4F, Et_3N·HF, and TBAF. [d]ND = not detectable. [e]Pyridine (2 equiv) was added.

Scheme 7. Intramolecular Fluoroamidation of Different Substrates[a]



[a]The reaction was carried out with 0.5 mmol of substrate, 0.55 mmol of PIDA, 1 mmol of BF_3·Et_2O, 1 mmol pyridine, and 20 mL of CH_2Cl_2.

Scheme 8. Possible Pathway for the Formation of Aminoacetoxylation Product

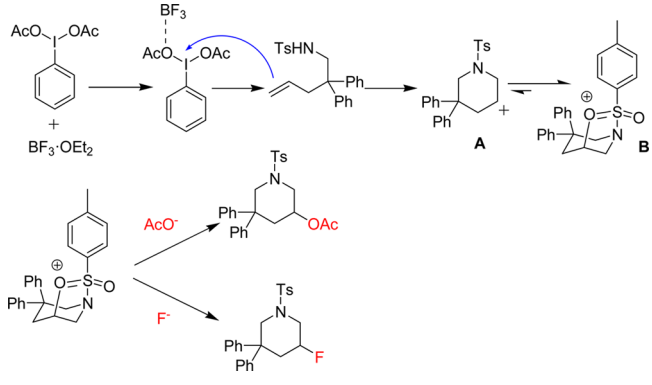


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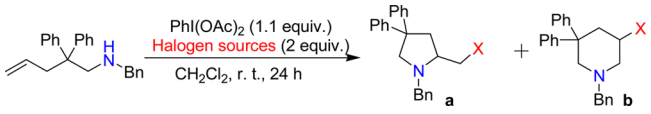
Table 5. PIDA-Promoted Haloamination of *N*-Benzyl 4-Penten-1-amine Substrate



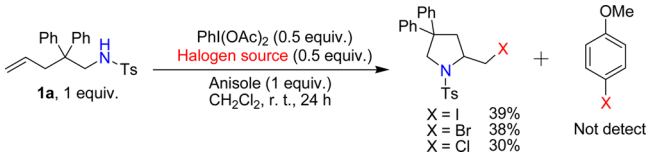
entry	halogen sources	conversion	a:b[a]
1	KI	>99	10:90
2	LiBr	>99	0:100
3	Py·HCl	>99	87:13
4	BF_3·Et_2O	0	

[a]Determined ^{1}H NMR analysis of the reaction mixture.

entry 3). Fluoroamination reaction was not observed under the current conditions possibly due to the strong interaction between the amino group and BF_3. Detailed results for haloamination of different *N*-benzyl substrates are summarized in Scheme 9, and electronic perperty of the phenyl group showed little effects on the reactions.

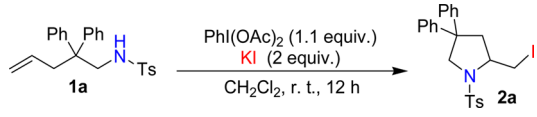
PIDA was known to produce Ph(AcO)I-X[30] or AcO-X[31] upon addition of metal halides, and a variety of X^+-involved reactions could be realized using PIDA in combination with different metal halides.[30,31] Several control experiments were then carried out under optimized conditions to see if the reaction was proceeded via PIDA-promoted C=C double bond activation or proceeded via the formation of Ph(AcO)I-X or AcO-X. At first, 1 equiv of substrate **1a**, 1 equiv of anisole, 0.5 equiv of PIDA, and 0.5 equiv of halogen source were allowed to react together under optimal conditions. Anisole was added as a competitive substrate based on the fact that it could be quickly halogenated by PIDA/metal halides,[30] and it was expected to capture any possible X^+ formed during the reaction. To our surprise, the haloamination reactions were not affected by the addition of anisole, and formation of *p*-haloanisoles was not observed under the current reaction conditions (Scheme 10). We reasoned that the interaction between PIDA and C=C double bonds was more favorable than the interaction between PIDA and halides X^-. Given that halogenation of anisole was faster than haloamination of **1a**, it was reasonable to believe that X^+ was not formed in the current reaction system.

Scheme 10. Haloamination of 1a in the Presence of Anisole



Iodoaminations of **1a** under dark environment and in the presence of TEMPO were also carried out (Table 6). A similar result was obtained when the reaction was carried out under dark environment at room temperature (Table 6, entries 1 and 2). No TEMPO-involved product was detected when the reaction was carried out in the presence of TEMPO (Table 6, entry 3). The conversion of **1a** and the yield of **2a** dropped possibly due to the consumption of PIDA by TEMPO,[32] and the current results could possibly rule out the formation of free radicals during the reaction.

Table 6. Influence of Light and TEMPO on Iodoamidation of 1a

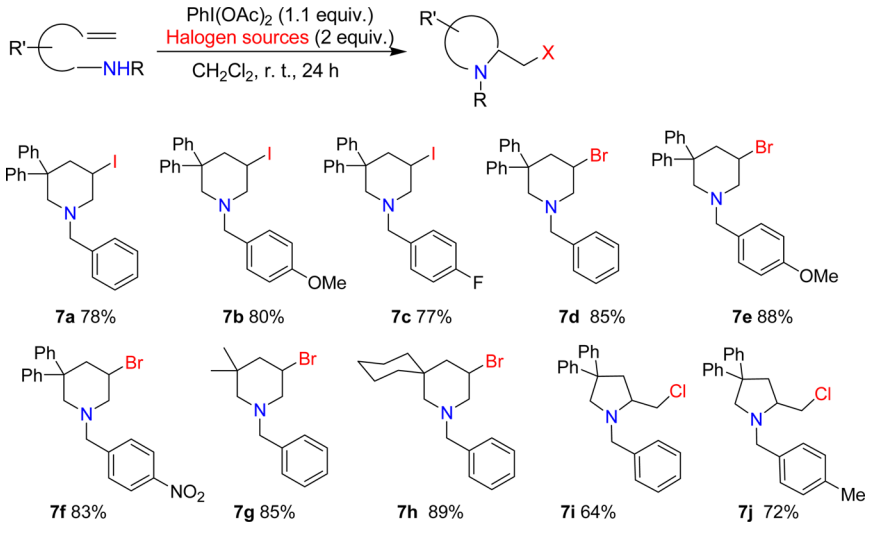


entry	condition	conversion[a]	isolated yield (%)
1	ambient light	>99	91
2	dark	>99	93
3	TEMPO (1.5 equiv)	42	30

[a]Determined by crude NMR analysis.

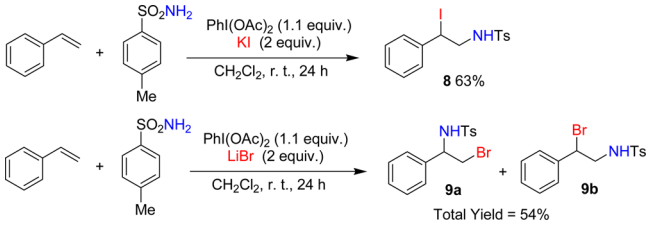
After intramolecular haloamidation of a variety of unfunctionalized olefins, intermolecular reactions of styrene with *p*-toluenesulfonamide were carried out in the presence of different halogen sources. After optimization of reaction conditions, iodoamidation of styrene gave α-iodo-β-sulfonamido-product in 63% isolated yield,[33] and bromoamidation of styrene gave a mixture of both isomers (Scheme 11). Chloro- and fluoroamidation of styrene was not successful under the current reaction conditions.

Scheme 9. Haloamination of Different *N*-Benzyl Substrates



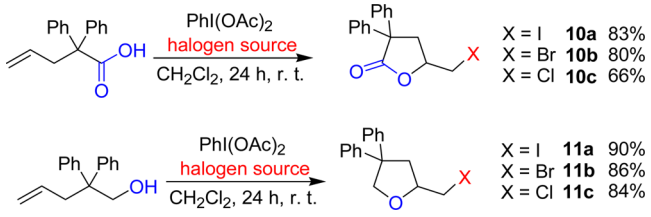
dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 11. Intermolecular Haloamidation of Styrene



Many γ-butyrolactone and substituted tetrahydrofuran skeletons have shown important biological acitivity,[34] and halomethyl lactone or halomethyl tetrahydrofuran compounds would be ideal intermediates for such structures. To further extend the application scope of PIDA-promoted halocyclization reactions, 2,2-diphenyl-4-penten-1-carboxylic acid and 2,2-diphenyl-4-penten-1-ol were subjected to halocyclization reactions, and both halomethyl substituted γ-butyrolactones and halomethyl substituted tetrahydrofurans could be obtained in good isolated yields (Scheme 12).

Scheme 12. I(III)-Promoted Halolactonization and Haloetherification Reactions



CONCLUSION

In summary, (diacetoxyiodo)benzene (PIDA) was effective for the functionalization of unactivated C=C double bonds. Intramolecular haloamidation (iodo-, bromo, and chloroamidation), haloetherification and halolactonization reactions could all be realized in the presence of 1.1 equiv of PIDA and suitable halogen sources, giving the corresponding halocyclization products in good to excellent isolated yields. Intramolecular fluoroamidation was relatively less successful; 3-fluoropiperidine compounds were isolated in moderate yields along with the formation of 3-acetoxy compounds as the byproducts. The iodomethylpyrrolidine compounds could be converted to many different pyrrolidine derivatives upon nucleophilic substitution reactions, and this method eventually offered an effective route to a variety of biologically active structures. The good isolated yields, high regioselectivity, mild conditions, and easy-to-operate feature made the current reaction a more attractive method for the syntheses of a variety of medicinal and agrochemical interesting compounds.

EXPERIMENTAL SECTION

General Experimental Information. Reagents were used as received without further purification unless otherwise specified. Solvents were dried and distilled prior to use. Reactions were monitored with thin layer chromatography using silica gel GF_{254} plates. Organic solutions were concentrated in vacuo using a rotary evaporator. Flash column chromatography was performed using silica gel (200−300 meshes). Petroleum ether used had a boiling point range of 60−90 °C. Melting points were measured on a digital melting point apparatus without correction of the thermometer. Nuclear magnetic resonance spectra were recorded at ambient temperature (unless otherwise stated) at 400 MHz (100 MHz for ^{13}C) in $CDCl_3$. Chemical shifts are reported in ppm (δ) using TMS as internal standard, and spin−spin coupling constants (J) are given in Hz. Infrared (IR) spectra were recorded with KBr pellet, and wavenumbers are given in cm^{-1}. High resolution mass spectrometry (HRMS) analyses were carried out on IonSpec 7.0T FTICR HR-ESI-MS. Substrates used were prepared according to our previous works[17a,c,18] or procedures described by Muniz et al.[20e]

General Procedure for Intramolecular Iodoamidation. The reaction was carried out in an open air system. To a 100 mL flask were added 0.5 mmol alkenylamine, 0.55 mmol $PhI(OAc)_2$, 1 mmol KI, and 20 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature for an indicated period. Then 10 mL of CH_2Cl_2 was added, and the mixture was washed with H_2O. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to give the corresponding product.

*2-(Iodomethyl)-4,4-diphenyl-1-tosylpyrrolidine (**2a**).* Compound **2a** was prepared according to the general procedure and isolated as a white solid (235.1 mg, 91% yield) after flash chromatography (petroleum ether:ethyl acetate = 80:1); mp = 180−182 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.50 (d, J = 8.1 Hz, 2H), 7.21−6.96 (m, 12H), 4.35 (d, J = 10.3 Hz, 1H), 3.82−3.72 (m, 1H), 3.67 (d, J = 10.3 Hz, 1H), 3.59 (dd, J = 9.5, 2.9 Hz, 1H), 2.77−2.71(m, 1H), 2.56 (dd, J = 13.1, 5.2 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.6, 143.3, 142.6, 132.8, 128.7, 127.7, 127.6, 126.3, 125.7, 125.5, 125.4, 125.2, 59.3, 58.1, 51.1, 42.7, 20.5, 10.5. The NMR data were in agreement with reported results.[15]

*2-(Iodomethyl)-1-(methylsulfonyl)-4,4-diphenylpyrrolidine (**2b**).* Compound **2b** was prepared according to the general procedure and isolated as a white solid (191.7 mg, 87% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); mp = 166−167 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.59−6.79 (m, 10H), 4.25 (d, J = 11.0 Hz, 1H), 4.13 (d, J = 11.1 Hz, 1H), 3.80−3.75 (m, 1H), 3.54 (dd, J = 9.8, 2.5 Hz, 1H), 3.26−3.16 (m, 2H), 2.38 (dd, J = 13.3, 8.4 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.6, 144.1, 129.0, 128.8, 127.3, 126.9, 126.9, 126.5, 60.2, 59.6, 53.4, 44.6, 36.8, 12.4. IR (KBr): 3053, 2960, 1590, 1493, 1333, 1263, 1147, 814, 754, 705, 662 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$calcd for $C_{18}H_{20}INO_2S$, 442.0338; found: 442.0337.

*2-(Iodomethyl)-4,4-diphenyl-1-(phenylsulfonyl)pyrrolidine (**2c**).* Compound **2c** was prepared according to the general procedure and isolated as a white solid (213.2 mg, 85% yield) after flash chromatography (petroleum ether:ethyl acetate = 80:1); mp = 153−154 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.71−7.60 (m, 2H), 7.45 (t, J = 7.5 Hz, 1H), 7.36−7.32 (m, 2H), 7.23−7.15 (m, 4H), 7.14−7.00 (m, 6H), 4.35 (d, J = 10.3 Hz, 1H), 3.85−3.77 (m, 1H), 3.74 (d, J = 10.3 Hz, 1H), 3.59 (dd, J = 9.6, 3.0 Hz, 1H), 2.82−2.69 (m, 2H), 2.60 (dd, J = 13.1, 5.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.5, 143.2, 136.1, 131.8, 128.1, 127.7, 127.6, 126.2, 125.8, 125.7, 125.0, 125.2, 59.4, 58.1, 51.1, 42.8, 10.3. IR (KBr): 3023, 2957, 1591, 1484, 1447, 1171, 1090, 753, 699, 662 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$calcd for $C_{23}H_{22}INO_2S$, 504.0494; found: 504.0485.

*2-(Iodomethyl)-1-(4-nitrophenylsulfonyl)-4,4-diphenylpyrrolidine (**2d**).* Compound **2d** was prepared according to the general procedure and isolated as a yellow solid (183.7 mg, 67% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 180−182 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.02(d, J = 8.9 Hz, 2H), 7.67(d, J = 8.9 Hz, 2H), 7.26−6.90 (m, 10H), 4.30 (d, J = 10.8 Hz, 1H), 4.09 (dd, J = 10.8, 1.3 Hz, 2H), 3.83−3.76 (m, 1H), 3.66 (dd, J = 9.8, 2.8 Hz, 1H), 3.16 (t, J = 9.4 Hz, 1H), 3.11−3.04 (m, 1H), 2.39 (dd, J = 13.5, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.8, 143.5, 142.4, 142.3, 127.8, 127.7, 127.0, 125.9, 125.7, 125.4, 125.3, 123.2, 59.3, 59.2, 51.7, 43.4, 10.5; IR (KBr): 3028, 2960, 1601, 1526, 1451, 1352, 1161, 1089, 804, 749, 700, 661 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{23}H_{21}IN_2O_4S$, 549.0345; found: 549.0334.

*2-(Iodomethyl)-1-tosylindoline (**2e**).* Compound **2e** was prepared according to the general procedure and isolated as a white solid (185.3 mg, 90% yield) after flash chromatography (petroleum ether:ethyl

dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

acetate = 50:1); mp = 151−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, J = 8.1 Hz, 1H), 7.48 (d, J = 8.1 Hz, 2H), 7.20−7.07 (m, 3H), 7.00−6.93 (m, 2H), 4.30−4.24 (m, 1H), 3.58 (dd, J = 9.7, 3.4 Hz, 1H), 3.18 (t, J = 9.9 Hz, 1H), 2.86 (dd, J = 16.7, 9.3 Hz, 1H), 2.76 (dd, J = 16.7, 3.0 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.3, 141.2, 134.4, 130.5, 129.8, 128.1, 127.1, 125.3, 124.9, 116.8, 62.5, 34.9, 21.6, 11.6. The NMR data were in agreement with reported results.[15]

*2-(Iodomethyl)-5-methyl-1-tosylindoline (**2f**).* Compound **2f** was prepared according to the general procedure and isolated as a white solid (196.1 mg, 92% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 153−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45 (t, J = 9.1 Hz, 3H), 7.09 (d, J = 8.1 Hz, 2H), 6.94 (d, J = 8.1 Hz, 1H), 6.78 (s, 1H), 4.27−4.21 (m, 1H), 3.55 (dd, J = 9.7, 3.5 Hz, 1H), 3.16 (t, J = 9.9 Hz, 1H), 2.79 (dd, J = 16.7, 9.2 Hz, 1H), 2.69 (dd, J = 16.7, 3.1 Hz, 1H), 2.27 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.1, 137.7, 133.7, 133.3, 129.5, 128.7, 127.6, 126.0, 124.8, 115.6, 61.6, 33.7, 20.6, 19.9, 10.5. The NMR data were in agreement with reported results.[15]

*2-(Iodomethyl)-6-methyl-1-tosylindoline (**2g**).* Compound **2g** was prepared according to the general procedure and isolated as a white solid (183.3 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 142−143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 (t, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 8.1 Hz, 2H), 7.05 (t, J = 7.8 Hz, 1H), 6.77 (d, J = 7.6 Hz, 1H), 4.34−4.21 (m, 1H), 3.62 (dd, J = 9.6, 3.3 Hz, 1H), 3.19 (t, J = 9.9 Hz, 1H), 2.79 (dd, J = 16.6, 9.5 Hz, 1H), 2.67 (dd, J = 16.6, 3.2 Hz, 1H), 2.28 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.2, 139.8, 133.8, 133.3, 128.7, 127.9, 127.1, 126.1, 124.7, 112.8, 61.3, 32.9, 20.5, 17.7, 10.9; IR (KBr): 3041, 2961, 1594, 1457, 1346, 1164, 1093, 1023, 807, 697, 662, 583 cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{17}H_{18}INO_2S$, 428.0181; found: 428.0173..

*2-(Iodomethyl)-7-methyl-1-tosylindoline (**2h**).* Compound **2h** was prepared according to the general procedure and isolated as a white solid (183.2 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (dd, J = 15.0, 8.2 Hz, 2H), 7.14−7.02 (m, 3H), 6.99 (t, J = 7.4 Hz, 1H), 6.79 (d, J = 7.2 Hz, 1H), 4.42−4.33 (m, 1H), 3.29 (dd, J = 9.9, 5.0 Hz, 1H), 2.91 (t, J = 9.9 Hz, 1H), 2.49 (s, 3H), 2.38 (d, J = 16.4 Hz, 1H), 2.31 (s, 3H), 2.05 (dd, J = 16.4, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.3, 139.9, 135.4, 133.9, 133.1, 130.6, 129.5, 127.6, 126.9, 122.5, 64.6, 33.8, 21.7, 20.0, 8.7; IR (KBr): 3056, 2962, 1596, 1504, 1354, 1169, 1086, 1023, 938, 810, 697, 662 cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{17}H_{18}INO_2S$, 428.0181; found: 428.0179.

*2-(Iodomethyl)-5-methoxy-1-tosylindoline (**2i**).* Compound **2i** was prepared according to the general procedure and isolated as a white solid (203.1 mg, 92% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 147−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 (d, J = 8.8 Hz, 1H), 7.43 (d, J = 8.2 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H), 6.69 (dd, J = 8.8, 2.4 Hz, 1H), 6.52 (d, J = 2.0 Hz, 1H), 4.31−4.17 (m, 1H), 3.68 (s, 3H), 3.53 (dd, J = 9.7, 3.6 Hz, 1H), 3.16 (t, J = 9.9 Hz, 1H), 2.78−2.60 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.6, 144.2, 134.4, 134.1, 132.5, 129.7, 127.1, 118.2, 113.2, 110.9, 62.9, 55.6, 34.9, 21.6, 11.3. The NMR data were in agreement with reported results.[11c]

*5-Fluoro-2-(iodomethyl)-1-tosylindoline (**2j**).* Compound **2j** was prepared according to the general procedure and isolated as a white solid (182.5 mg, 85% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 114−115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.52 (dd, J = 8.8, 4.6 Hz, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 6.85 (td, J = 8.8, 2.6 Hz, 1H), 6.73−6.64 (m, 1H), 4.31−4.25 (m, 1H), 3.54 (dd, J = 9.8, 3.5 Hz, 1H), 3.19 (t, J = 9.9 Hz, 1H), 2.80 (dd, J = 17.0, 9.1 Hz, 1H), 2.72 (dd, J = 17.0, 3.3 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.5 (d, J = 243.2 Hz), 144.5, 137.2, 134.0, 132.8 (d, J = 9.2 Hz), 129.9, 127.1, 118.1 (d, J = 8.6 Hz), 114.7 (d, J = 23.4 Hz), 112.5 (d, J = 24.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ = −117.7. The NMR data were in agreement with reported results.[11c]

*5-Chloro-2-(iodomethyl)-1-tosylindoline (**2k**).* Compound **2k** was prepared according to the general procedure and isolated as a white solid (191.3 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48 (dd, J = 8.2, 6.0 Hz, 3H), 7.11 (dd, J = 15.2, 4.9 Hz, 3H), 6.95 (s, 1H), 4.29−4.23 (m, 1H), 3.55 (dd, J = 9.8, 3.3 Hz, 1H), 3.20 (t, J = 9.8 Hz, 1H), 2.84 (dd, J = 16.9, 9.4 Hz, 1H), 2.73 (dd, J = 16.9, 3.1 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.7, 139.9, 134.1, 132.4, 130.1, 129.9, 128.1, 127.1, 125.5, 117.7, 62.7, 34.8, 21.7, 11.4. The NMR data were in agreement with reported results.[11c]

*5-Bromo-2-(iodomethyl)-1-tosylindoline (**2l**).* Compound **2l** was prepared according to the general procedure and isolated as a white solid (203.5 mg, 83% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48 (dd, J = 8.3, 5.4 Hz, 3H), 7.16−7.04 (m, 3H), 6.94 (s, 1H), 4.29−4.22 (m, 1H), 3.54 (dd, J = 9.8, 3.3 Hz, 1H), 3.21 (t, J = 7.9 Hz, 1H), 2.84 (dd, J = 16.9, 9.4 Hz, 1H), 2.73 (dd, J = 16.9, 3.0 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.6, 139.9, 134.1, 132.4, 130.2, 129.9, 128.1, 127.1, 125.5, 117.7, 62.7, 34.7, 21.6, 11.2. IR (KBr): 3042, 2964, 1594, 1471, 1351, 1163, 1085, 743, 662, cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{16}H_{15}BrINO_2S$, 491.9130; found: 491.9139.

*2-(Iodomethyl)-1-tosylindoline-5-carbonitrile (**2m**).* Compound **2m** was prepared according to the general procedure and isolated as a white solid (188.0 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 151−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.63 (d, J = 8.4 Hz, 1H), 7.53 (d, J = 8.1 Hz, 2H), 7.45 (d, J = 8.4 Hz, 1H), 7.27 (s, 1H), 7.18 (d, J = 8.0 Hz, 2H), 4.34−4.29 (m, 1H), 3.59 (dd, J = 9.9, 2.8 Hz, 1H), 3.29 (t, J = 9.5 Hz, 1H), 3.01 (dd, J = 17.0, 9.8 Hz, 1H), 2.84 (dd, J = 17.1, 3.1 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.3, 145.2, 134.2, 132.9, 131.3, 130.2, 128.9, 126.9, 118.8, 116.1, 107.7, 62.5, 34.8, 21.7, 11.4. The NMR data were in agreement with reported results.[11c]

*2-(Iodomethyl)-4,4-dimethyl-1-tosylpyrrolidine (**2n**).* Compound **2n** was prepared according to the general procedure and isolated as a white solid (190.5 mg, 97% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.66 (d, J = 8.2 Hz, 1H), 7.26 (d, J = 8.0 Hz, 2H), 3.69 (dd, J = 9.5, 2.8 Hz, 1H), 3.65−3.57 (m, 1H), 3.31 (t, J = 9.2 Hz, 1H), 3.18−3.06 (m, 2H), 2.36 (s, 3H), 1.84 (dd, J = 12.8, 7.2 Hz, 1H), 1.52 (dd, J = 12.8, 8.5 Hz, 1H), 0.96 (s, 3H), 0.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.8, 134.8, 129.8, 127.5, 62.0, 60.1, 47.8, 37.5, 26.0, 25.9, 21.6, 13.4. The NMR data were in agreement with reported results.[11c]

*3-(Iodomethyl)-2-tosyl-2-azaspiro[4.5]decane (**2o**).* Compound **2o** was prepared according to the general procedure and isolated as a white solid (199.3 mg, 92% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 3.69 (dd, J = 9.5, 2.7 Hz, 1H), 3.54 (td, J = 8.8, 2.6 Hz, 1H), 3.37−3.23 (m, 2H), 3.09 (d, J = 11.0 Hz, 1H), 2.36 (s, 3H), 1.92 (dd, J = 12.9, 7.2 Hz, 1H), 1.45 (dd, J = 13.0, 8.6 Hz, 1H), 1.39−1.26 (m, 4H), 1.20−0.95 (m, 4H), 0.72−0.65 (m, 1H), 0.54 (dd, J = 11.5, 5.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 134.7, 129.7, 127.5, 59.3, 59.2, 45.9, 41.4, 36.1, 33.9, 25.9, 23.7, 22.7, 21.6, 13.7; IR (KBr): 3037, 2926, 2855, 1595, 1486, 1449, 1343, 1159, 1091, 1023, 815, 660 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{17}H_{24}INO_2S$, 434.0651; found: 434.0642.

*4,4-Diallyl-2-(iodomethyl)-1-tosylpyrrolidine (**2p**).* Compound **2p** was prepared according to the general procedure and isolated as an oil (213.2 mg, 96% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 5.67−5.56 (m, 1H), 5.49−5.39 (m, 1H), 5.05−4.88 (m, 3H), 4.73 (d, J = 16.9 Hz, 1H), 3.68−3.56 (m, 2H), 3.33 (t, J = 8.8 Hz, 1H), 3.22−3.11 (m, 2H), 2.36 (s, 3H), 2.03 (d, J = 7.3 Hz, 2H), 1.93 (dd, J = 13.1, 7.2 Hz, 1H), 1.62−1.50 (m, 2H), 1.42 (dd, J = 14.0, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, CDCl $_3$) δ = 143.9, 135.1, 133.5, 133.1, 129.8, 127.5, 118.7, 59.4, 58.7, 43.7, 43.3, 40.4, 39.2, 21.6, 13.5; IR (KBr): 3072, 2971,

dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

1640, 1597, 1487, 1442, 1344, 1159, 1095, 1011, 814, 665 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{18}H_{24}INO_2S$, 446.0651; found: 446.0652.

*2-(Iodomethyl)-1-tosylpyrrolidine (**2q**).* Compound **2q** was prepared according to the general procedure and isolated as a white solid (167.6 mg, 92% yield) after flash chromatography (petroleum ether:ethyl acetate = 60:1); mp = 90 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.65 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 3.65 (dd, J = 11.2, 5.4 Hz, 1H), 3.53 (dd, J = 9.5, 2.5 Hz, 1H), 3.40 (dd, J = 10.0, 5.9 Hz, 1H), 3.21−3.06 (m, 2H), 2.36 (s, 3H), 1.88−1.64 (m, 3H), 1.44 (dd, J = 11.3, 5.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.8, 134.1, 129.9, 127.5, 60.7, 50.1, 31.9, 23.9, 21.6, 11.7. The NMR data were in agreement with reported results.[15]

*2-(Iodomethyl)-1-(phenylsulfonyl)pyrrolidine (**2r**).* Compound **2r** was prepared according to the general procedure and isolated as a white solid (154.3 mg, 88% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 64−65 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.77 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 3.70−3.64 (m, 1H), 3.53 (dd, J = 9.7, 2.9 Hz, 1H), 3.46−3.38 (m, 1H), 3.19−3.09 (m, 1H), 1.86−1.64 (m, 3H), 1.48−1.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.9, 133.1, 129.3, 127.4, 60.7, 50.1, 31.9, 23.9, 11.7; IR (KBr): 3064, 2973, 1581, 1448, 1342, 1161, 1095, 817, 788, 710, 661 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_{14}INO_2S$, 351.9868; found: 351.9861.

*2-(Iodomethyl)-1-(o-tolylsulfonyl)pyrrolidine (**2s**).* Compound **2s** was prepared according to the general procedure and isolated as a white solid (156.4 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 36−37 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.85 (d, J = 8.3 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.27−7.23 (m, 2H), 4.01−3.90 (m, 1H), 3.37 (dd, J = 9.8, 2.9 Hz, 1H), 3.32−3.20 (m, 2H), 3.07 (t, J = 9.5 Hz, 1H), 2.60 (s, 3H), 2.06−1.95 (m, 1H), 1.94−1.80 (m, 2H), 1.80−1.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.1, 136.9, 133.1, 132.9, 129.6, 126.3, 59.8, 49.9, 32.4, 24.2, 20.9, 11.3; IR (KBr): 3047, 2974, 1590, 1453, 1337, 1159, 1097, 989, 814, 765, 701, 663 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{12}H_{16}INO_2S$, 366.0025, found 366.0021.

*2-(1-Iodoethyl)-4,4-diphenyl-1-tosylpyrrolidine (**2t**).* Compound **2t** was prepared according to the general procedure and isolated as a white solid (231.2 mg, 87% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); mp = 197−198 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, J = 8.1 Hz, 2H), 7.21−6.99 (m, 12H), 4.94 (dd, J = 7.0, 3.0 Hz, 1H), 4.40 (d, J = 10.6 Hz, 1H), 3.99 (d, J = 10.8 Hz, 1H), 3.01 (dd, J = 12.3, 6.1 Hz, 1H), 2.86 (dd, J = 12.6, 6.1 Hz, 1H), 2.48 (dd, J = 12.9, 9.5 Hz, 1H), 2.29 (s, 3H), 1.75 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.4, 144.2, 142.9, 136.9, 129.5, 128.6, 128.6, 126.8, 126.7, 126.6, 126.3, 64.7, 59.1, 52.9, 42.1, 37.4, 24.5, 21.5; IR (KBr): 3058, 2984, 1596, 1492, 1340, 1156, 1085, 1033, 1011, 924, 805, 757, 698, 663 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{25}H_{26}INO_2S$, 532.0807; found: 532.0797.

*2-(2-Iodopropan-2-yl)-4,4-diphenyl-1-tosylpyrrolidine (**2u**).* Compound **2u** was prepared according to the general procedure and isolated as a white solid (117.6 mg, 43% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 64−65 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.51 (d, J = 7.4 Hz, 2H), 7.42 (t, J = 7.7 Hz, 2H), 7.36−7.26 (m, 3H), 7.23−7.16 (m, 3H), 7.13 (d, J = 8.3 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 5.29 (dd, J = 13.8, 2.7 Hz, 1H), 4.41 (dd, J = 13.3, 3.5 Hz, 1H), 3.70 (d, J = 13.8 Hz, 1H), 3.45−3.40 (m, 1H), 2.92 (t, J = 13.8 Hz, 1H), 2.35 (s, 3H), 1.48 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.0, 143.1, 142.7, 140.1, 129.5, 129.1, 128.7, 128.0, 127.2, 126.8, 126.6, 125.9, 61.0, 50.1, 49.9, 46.0, 40.2, 30.3, 21.4, 18.1; IR (KBr): 3056, 2986, 1596, 1493, 1368, 1150, 1081, 1035, 954, 810, 774, 701, 629 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{26}H_{28}INO_2S$, 546.0964; found: 546.0959.

*2-(Iodomethyl)-4-phenyl-1-tosylpyrrolidine (**2v**).* Compound **2v** was prepared according to the general procedure and isolated as a white solid (196.5 mg, 89% yield) after flash chromatography (petroleum ether:ethyl acetate = 80:1); mp = 130 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.72 (d, J = 7.6 Hz, 2H), 7.30 (d, J = 7.6 Hz, 2H), 7.25−7.12 (m, 3H), 7.03 (d, J = 7.1 Hz, 2H), 3.87−3.80 (m, 1H), 3.71 (d, J = 7.5 Hz, 1H), 3.64 (d, J = 9.6 Hz, 1H), 3.45−3.31 (m, 2H), 2.66−2.55 (m, 1H), 2.48−2.42 (m, 1H), 2.39 (s, 3H), 1.82 (dd, J = 21.9, 11.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.1, 138.8, 134.8, 130.1, 128.8, 127.5, 127.3, 127.1, 60.6, 55.8, 43.2, 41.1, 21.7, 13.2; IR (KBr): 3063, 2964, 1596, 1493, 1441, 1340, 1159, 998, 821, 759, 706, 661 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{18}H_{20}INO_2S$, 442.0338; found: 442.0336.

*Crystal data for **2v**.* $C_{18}H_{20}INO_2S$, M = 441.31, monoclinic, a = 10.911(2) Å, b = 15.095(3) Å, c = 11.664(2) Å, α = 90.00°, β = 113.30(3)°, γ = 90.00°, V = 1764.4(6) $Å^3$, T = 113(2) K, space group $P2(1)/c$, Z = 4, 20423 reflections measured, 4238 independent reflections (R_{int} = 0.0501). The final R_1 values were 0.0307 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.0738 ($I > 2\sigma(I)$). The final R_1 values were 0.0421 (all data). The final $wR(F^2)$ values were 0.0809 (all data). The goodness of fit on F^2 was 0.973.

*4-Allyl-2-(iodomethyl)-1-tosylpyrrolidine (**2w**).* Compound **2w** was prepared according to the general procedure and isolated as a white solid (173.9 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 80:1); mp = 67−68 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.65 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 5.61−5.48 (m, 1H), 4.96−4.87 (m, 2H), 3.62−3.52 (m, 3H), 3.29 (t, J = 9.0 Hz, 1H), 2.94 (t, J = 11.1 Hz, 1H), 2.37 (s, 3H), 2.21−2.25 (m, 1H), 2.03−1.88 (m, 2H), 1.57−1.44 (m, 1H), 1.33−1.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.9, 135.5, 134.7, 129.9, 127.4, 116.6, 60.7, 55.0, 39.8, 37.7, 36.1, 21.6, 13.2; IR (KBr): 3060, 2970, 1645, 1594, 1488, 1430, 1159, 1024, 998, 820, 761, 705, 660 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{15}H_{20}INO_2S$, 406.0338; found: 406.0338.

*4-Allyl-2-(iodomethyl)-4-phenyl-1-tosylpyrrolidine (**2x**).* Compound **2x** was prepared according to the general procedure and isolated as an oil (218.3 mg, 91% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.45 (d, J = 8.2 Hz, 2H), 7.12−7.03 (m, 5H), 6.90 (dd, J = 7.5, 1.9 Hz, 2H), 5.33−5.17 (m, 1H), 4.89 (dd, J = 12.8, 8.5 Hz, 2H), 3.86 (dd, J = 9.5, 2.9 Hz, 1H), 3.74 (d, J = 10.1 Hz, 1H), 3.64−3.55 (m, 1H), 3.47 (d, J = 10.1 Hz, 1H), 3.34 (t, J = 9.8 Hz, 1H), 2.52−2.36 (m, 3H), 2.30 (s, 3H), 2.08 (dd, J = 13.5, 6.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.5, 142.3, 132.4, 132.3, 128.6, 127.4, 126.4, 125.3, 125.2, 117.6, 59.5, 59.2, 47.0, 44.6, 41.1, 20.5, 11.3.IR (KBr): 3058, 2961, 1597, 1492, 1448, 1343, 1159, 1092, 1022, 958, 806, 754, 701, 660 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{21}H_{24}INO_2S$, 482.0651; found: 482.0644.

General Procedure for Derivatization of 2-Iodomethypyrrolidine. 2-Iodomethypyrrolidine (**2n**) was dissolved in 2 mL of DMF, the nucleophile of interest was added, and the reaction mixture was stirred for a given time. Then 30 mL of CH_2Cl_2 was added, and the reaction mixture was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to give the corresponding product.

*2-(Azidomethyl)-4,4-dimethyl-1-tosylpyrrolidine (**3a**).* Compound **3a** was prepared according to the general procedure and isolated as a white solid (146.6 mg, 95% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 71 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.66 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 3.71−3.60 (m, 2H), 3.56−3.51 (m, 1H), 3.08 (q, J = 10.8 Hz, 2H), 2.36 (s, 3H), 1.63 (dd, J = 7.5, 2.7 Hz, 2H), 0.98 (s, 3H), 0.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.8, 134.6, 129.8, 127.5, 61.6, 59.0, 55.0, 43.8, 37.5, 26.1, 25.6, 21.6; IR (KBr): 3031, 2960,2101, 1595, 1488, 1456, 1337, 1156, 1094, 1037, 917, 813, 730, 664, 590 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{14}H_{20}N_4O_2S$, 309.1385; found: 309.1382.

*2-((4,4-Dimethyl-1-tosylpyrrolidin-2-yl)methyl)isoindoline-1,3-dione (**3b**).* Compound **3b** was prepared according to the general procedure and isolated as a white solid (171.1 mg, 83% yield) after flash chromatography (petroleum ether:ethyl acetate = 20:1); mp = 177−179 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.84−7.61 (m, 6H), 7.26 (d, J = 7.8 Hz, 2H), 4.35 (dd, J = 12.9, 4.5 Hz, 1H), 3.92−3.69 (m, 2H), 3.24 (d, J = 10.7 Hz, 1H), 3.04 (d, J = 10.7 Hz, 1H), 2.35 (s, 3H), 1.56 (dd, J = 12.5, 7.6 Hz, 1H), 1.49 (dd, J = 12.3, 7.4 Hz, 1H), 1.02 (s, 3H), 0.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.4,

dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

143.6, 134.3, 134.1, 131.9, 129.7, 127.9, 123.6, 123.4, 62.2, 57.4, 44.6, 43.2, 37.3, 26.6, 26.1, 21.6; IR (KBr): 3204, 3031, 2959, 1767, 1718, 1602, 1463, 1390, 1365, 1166, 1088, 812, 716, 661, 590 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{22}H_{24}N_2O_4S$, 413.1535; found: 413.1534.

*(4,4-Dimethyl-1-tosylpyrrolidin-2-yl)methyl acetate (**3c**).* Compound **3c** was prepared according to the general procedure and isolated as a white solid (141.4 mg, 87% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 79−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 4.39 (dd, J = 11.0, 3.8 Hz, 1H), 4.13 (dd, J = 11.0, 7.1 Hz, 1H), 3.82−3.75 (m, 1H), 3.07 (s, 2H), 2.36 (s, 3H), 1.95 (s, 3H), 1.65 (dd, J = 12.8, 7.7 Hz, 1H), 1.54 (dd, J = 11.3, 6.7 Hz, 1H), 0.98 (d, J = 7.4 Hz, 3H), 0.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.7, 142.5, 134.0, 128.6, 126.4, 65.7, 60.5, 56.8, 42.6, 36.5, 25.3, 24.9, 20.5, 19.8; IR (KBr): 2961, 1734, 1597, 1337, 1158, 1093, 1044, 807, 665, 590 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{16}H_{23}NO_4S$, 326.1426; found: 326.1422.

*4,4-Dimethyl-2-(p-tolylthiomethyl)-1-tosylpyrrolidine (**3d**).* Compound **3d** was prepared according to the general procedure and isolated as a white solid (178.6 mg, 92% yield) after flash chromatography (petroleum ether:ethyl acetate = 60:1); mp = 103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 3.82 (dd, J = 13.3, 3.0 Hz, 1H), 3.55−3.48 (m, 1H), 3.12 (d, J = 10.5 Hz, 1H), 2.93 (d, J = 10.4 Hz, 1H), 2.78 (dd, J = 13.3, 10.4 Hz, 1H), 2.30 (s, 3H), 2.28 (s, 3H), 1.76 (dd, J = 12.8, 7.6 Hz, 1H), 1.53 (dd, J = 12.9, 7.8 Hz, 1H), 0.95 (s, 3H), 0.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.4, 135.2, 132.9, 130.6, 129.1, 128.8, 128.5, 126.5, 60.9, 58.1, 44.9, 39.2, 36.2, 25.4, 24.8, 20.5, 20.0; IR (KBr): 3030, 2961, 1695, 1494, 1449, 1333, 1154, 1092, 810, 710, 682 cm $^{-1}$; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{21}H_{27}NO_2S_2$,390.1561; found: 390.1560.

General Procedure for the Intramolecular Bromoamidation. The reaction was carried out in an open air system. To a 100 mL flask were added 0.5 mmol alkenylamine, 0.55 mmol $PhI(OAc)_2$, 1 mmol LiBr, and 20 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature for an indicated period. Then 10 mL of CH_2Cl_2 was added, and the mixture was washed with H_2O. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to give the corresponding product.

*2-(Bromomethyl)-4,4-diphenyl-1-tosylpyrrolidine (**4a**).* Compound **4a** was prepared according to the general procedure and isolated as a white solid (206.1 mg, 88% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 163 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53 (d, J = 8.0 Hz, 2H), 7.25−6.85 (m, 12H), 4.33 (d, J = 10.2 Hz, 1H), 3.96−3.81 (m, 1H), 3.72 (dd, J = 9.7, 3.1 Hz, 1H), 3.63 (d, J = 10.2 Hz, 1H), 2.86 (t, J = 9.9 Hz, 1H), 2.72−2.62 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ= 144.7, 144.4, 143.8, 133.8, 129.9, 128.8, 128.0, 127.5, 126.8, 126.6, 126.6, 126.4, 60.1, 58.9, 52.3, 42.1, 35.9, 21.6; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{24}H_{24}BrNO_2S$, 470.0789; found: 470.0789. The NMR data were in agreement with reported results.[3s]

*2-(Bromomethyl)-1-(methylsulfonyl)-4,4-diphenylpyrrolidine (**4b**).* Compound **4b** was prepared according to the general procedure and isolated as a white solid (167.3 mg, 85% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 143−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41−6.91 (m, 10H), 4.22 (dd, J = 11.0, 1.7 Hz, 1H), 4.09 (d, J = 11.0 Hz, 1H), 4.00−3.93 (m, 1H), 3.68 (dd, J = 10.1, 2.9 Hz, 1H), 3.35 (dd, J = 10.1, 8.3 Hz, 1H), 3.15 (dd, J = 13.3, 6.9, 1H), 2.53 (dd, J = 13.4, 8.3 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.6, 144.1, 129.0, 128.8, 127.2, 126.9, 126.8, 126.5, 59.9, 59.5, 53.3, 42.7, 36.7, 36.6. HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{18}H_{20}BrNO_2S$, 394.0476; found: 394.0468. The NMR data were in agreement with reported results.[17c]

*2-(Bromomethyl)-4,4-diphenyl-1-(phenylsulfonyl)pyrrolidine (**4c**).* Compound **4c** was prepared according to the general procedure and isolated as a white solid (182.1 mg, 80% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 162−163 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.70−7.64 (m, 2H), 7.46 (t, J = 7.4 Hz, 1H), 7.36 (t, J = 7.7 Hz, 2H), 7.25−7.17 (m, 4H), 7.16−6.98 (m, 6H), 4.32 (d, J = 10.2 Hz, 1H), 3.94−3.80 (m, 1H), 3.80−3.60 (m, 2H), 2.89 (t, J = 9.9 Hz, 1H), 2.78−2.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.6, 144.3, 137.1, 132.9, 129.2, 128.8, 128.7, 127.4, 126.9, 126.8, 126.6, 126.3, 60.0, 58.8, 52.3, 42.1, 35.7; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{23}H_{22}BrNO_2S$, 456.0633; found: 456.0625. The NMR data were in agreement with reported results.[17c]

*2-(Bromomethyl)-1-tosylindoline (**4d**).* Compound **4d** was prepared according to the general procedure and isolated as a white solid (147.2 mg, 81% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 148−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, J = 8.1 Hz, 1H), 7.48 (d, J = 8.1 Hz, 2H), 7.19−7.07 (m, 3H), 7.00−6.94 (m, 2H), 4.39−4.32 (m, 1H), 3.73 (dd, J = 9.9, 3.6 Hz, 1H), 3.33 (t, J = 9.8 Hz, 1H), 2.84 (d, J = 6.0 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.3, 140.0, 133.3, 129.6, 128.7, 126.9, 125.9, 124.3, 123.9, 115.8, 61.1, 34.9, 32.1, 20.5. The NMR data were in agreement with reported results.[11b]

*2-(Bromomethyl)-5-methyl-1-tosylindoline (**4e**).* Compound **4e** was prepared according to the general procedure and isolated as a white solid (147.5 mg, 78% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 156−158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 (t, J = 8.6 Hz, 3H), 7.11 (d, J = 8.1 Hz, 2H), 6.95 (d, J = 8.2 Hz, 1H), 6.80 (s, 1H), 4.36−4.29 (m, 1H), 3.72 (dd, J = 9.9, 3.8 Hz, 1H), 3.32 (t, J = 9.9 Hz, 1H), 2.83−2.70 (m, 2H), 2.28 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.2, 137.6, 133.8, 133.3, 129.7, 128.7, 127.6, 126.1, 124.8, 115.7, 61.2, 34.9, 32.1, 20.5, 19.9; IR (KBr): 3021, 2961,1595, 1486, 1348, 1162, 1093, 809, 755, 662 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{17}H_{18}BrNO_2S$, 380.0320; found: 380.0317.

*2-(Bromomethyl)-5-methoxy-1-tosylindoline (**4f**).* Compound **4f** was prepared according to the general procedure and isolated as a white solid (167.4 mg, 85% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 144−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 (dd, J = 17.1, 8.3 Hz, 3H), 7.11 (d, J = 7.9 Hz, 2H), 6.69 (d, J = 8.4 Hz, 1H), 6.53 (s, 1H), 4.34−4.30 (m, 1H), 3.72−3.67 (m, 4H), 3.30 (t, J = 9.9 Hz, 1H), 2.82−2.63 (m, 2H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.6, 143.2, 133.3, 133.1, 131.6, 128.7, 126.1, 117.2, 112.1, 109.8, 61.5, 54.5, 34.8, 32.2, 20.6; IR (KBr): 3017, 2961, 1601, 1489, 1347, 1159, 1090, 1029, 960, 817, 806, 754, 700 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{17}H_{18}BrNO_3S$, 396.0269; found: 396.0257.

*2-(Bromomethyl)-5-fluoro-1-tosylindoline (**4g**).* Compound **4g** was prepared according to the general procedure and isolated as a white solid (164.2 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 103−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.52 (dd, J = 8.8, 4.6 Hz, 1H), 7.46 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 6.85 (td, J = 8.8, 2.1 Hz, 1H), 6.70 (d, J = 7.9 Hz, 1H), 4.40−4.33 (m, 1H), 3.70 (dd, J = 10.0, 3.7 Hz, 1H), 3.34 (t, J = 9.8 Hz, 1H), 2.85−2.71 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.4 (d, J = 243.9 Hz), 143.5, 136.1, 132.9, 131.9 (d, J = 8.6 Hz), 128.8, 126.1, 117.1 (d, J = 8.7 Hz), 113.7(d, J = 23.4 Hz), 111.4 (d, J = 24.3 Hz), 61.2, 34.7, 32.1, 20.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −117.6; IR (KBr): 3035, 2961,1601, 1599, 1481, 1353, 1170, 1090, 1028, 967, 993, 811, 755, 700 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{16}H_{15}BrFNO_2S$, 384.0069; found: 384.0061.

*2-(Bromomethyl)-5-chloro-1-tosylindoline (**4h**).* Compound **4h** was prepared according to the general procedure and isolated as a white solid (159.3 mg, 80% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 123−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 (t, J = 8.0 Hz, 3H), 7.20−7.09 (m, 3H), 6.97 (d, J = 0.7 Hz, 1H), 4.40−4.31 (m, 1H), 3.71 (dd, J = 10.0, 3.6 Hz, 1H), 3.35 (t, J = 9.8 Hz, 1H), 2.88−2.76 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.6, 138.9, 133.1, 131.6, 129.2, 128.9, 127.1, 125.9, 124.4, 116.7, 61.3, 34.8, 32.0, 20.6; IR (KBr): 3030, 2960, 1694, 1470, 1354, 1166, 1027, 956, 878, 812, 702 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{16}H_{15}BrClNO_2S$, 399.9774; found: 399.9756.

dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

*5-Bromo-2-(bromomethyl)-1-tosylindoline (**4i**).* Compound **4i** was prepared according to the general procedure and isolated as a white solid (190.3 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 120−121 °C; ^{1}H NMR (400 MHz, CDCl $_3$) δ = 7.49 (t, J = 8.1 Hz, 3H), 7.27−7.06 (m, 3H), 6.97 (d, J = 0.7 Hz, 1H), 4.44−4.29 (m, 1H), 3.72 (dd, J = 10.0, 3.7 Hz, 1H), 3.35 (t, J = 9.8 Hz, 1H), 2.96−2.70 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.6, 138.9, 133.0, 131.6, 129.2, 128.9, 127.1, 126.0, 124.4, 116.7, 61.3, 34.8, 32.0, 20.6.IR (KBr): 3029, 2960,1694, 1468, 1354, 1325, 1150, 1027, 959, 814, 702, 664 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$calcd for $C_{16}H_{15}Br_2NO_2S$, 443.9268; found: 443.9253.

*2-(Bromomethyl)-1-(phenylsulfonyl)pyrrolidine (**4j**).* Compound **4j** was prepared according to the general procedure and isolated as a white solid (125.6 mg, 83% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 58−59 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (d, J = 7.6 Hz, 2H), 7.58−7.52 (m, 1H), 7.48 (t, J = 7.6 Hz, 2H), 3.81−3.73 (m, 1H), 3.68 (dd, J = 9.8, 3.2 Hz, 1H), 3.45−3.37 (m, 1H), 3.30 (t, J = 9.7 Hz, 1H), 3.11−3.05 (m, 1H), 1.91−1.82 (m, 1H), 1.82−1.72 (m, 1H), 1.64 (dq, J = 19.9, 7.5 Hz, 1H), 1.53−1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.8, 133.1, 129.3, 127.5, 60.4, 49.9, 36.1, 30.2, 23.8. The NMR data were in agreement with reported results.[31a]

*2-(Bromomethyl)-1-(o-tolylsulfonyl)pyrrolidine (**4k**).* Compound **4k** was prepared according to the general procedure and isolated as an oil (120.5 mg, 76% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.85 (d, J = 8.3 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.25 (dd, J = 7.2, 4.1 Hz, 2H), 4.10−4.04 (m, 1H), 3.52 (dd, J = 10.0, 3.1 Hz, 1H), 3.31−3.15 (m, 3H), 2.60 (s, 3H), 2.01−1.92 (m, 2H), 1.92−1.80 (m, 1H), 1.80−1.69 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.1, 136.8, 133.1, 132.9, 129.6, 126.3, 59.5, 49.4, 35.9, 30.5, 24.2, 20.9; IR (KBr): 3060, 2970,1640, 1592, 1460, 1326, 1159, 1073, 984, 874, 812, 761, 969 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{12}H_{16}BrNO_2S$, 318.0163; found: 318.0155.

*2-(Bromomethyl)-1-tosylpyrrolidine (**4l**).* Compound **4l** was prepared according to the general procedure and isolated as a white solid (134.9 mg, 85% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 86 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 3.79−3.73 (m, 1H), 3.68 (dd, J = 9.9, 3.1 Hz, 1H), 3.42−3.35 (m, 1H), 3.29 (t, J = 9.7 Hz, 1H), 3.11−3.05 (m, 1H), 2.36 (s, 3H), 1.90−1.81 (m, 1H), 1.81−1.73 (m, 1H), 1.71−1.62 (m, 1H), 1.56−1.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.9, 133.9, 129.9, 127.5, 60.4, 49.8, 36.2, 30.3, 23.8, 21.6. The NMR data were in agreement with reported results.[31a]

*7-Allyl-2-(bromomethyl)-5-methyl-1-tosylindoline (**4m**).* Compound **4m** was prepared according to the general procedure and isolated as a white solid (161.7 mg, 77% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 123−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 6.89 (s, 1H), 6.64 (s, 1H), 5.95−5.86 (m, 1H), 5.14−4.95 (m, 2H), 4.41−4.34 (m, 1H), 3.79 (dd, J = 15.7, 6.4 Hz, 1H), 3.57 (dd, J = 15.8, 7.3 Hz, 1H), 3.46 (dd, J = 10.0, 5.0 Hz, 1H), 3.01 (t, J = 10.0 Hz, 1H), 2.32 (s, 3H), 2.26 (dd, J = 12.8, 4.9 Hz, 1H), 2.21 (s, 3H), 2.01 (dd, J = 16.4, 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.3, 136.2, 136.1, 136.1, 134.5, 133.4, 132.8, 129.2, 128.5, 126.7, 122.7, 115.1, 63.2, 35.8, 32.8, 31.2, 20.6, 20.1; IR (KBr): 3014, 2966, 1640, 1598, 1467, 1434, 1344, 1166, 1090, 910, 874, 815, 702 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{20}H_{22}BrNO_2S$, 420.0633; found: 420.0623.

*2-(Bromomethyl)-4,4-dimethyl-1-tosylpyrrolidine (**4n**).* Compound **4n** was prepared according to the general procedure and isolated as a white solid (155.4 mg, 90% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 94−96 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 3.86 (dd, J = 9.6, 3.0 Hz, 1H), 3.83−3.77 (m, 1H), 3.45 (t, J = 9.1 Hz, 1H), 3.10 (q, J = 10.9 Hz, 2H), 2.36 (s, 3H), 1.81 (dd, J = 12.9, 7.2 Hz, 1H), 1.63 (dd, J = 12.9, 8.2 Hz, 1H), 0.98 (s, 3H), 0.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 134.9, 129.7, 127.5, 61.9, 60.0, 45.9, 37.5, 37.5, 26.1, 25.8, 21.6. The NMR data were in agreement with reported results.[31a]

*3-(Bromomethyl)-2-tosyl-2-azaspiro[4.5]decane (**4o**).* Compound **4o** was prepared according to the general procedure and isolated as a white solid (177.5 mg, 92% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 86−88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 3.86 (dd, J = 9.7, 3.0 Hz, 1H), 3.76−3.69 (m, 1H), 3.46−3.40 (m, 1H), 3.27 (d, J = 10.9 Hz, 1H), 3.07 (d, J = 10.9 Hz, 1H), 2.36 (s, 3H), 1.88 (dd, J = 13.1, 7.4 Hz, 1H), 1.56 (dd, J = 13.1, 8.4 Hz, 1H), 1.35−0.98 (m, 8H), 0.76−0.69 (m, 1H), 0.64−0.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 134.8, 129.7, 127.5, 59.3, 59.1, 44.1, 41.4, 37.7, 36.2, 34.0, 25.8, 23.7, 22.8, 21.5. The NMR data were in agreement with reported results.[31a]

*4,4-Diallyl-2-(bromomethyl)-1-tosylpyrrolidine (**4p**).* Compound **4p** was prepared according to the general procedure and isolated as an oil (182.3 mg, 92% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 5.67−5.56 (m, 1H), 5.53−5.39 (m, 1H), 5.05−4.88 (m, 3H), 4.74 (d, J = 17.0 Hz, 1H), 3.83−3.77 (m, 2H), 3.55−3.45 (m, 1H), 3.19−3.07 (m, 2H), 2.36 (s, 3H), 2.04 (d, J = 7.3 Hz, 2H), 1.96−1.85 (m, 1H), 1.71−1.54 (m, 2H), 1.44 (dd, J = 14.1, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.9, 134.9, 133.4, 133.1, 129.8, 127.5, 118.7, 59.3, 58.6, 43.8, 41.3, 40.5, 39.2, 37.5, 21.6; IR (KBr): 3072, 2972,1640, 1598, 1444, 1346, 1162, 1097, 920, 813, 772, 665, 591 cm^{-1}HRMS-ESI (m/z): [M + H] $^+$ calcd for $C_{18}H_{24}BrNO_2S$, 398.0789; found: 398.0784.

*2-(2-Bromopropan-2-yl)-4,4-diphenyl-1-tosylpyrrolidine (**4q**).* Compound **4q** was prepared according to the general procedure and isolated as a white solid (149.3 mg, 60% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 89−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 (d, J = 7.7 Hz, 2H), 7.33 (t, J = 7.7 Hz, 2H), 7.24−7.18 (m, 3H), 7.17−7.11 (m, 5H), 7.01 (d, J = 8.1 Hz, 2H), 5.16 (dd, J = 13.8, 2.6 Hz, 1H), 4.09 (dd, J = 13.0, 3.7 Hz, 1H), 3.55 (d, J = 13.8 Hz, 1H), 3.18−3.13 (m, 1H), 2.65 (t, J = 13.5 Hz, 1H), 2.28 (s, 3H), 1.33 (s, 3H), 1.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.1, 143.1, 142.8, 140.1, 129.5, 129.0, 128.7, 127.9, 127.2, 126.8, 126.6, 125.9, 61.8, 58.2, 49.9, 48.8, 42.9, 27.9, 21.4, 16.3. HRMS-ESI (m/z): [M + H]+ calcd for $C_{26}H_{28}BrNO_2S$, 498.1102; found: 498.1101. The NMR data were in agreement with reported results.[17c]

*2-(1-Bromoethyl)-4,4-diphenyl-1-tosylpyrrolidine (**4r**).* Compound **4r** was prepared according to the general procedure and isolated as a white solid (152.2 mg, 63% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 186−187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45 (d, J = 8.2 Hz, 2H), 7.20−7.16 (m, 2H), 7.14−7.09 (m, 3H), 7.08−6.99 (m, 7H), 4.86−4.80 (m, 1H), 4.42 (dd, J = 10.6, 1.3 Hz, 1H), 3.90 (d, J = 10.7 Hz, 1H), 3.74 (ddd, J = 9.5, 6.7, 2.9 Hz, 1H), 2.79 (dd, J = 12.3, 6.2 Hz, 1H), 2.66 (dd, J = 12.9, 9.4 Hz, 1H), 2.29 (s, 3H), 1.56 (d, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.3, 142.9, 141.8, 135.9, 128.4, 127.5, 125.7, 125.6, 125.5, 125.3, 63.1, 57.9, 53.9, 51.9, 38.1, 21.4, 20.5. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{25}H_{26}BrNO_2S$, 484.0946; found: 484.0937.

*2-(Bromomethyl)-4-phenyl-1-tosylpyrrolidine (**4s**).* Compound **4s** was prepared according to the general procedure and isolated as a white solid (159.5 mg, 81% yield) after flash chromatography (petroleum ether:ethyl acetate = 80:1); mp = 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.70 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 7.23−7.10 (m, 3H), 7.06−6.96 (m, 2H), 3.94−3.88 (m, 1H), 3.82−3.75 (m, 2H), 3.52 (dd, J = 9.7, 8.4 Hz, 1H), 3.30 (t, J = 11.4 Hz, 1H), 2.62−2.53 (m, 1H), 2.46−2.33 (m, 4H), 1.96−1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.0, 138.8, 134.9, 130.0, 128.7, 127.5, 127.3, 127.0, 60.5, 55.7, 43.1, 39.1, 37.6, 21.6; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{18}H_{20}BrNO_2S$, 394.0476; found: 394.0476. The NMR data were in agreement with reported results.[17c]

*2-(Bromomethyl)-5,5-diphenyl-1-tosylpiperidine (**4t**).* Compound **4t** was prepared according to the general procedure and isolated as a white solid (152.3 mg, 63% yield) after flash chromatography (petroleum ether:ethyl acetate = 70:1); mp = 134−135 °C; ^{1}H

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NMR (400 MHz, $CDCl_3$) δ = 7.49 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 7.9 Hz, 2H), 7.21−7.06 (m, 10H), 4.54 (d, J = 13.4 Hz, 1H), 4.03−3.94 (m, 1H), 3.45 (t, J = 10.8 Hz, 1H), 3.26 (dd, J = 9.9, 3.2 Hz, 1H), 3.08 (d, J = 13.4 Hz, 1H), 2.40 (dd, J = 14.1, 2.4 Hz, 1H), 2.33 (s, 3H), 2.21−2.13 (m, 1H), 2.07 (dd, J = 14.2, 1.8 Hz, 1H), 1.59 (t, J = 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.9, 142.8, 142.3, 135.5, 128.8, 127.5, 127.4, 126.8, 126.4, 125.6, 125.3, 125.1, 52.1, 47.6, 44.6, 27.6, 27.4, 20.7, 20.5; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{25}H_{26}BrNO_2S$, 484.0946; found: 484.0937. The NMR data were in agreement with reported results.[17c]

*2-(Bromomethyl)-5,5-dimethyl-1-tosylpiperidine (**4u**).* Compound **4u** was prepared according to the general procedure and isolated as a white solid (125.7 mg, 70% yield) after flash chromatography (petroleum ether:ethyl acetate = 70:1); mp = 75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.62 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.1 Hz, 2H), 4.19 (dd, J = 17.3, 11.7 Hz, 1H), 3.38 (t, J = 10.5 Hz, 1H), 3.21 (d, J = 13.1 Hz, 1H), 3.10 (dd, J = 9.9, 4.0 Hz, 1H), 2.56 (d, J = 13.1 Hz, 1H), 2.34 (s, 3H), 1.91 (d, J = 14.3 Hz, 1H), 1.75−1.65 (m, 1H), 1.32−1.12 (m, 2H), 0.82 (s, 3H), 0.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.4, 137.8, 129.8, 126.9, 52.8, 51.4, 31.3, 30.1, 29.3, 28.8, 23.2, 21.6; IR (KBr): 3020, 2953, 1595, 1451, 1333, 1154, 1089, 977, 909, 810, 773, 662 cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{15}H_{22}BrNO_2S$, 360.0633; found: 360.0625.

*3-(Bromomethyl)-2-tosyl-2-azaspiro[5.5]undecane (**4v**).* Compound **4v** was prepared according to the general procedure and isolated as an oil (135.2 mg, 68% yield) after flash chromatography (petroleum ether:ethyl acetate = 80:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.63 (d, J = 7.8 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 4.22−4.04 (m, 1H), 3.55 (d, J = 13.3 Hz, 1H), 3.40 (t, J = 10.5 Hz, 1H), 3.19−3.07 (m, 1H), 2.45 (d, J = 13.3 Hz, 1H), 2.36 (s, 3H), 1.86 (d, J = 14.1 Hz, 1H), 1.74−1.66 (m, 1H), 1.43−1.04 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.3, 136.8, 128.7, 125.9, 52.3, 47.8, 36.9, 31.4, 29.6, 28.6, 28.5, 25.4, 20.5, 20.3, 20.3, 19.7; IR (KBr): 3031, 2927, 1597, 1490, 1452, 1338, 1158, 1093, 940, 811, 766, 676 cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{18}H_{26}BrNO_2S$, 400.0946; found: 400.0938.

*2-(Bromomethyl)-1-tosylpiperidine (**4w**).* Compound **4w** was prepared according to the general procedure and isolated as an oil (94.4 mg, 57% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 4.26−4.05 (m, 1H), 3.68 (d, J = 11.2 Hz, 1H), 3.44 (t, J = 10.1 Hz, 1H), 3.35 (dd, J = 10.1, 5.4 Hz, 1H), 2.93−2.83 (m, 1H), 2.36 (s, 3H), 1.96 (d, J = 10.6 Hz, 1H), 1.47 (d, J = 11.9 Hz, 2H), 1.42−1.35 (m, 2H), 1.27−1.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.4, 136.9, 128.9, 126.0, 52.4, 40.1, 29.4, 24.2, 23.3, 20.6, 16.9. The NMR data were in agreement with reported results.[11b]

General Procedure for the Intramolecular Chloroamidation. The reaction was carried out in an open air system. To a 100 mL flask were added 0.5 mmol alkenylamine, 0.55 mmol $PhI(OAc)_2$, 1 mmol pyridium chloride, and 20 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature for an indicated period. Then 10 mL of 1 N HCl were added and the mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to give the corresponding product.

*2-(Chloromethyl)-4,4-diphenyl-1-tosylpyrrolidine (**5a**).* Compound **5a** was prepared according to the general procedure and isolated as a white solid (174.3 mg, 82% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 162−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.55 (d, J = 8.2 Hz, 2H), 7.23−6.93 (m, 12H), 4.31 (d, J = 10.2 Hz, 1H), 3.86−3.78 (m, 2H), 3.61 (d, J = 10.2 Hz, 1H), 2.98 (dd, J = 14.8, 7.0 Hz, 1H), 2.65 (d, J = 6.2 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.7, 144.5, 143.7, 133.8, 129.8, 128.8, 128.7, 127.5, 126.8, 126.6, 126.5, 126.4, 60.2, 58.6, 52.3, 46.5, 40.9, 21.6; IR (KBr): 3031, 2960,1594, 1487, 1445, 1354, 1171, 1089, 1028, 867, 814, 734, 700, 661 cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{24}H_{24}ClNO_2S$, 426.1295; found: 426.1292.

*2-(Chloromethyl)-4,4-dimethyl-1-tosylpyrrolidine (**5b**).* Compound **5b** was prepared according to the general procedure and isolated as a white solid (132.6 mg, 88% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 92−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.66 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 4.00−3.93 (m, 1H), 3.82−3.75 (m, 1H), 3.60 (dd, J = 10.4, 8.5 Hz, 1H), 3.07 (q, J = 10.5 Hz, 2H), 2.36 (s, 3H), 1.76 (dd, J = 12.9, 7.4 Hz, 1H), 1.70−1.60 (m, 1H), 0.98 (s, 3H), 0.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 134.8, 129.7, 127.5, 61.8, 60.3, 48.1, 44.6, 37.5, 26.1, 25.8, 21.6. The NMR data were in agreement with reported results.[11g]

*3-(Chloromethyl)-2-tosyl-2-azaspiro[4.5]decane (**5c**).* Compound **5c** was prepared according to the general procedure and isolated as a white solid (129.9 mg, 76% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 73−75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 3.96 (dd, J = 10.5, 2.9 Hz, 1H), 3.75−3.69 (m, 1H), 3.57 (dd, J = 10.3, 8.6 Hz, 1H), 3.25 (d, J = 10.8 Hz, 1H), 3.05 (d, J = 10.9 Hz, 1H), 2.35 (s, 3H), 1.83 (dd, J = 13.0, 7.4 Hz, 1H), 1.60 (dd, J = 13.0, 8.3 Hz, 1H), 1.34−1.26 (m, 3H), 1.22−1.01 (m, 4H), 0.81−0.68 (m, 2H), 0.62−0.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 134.7, 129.7, 127.5, 59.5, 58.9, 48.4, 42.8, 41.4, 36.2, 33.9, 25.8, 23.7, 22.8, 21.5; IR (KBr): 3030, 2928, 1698, 1449, 1344, 1157, 1093, 1040, 966, 811 cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{17}H_{24}ClNO_2S$, 342.1295; found: 342.1291.

*2-(Chloromethyl)-1-tosylpyrrolidine (**5d**).* Compound **5d** was prepared according to the general procedure and isolated as a white solid (103.1 mg, 76% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 56−57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.66 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 3.80 (dd, J = 10.6, 3.3 Hz, 1H), 3.76−3.69 (m, 1H), 3.48−3.31 (m, 2H), 3.12−3.00 (m, 1H), 2.36 (s, 3H), 1.91−1.82 (m, 1H), 1.82−1.70 (m, 1H), 1.68−1.56 (m, 1H), 1.54−1.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.8, 133.0, 128.9, 126.6, 59.5, 48.7, 46.0, 28.3, 22.8, 20.6. The NMR data were in agreement with reported results.[11g]

*4,4-Diallyl-2-(chloromethyl)-1-tosylpyrrolidine (**5e**).* Compound **5e** was prepared according to the general procedure and isolated as an oil (155.6 mg, 88% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 7.6 Hz, 2H), 7.27 (d, J = 7.6 Hz, 2H), 5.67−5.57 (m, 1H), 3.52−3.42 (m, 1H), 5.07−4.91 (m, 3H), 4.76 (d, J = 16.9 Hz, 1H), 3.92 (d, J = 10.7 Hz, 1H), 3.81 (q, J = 7.8 Hz, 1H), 3.62 (t, J = 9.2 Hz, 1H), 3.23−3.04 (m, 2H), 2.37 (s, 3H), 2.05 (d, J = 7.3 Hz, 2H), 1.87 (dd, J = 13.1, 7.5 Hz, 1H), 1.74−1.58 (m, 2H), 1.53−1.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.9, 134.9, 133.5, 133.2, 129.8, 127.5, 118.7, 59.6, 58.5, 48.1, 43.8, 40.5, 40.1, 39.2, 21.6; IR (KBr): 3072, 2967, 1640, 1597, 1444, 1344, 1159, 1094, 919, 808 cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{18}H_{24}ClNO_2S$, 354.1295; found: 354.1291.

*2-(Chloromethyl)-1-tosylindoline (**5f**).* Compound **5f** was prepared according to the general procedure and isolated as a white solid (98.0 mg, 61% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 130−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.68 (d, J = 8.1 Hz, 1H), 7.58 (d, J = 7.6 Hz, 2H), 7.30−7.17 (m, 3H), 7.07 (q, J = 7.4 Hz, 2H), 4.44−4.40 (m, 1H), 3.95 (d, J = 10.6 Hz, 1H), 3.57 (t, J = 9.9 Hz, 1H), 3.02−2.81 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.3, 141.1, 134.5, 130.8, 129.8, 127.9, 127.1, 125.3, 125.0, 116.9, 62.3, 46.9, 32.3, 21.6. The NMR data were in agreement with reported results.[11b]

*2-(2-Chloropropan-2-yl)-4,4-diphenyl-1-tosylpyrrolidine (**5g**).* Compound **5g** was prepared according to the general procedure and isolated as a white solid (84.1 mg, 37% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 55−57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 (d, J = 7.6 Hz, 2H), 7.32 (t, J = 7.7 Hz, 2H), 7.26−7.10 (m, 8H), 7.03 (d, J = 8.1 Hz, 2H), 5.13 (dd, J = 13.7, 2.5 Hz, 1H), 3.89 (dd, J = 12.7, 3.7 Hz, 1H), 3.48 (d, J = 13.7 Hz, 1H), 3.03−2.98 (m, 1H), 2.48 (t, J = 13.3 Hz, 1H), 2.29 (s, 3H), 1.32 (s, 3H), 1.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.1, 143.2, 142.9, 139.9, 129.5, 128.9, 128.7, 127.9, 127.2, 126.8, 126.6, 126.0, 63.9, 62.2, 50.0, 47.7, 41.6, 26.6, 21.5, 15.2. HRMS-ESI

dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

(m/z): [M + H]+ calcd for $C_{25}H_{26}ClNO_2S$, $C_{26}H_{28}ClNO_2S$, 454.1608; found: 454.1611.

*2-(1-Chloroethyl)-4,4-diphenyl-1-tosylpyrrolidine (**5h**).* Compound **5h** was prepared according to the general procedure and isolated as a white solid (131.2 mg, 60% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 166−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 (d, J = 8.2 Hz, 2H), 7.22−7.01 (m, 12H), 7.76−7.70 (m, 1H), 4.44 (d, J = 10.6 Hz, 1H), 3.98−3.90 (m, 1H), 3.83 (d, J = 10.6 Hz, 1H), 2.83−2.60 (m, 2H), 2.29 (s, 3H), 1.38 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.4, 142.9, 141.8, 136.0, 128.4, 127.5, 127.5, 125.7, 125.6, 125.5, 125.5, 125.3, 63.0, 59.1, 57.9, 51.9, 36.4, 20.5, 20.5. HRMS−ESI (m/z): [M + H]$^+$ calcd for $C_{25}H_{26}ClNO_2S$, 440.1451; found: 440.1453.

General Procedure for Intramolecular Fluoroamidation. The reaction was carried out in an open air system. To a 100 mL flask were added 0.5 mmol alkenylamine, 0.55 mmol $PhI(OAc)_2$, 1 mmol $BF_3{\cdot}OEt_2$, 1 mmol pyridine, and 20 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature for an indicated period. The reaction mixture was treated with sat. aqueous K_2CO_3 (10 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was washed with 1 N HCl, dried over anhydrous $MgSO_4$ and concentrated in vacuo to afford the crude product which was purified by flash column chromatography.

*5-Fluoro-3,3-diphenyl-1-tosylpiperidine (**6a**).* Compound **6a** was prepared according to the general procedure and isolated as a white solid (110.6 mg, 54% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 165−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 7.7 Hz, 2H), 7.26−7.04 (m, 10H), 4.52 (dm, J = 47.2 Hz, 1H), 4.43 (d, J = 12.4 Hz, 1H), 4.00−3.93 (m, 1H), 2.97−2.83 (m, 1H), 2.35 (s, 3H), 2.32 (d, J = 12.4 Hz, 1H), 2.23−2.18 (m, 1H), 2.08 (dd, J = 21.3, 11.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.4, 144.1, 143.2, 132.1, 129.9, 128.7, 128.6, 127.8, 127.8, 126.9, 126.6, 126.5, 85.6 (d, J = 173.6 Hz), 53.9, 49.9 (d, J = 31.3 Hz), 46.5, 41.1 (d, J = 18.7 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −185.5 (d, J = 47.7 Hz). The NMR data were in agreement with reported results.[21h]

*5-Fluoro-1-(methylsulfonyl)-3,3-diphenylpiperidine (**6b**).* Compound **6b** was prepared according to the general procedure and isolated as a white solid (103.3 mg, 62% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 161−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.59−6.25 (m, 10H), 4.61−4.43 (m, 2H), 3.97 (dd, J = 10.3, 5.1 Hz, 1H), 2.97 (t, J = 11.0 Hz, 1H), 2.88 (d, J = 12.6 Hz, 1H), 2.71 (dd, J = 10.1, 5.8 Hz, 1H), 2.67 (s, 3H), 2.31 (dd, J = 21.7, 10.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.1, 141.9, 127.7, 127.7, 126.5, 125.9, 125.6, 125.4, 84.4 (d, J = 174.5 Hz), 52.8, 48.7 (d, J = 30.8 Hz), 45.6 (d, J = 10.3 Hz), 40.1 (d, J = 18.7 Hz), 33.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −184.9 (d, J = 47.3 Hz). The NMR data were in agreement with reported results.[21h]

*5-Fluoro-1-(4-nitrophenylsulfonyl)-3,3-diphenylpiperidine (**6c**).* Compound **6c** was prepared according to the general procedure and isolated as a white solid (101.4 mg, 46% yield) after flash chromatography (petroleum ether:ethyl acetate = 20:1);mp = 205−206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.30 (d, J = 8.7 Hz, 2H), 7.87 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 7.7 Hz, 2H), 7.29 (t, J = 7.7 Hz, 2H), 7.21−7.13 (m, 4H), 7.07 (d, J = 7.4 Hz, 2H), 4.61−4.52 (dm, J = 47.5 Hz, 1H), 4.45 (d, J = 13.5 Hz, 1H), 4.02−3.94 (m, 1H), 2.92 (t, J = 9.9 Hz, 1H), 2.46 (d, J = 12.3 Hz, 1H), 2.35−2.28 (m, 1H), 2.14 (dd, J = 21.6, 10.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.4, 144.9, 142.7, 141.1 128.9, 128.9, 128.8, 127.5, 127.2, 126.8, 126.4, 124.6, 85.1 (d, J = 175.0 Hz), 53.9, 49.7 (d, J = 31.4 Hz), 46.6 (d, J = 10.9 Hz), 40.9 (d, J = 18.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ = −185.3 (d, J = 47.5 Hz). IR (KBr): 3031, 2961, 1600, 1499, 1355, 1167, 798, 754, 700, 661, 603 cm^{-1}; HRMS-ESI (m/z): [M + H]$^+$calcd for $C_{23}H_{21}FN_2O_4S$, 441.1284; found: 441.1273.

*5-Fluoro-3,3-diphenyl-1-(phenylsulfonyl)piperidine (**6d**).* Compound **6d** was prepared according to the general procedure and isolated as a white solid (108.4 mg, 55% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 178−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.70 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.40 (d, J = 7.6 Hz, 2H), 7.27 (t, J = 7.7 Hz, 2H), 7.23−7.16 (m, 3H), 7.16−7.12 (m, 1H), 7.09 (t, J = 6.3 Hz, 2H), 4.45 (dm, J = 47.5 Hz, 1H), 4.46 (d, J = 13.2 Hz, 1H), 4.01−3.94 (m, 1H), 2.90 (t, J = 8.6 Hz, 1H), 2.35 (d, J = 12.4 Hz, 1H), 2.26−2.20 (m, 1H), 2.09 (dd, J = 21.3, 11.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.3, 142.0, 134.1, 132.2, 128.3, 127.7, 127.6, 126.6, 125.9, 125.5, 125.4, 84.5 (d, J = 174.0 Hz), 52.8, 48.8 (d, J = 31.2 Hz), 45.4 (d, J = 10.9 Hz), 39.9 (d, J = 18.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ = −185.5 (d, J = 47.6 Hz). The NMR data were in agreement with reported results.[21h]

*5-Fluoro-3,3-dimethyl-1-tosylpiperidine (**6e**).* Compound **6e** was prepared according to the general procedure and isolated as a white solid (78.4 mg, 55% yield) after flash chromatography (petroleum ether:ethyl acetate = 30:1); mp = 83−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 4.81−4.60 (dm, J = 43.3 Hz, 1H), 3.56−3.46 (m, 1H), 2.87 (d, J = 11.4 Hz, 1H), 2.60−2.53 (m, 1H), 2.36 (s, 3H), 2.32 (d, J = 11.4 Hz, 1H), 1.68−1.58 (m, 1H), 1.32−1.18 (m, 1H), 0.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.8, 133.3, 129.8, 127.5, 85.8 (d, J = 175.3 Hz), 56.7, 49.8 (d, J = 28.6 Hz), 42.6 (d, J = 17.4 Hz), 31.9 (d, J = 7.4 Hz), 27.8, 25.9, 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −183.0 (d, J = 43.3 Hz). The NMR data were in agreement with reported results.[21h]

*4-Fluoro-2-tosyl-2-azaspiro[5.5]undecane (**6f**).* Compound **6f** was prepared according to the general procedure and isolated as a white solid (94.6 mg, 58% yield) after flash chromatography (petroleum ether:ethyl acetate = 20:1); mp = 104−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.58 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 4.83−4.59 (dm, J = 43.5 Hz, 1H), 3.58−3.51 (m, 1H), 3.12 (d, J = 11.6 Hz, 1H), 2.61−2.54 (m, 1H), 2.37 (s, 3H), 2.34 (d, J = 11.7 Hz, 1H), 1.82−1.69 (m, 1H), 1.48−1.11 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 133.6, 129.8, 127.5, 86.4, 85.6 (d, J = 175.1 Hz), 84.7, 54.0, 50.2 (d, J = 28.6 Hz), 40.9, 36.3, 34.6 (d, J = 6.9 Hz), 33.9, 26.18, 21.6, 21.5, 21.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ = −182.5 (d, J = 43.5 Hz). The NMR data were in agreement with reported results.[20f]

*3,3-Diallyl-5-fluoro-1-tosylpiperidine (**6g**).* Compound **6g** was prepared according to the general procedure and isolated as a white solid (101.4 mg, 60% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 62−63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 5.76−5.63 (m, 2H), 5.12−4.95 (m, 4H), 4.84−4.60 (dm, J = 43.5 Hz, 1H), 3.54−3.41 (m, 1H), 2.95 (d, J = 11.6 Hz, 1H), 2.64−2.56 (m, 1H), 2.39 (d, J = 11.7 Hz, 1H), 2.37 (s, 3H), 2.13−1.99 (m, 4H), 1.73−1.64 (m, 1H), 1.34−1.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.8, 133.1, 132.8, 132.6, 129.8, 127.6, 119.2, 119.1, 85.5 (d, J = 175.6 Hz), 53.6, 49.9 (d, J = 28.3 Hz), 40.9, 39.1, 38.3 (d, J = 18.0 Hz), 37.5 (d, J = 6.4 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −182.1 (d, J = 43.5 Hz). IR (KBr): 3065, 2929,1638, 1596, 1448, 1341, 1163, 1097, 923, 812, 710, 655 cm^{-1}; HRMS-ESI (m/z): [M + H] $^+$calcd for $C_{18}H_{24}FNO_2S$, 338.1590; found: 338.1584.

*3-Fluoro-1-tosylpiperidine (**6h**).* Compound **6h** was prepared according to the general procedure and isolated as a white solid (51.6 mg, 40% yield) after flash chromatography (petroleum ether:ethyl acetate = 20:1);mp = 101−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.59 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 4.60 (dm, J = 47.4, 1H), 3.34−3.35 (m, 1H), 3.10−3.00 (m, 1H), 2.95−2.89 (m, 1H), 2.87−2.76 (m, 1H), 2.37 (s, 3H), 1.86−1.68 (m, 2H), 1.59−1.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 133.4, 129.7, 127.7, 86.1 (d, J = 176.3 Hz), 49.7 (d, J = 26.8 Hz), 45.8, 29.3 (d, J = 20.0 Hz), 21.6, 21.2 (d, J = 7.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ = −182.7 (m). The NMR data were in agreement with reported results.[20f]

*1-Benzyl-5-iodo-3,3-diphenylpiperidine (**7a**).* Compound **7a** was prepared according to the general procedure and isolated as an oil (176.3 mg, 78% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33−6.85 (m, 15H), 4.07−3.96 (m, 1H), 3.59 (d, J = 11.8 Hz, 1H), 3.50 (s, 2H), 3.25 (dd, J = 10.5, 3.8 Hz, 1H), 3.13 (d, J = 12.8 Hz, 1H), 2.58 (t, J = 12.7 Hz, 1H), 2.44 (t, J = 11.0 Hz, 1H), 2.29 (d, J = 12.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.3, 144.6, 137.6, 137.5, 130.3, 129.3, 128.7, 128.4, 128.1, 127.4, 126.4, 125.9, 63.9, 62.4, 61.9,

dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

50.2, 48.8, 23.1. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{24}H_{24}IN$, 454.1032; found: 454.1073.

*5-Iodo-1-(4-methoxybenzyl)-3,3-diphenylpiperidine (**7b**).* Compound **7b** was prepared according to the general procedure and isolated as an oil (192.8 mg, 80% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25−7.04 (m, 10H), 6.99 (d, J = 7.5 Hz, 2H), 6.79 (d, J = 8.4 Hz, 2H), 4.04−3.94 (m, 1H), 3.73 (s, 3H), 3.58 (d, J = 12.1 Hz, 1H), 3.46 (d, J = 13.0 Hz, 1H), 3.40 (d, J = 13.0 Hz, 1H), 3.27−3.19 (m, 1H), 3.12 (d, J = 12.6 Hz, 1H), 2.57 (t, J = 12.7 Hz, 1H), 2.42 (t, J = 11.0 Hz, 1H), 2.23 (d, J = 12.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 146.2, 143.6, 129.4, 128.5, 127.7, 127.3, 127.0, 126.1, 125.3, 124.8, 112.6, 62.8, 60.6, 60.6, 54.2, 49.1, 47.8, 22.2. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{25}H_{26}INO$, 484.1137; found: 484.1139.

*1-(4-Fluorobenzyl)-5-iodo-3,3-diphenylpiperidine (**7c**).* Compound **7c** was prepared according to the general procedure and isolated as an oil (181.6 mg, 77% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.21−6.84 (m, 14H), 4.03−4.95 (m, 1H), 3.55 (d, J = 12.1 Hz, 1H), 3.47−3.36 (m, 2H), 3.19 (dd, J = 10.5, 3.7 Hz, 1H), 3.12 (d, J = 12.7 Hz, 1H), 2.55 (t, J = 12.7 Hz, 1H), 2.47−2.38 (m, 1H), 2.23 (dd, J = 21.2, 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.1 (d, J = 245.4 Hz), 146.1, 143.4, 132.2 129.6 (d, J = 7.8 Hz), 127.5, 127.3, 127.1, 125.3, 125.2, 124.9, 114.09 (d, J = 21.1 Hz), 62.7, 60.7, 60.4, 49.0, 47.6, 21.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ = −115.0; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{24}H_{23}FIN$, 472.0937; found: 472.0925.

*1-Benzyl-5-bromo-3,3-diphenylpiperidine (**7d**).* Compound **7d** was prepared according to the general procedure and isolated as an oil (172.1 mg, 85% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26−6.98 (m, 15H), 3.90−3.85 (m, 1H), 3.49 (q, J = 13.2 Hz, 3H), 3.18 (dd, J = 10.4, 3.8 Hz, 1H), 3.01 (d, J = 12.5 Hz, 1H), 2.40 (t, J = 12.4 Hz, 1H), 2.30−2.18 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.4, 144.8, 137.6, 129.4, 128.7, 128.5, 128.2, 127.5, 126.5, 126.1, 62.6, 62.0, 49.2, 46.8, 45.5. The NMR data were in agreement with reported results.[17c]

*5-Bromo-1-(4-methoxybenzyl)-3,3-diphenylpiperidine (**7e**).* Compound **7e** was prepared according to the general procedure and isolated as a white solid (191.1 mg, 88% yield) after flash chromatography (petroleum ether:ethyl acetate = 80:1); mp = 88−91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41−6.92 (m, 12H), 6.78 (d, J = 7.7 Hz, 2H), 3.87 (t, J = 11.3 Hz, 1H), 3.71 (s, 3H), 3.51 (d, J = 12.1 Hz, 1H), 3.44 (s, 2H), 3.21−3.16 (m, 1H), 3.01 (d, J = 12.3 Hz, 1H), 2.40 (t, J = 12.4 Hz, 1H), 2.30−2.14 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.0, 147.4, 144.8, 130.5, 129.3, 128.7, 128.4, 128.1, 127.8, 126.4, 125.9, 113.7, 61.9, 61.9, 61.7, 55.3, 49.2, 46.8, 45.6. The NMR data were in agreement with reported results.[17c]

*5-Bromo-1-(4-nitrobenzyl)-3,3-diphenylpiperidine (**7f**).* Compound **7f** was prepared according to the general procedure and isolated as a white solid (187.2 mg, 83% yield) after flash chromatography (petroleum ether:ethyl acetate = 60:1); mp = 149−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.10 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), 7.29−7.06(m, 8H), 7.04(d, J = 7.3 Hz, 2H), 3.94−3.87 (m, 1H), 3.66−3.50 (m, 3H), 3.12 (dd, J = 10.2, 4.6 Hz, 1H), 3.06 (d, J = 12.8 Hz, 1H), 2.43−2.29 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.3, 145.8, 144.4, 143.3, 128.6, 127.4, 127.3, 127.2, 125.5, 125.3, 125.1, 122.6, 61.15, 60.8, 60.5, 48.1, 45.3, 43.6. The NMR data were in agreement with reported results.[17c]

*1-Benzyl-5-bromo-3,3-dimethylpiperidine (**7g**).* Compound **7g** was prepared according to the general procedure and isolated as an oil (119.5 mg, 85% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); ^{1}H NMR(400 MHz, $CDCl_3$) δ = 7.29−7.16 (m, 5H), 4.19−4.13 (m, 1H), 3.48 (d, J = 13.4 Hz, 1H), 3.35 (d, J = 13.4 Hz, 1H), 3.15 (d, J = 6.6 Hz, 1H), 2.35 (d, J = 11.1 Hz, 1H), 2.07 (t, J = 10.8 Hz, 1H), 1.99−1.94 (m, 1H),1.70 (d, J = 11.0 Hz, 1H), 1.46 (t, J = 12.5 Hz, 1H), 0.99 (s, 3H), 0.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.4, 127.6, 127.2, 126.0, 63.4, 61.4, 61.2, 48.2, 45.4, 33.4, 28.2, 23.8. The NMR data were in agreement with reported results.[17c]

*2-Benzyl-4-bromo-2-azaspiro[5.5]undecane (**7h**).* Compound **7h** was prepared according to the general procedure and isolated as an oil (143.6 mg, 89% yield) after flash chromatography (petroleum ether:ethyl acetate = 70:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.23−7.15 (m, 5H), 4.20−4.14 (m, 1H), 3.48 (d, J = 13.4 Hz, 1H), 3.35 (dd, J = 13.4, 5.4 Hz, 1H), 3.15 (dd, J = 10.5, 4.3 Hz, 1H), 2.65 (d, J = 11.3 Hz, 1H), 2.19 (dd, J = 11.0, 1.8 Hz, 1H), 2.12 (t, J = 10.8 Hz, 1H), 1.57 (d, J = 11.3 Hz, 2H), 1.36−1.08 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.6, 127.5, 127.2, 126.0, 62.1, 61.3, 45.3, 37.3, 36.1, 31.6, 25.6, 20.5, 20.5. The NMR data were in agreement with reported results.[17c]

*1-Benzyl-2-(chloromethyl)-4,4-diphenylpyrrolidine (**7i**).* Compound **7i** was prepared according to the general procedure and isolated as an oil (115.8 mg, 64% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54−7.27 (m, 15H), 4.20 (d, J = 13.2, 1H), 4.01 (d, J = 9.8, 1H), 3.74 (d, J = 13.2, 1H), 3.50 (dd, J = 10.4, 4.2, 1H), 3.40−3.35 (m, 1H),3.17−3.07 (m, 3H), 2.79 (dd, J = 13.1, 3.4,1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 129.4, 128.7, 128.6, 128.5, 128.3, 127.9, 127.4, 127.3, 126.9, 126.6, 126.3, 126.0, 65.3, 64.4, 59.7, 53.0, 47.3, 42.5. The NMR data were in agreement with reported results.[17a]

*2-(Chloromethyl)-1-(4-methylbenzyl)-4,4-diphenylpyrrolidine (**7j**).* Compound **7j** was prepared according to the general procedure and isolated as an oil (135.3 mg, 72% yield) after flash chromatography (petroleum ether:ethyl acetate = 100:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29−7.05 (m, 14H), 3.95 (d, J = 13.1, 1H), 3.78 (d, J = 9.8, 1H), 3.51 (s, 1H), 3.28 (dd, J = 10.3, 3.8, 1H), 3.17−3.14 (m, 1H), 2.95−2.84 (m, 3H), 2.56 (dd, J = 13.1, 2.5, 1H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 129.4, 129.3, 128.8, 128.7, 128.5, 128.3, 128.2, 127.4, 126.9, 126.6, 126.3, 125.9, 65.2, 64.3, 59.4, 52.9, 47.3, 42.5, 21.4. The NMR data were in agreement with reported results.[17a]

*N-(2-Iodo-2-phenylethyl)-4-methylbenzenesulfonamide (**8**).* Compound **8** was prepared according to the general procedure and isolated as a white solid (126.4 mg, 63% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 7.20−7.18 (m, 5H), 4.94 (t, J = 7.8 Hz, 1H), 4.69 (t, J = 6.4 Hz, 1H), 3.66−3.59 (m, 1H), 3.48−3.41 (m, 1H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.9, 139.9, 137.0, 129.9, 129.1, 128.8, 127.6, 127.1, 51.3, 29.9, 21.6. The NMR data were in agreement with reported results. [33]

Compounds **9a** and **9b** could be separated. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.73 (d, 2H, J = 8.4 Hz, **9a**); 7.62 (d, J = 8.4 Hz, **9b**), 7.19−7.34 (m, **9a** and **9b**), 7.10−7.13 (m, **9b**), 5.38 (d, J = 6.7 Hz, **9b**), 4.92 (t, J = 6.4 Hz, **9a**), 4.82 (dd, J = 13.9, 6.2 Hz, **9a**), 4.570 (q, J = 6.2 Hz, **9b**), 3.61−3.41(m, **9a** and **9b**), 2.36 (s, **9a**), 2.31 (s, **9b**). ^{13}C NMR (100 MHz, $CDCl_3$) (**9a** + **9b**) δ = 143.9, 143.6, 138.2, 137.7, 136.9, 136.9, 129.9, 129.6, 129.2, 129.1, 128.7, 128.3, 127.7, 127.2, 127.1, 126.8, 58.1, 52.6, 50.1, 36.7, 21.6, 21.6. The NMR data were in agreement with reported results.[36]

*5-(Iodomethyl)-3,3-diphenyldihydrofuran-2(3H)-one (**10a**).* Compound **10a** was prepared according to the general procedure and isolated as a white solid (156.9 mg, 83% yield) after flash chromatography (petroleum ether:ethyl acetate = 60:1); mp = 115−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42−7.23 (m, 10H), 4.27−4.18 (m, 1H), 3.44 (dd, J = 10.3, 4.8 Hz, 1H), 3.33 (dd, J = 10.3, 7.1 Hz, 1H), 3.09 (dd, J = 12.7, 4.8 Hz, 1H), 2.80 (dd, J = 12.7, 10.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.3, 142.1, 140.8, 128.9, 128.6, 128.2, 127.9, 127.7, 127.5, 76.5, 59.9, 45.8, 6.7. The NMR data were in agreement with reported results.[37]

*5-(Bromomethyl)-3,3-diphenyldihydrofuran-2(3H)-one (**10b**).* Compound **10b** was prepared according to the general procedure and isolated as a white solid (132.3 mg, 80% yield) after flash chromatography (petroleum ether:ethyl acetate = 40:1); mp = 86−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40−7.01 (m, 10H), 4.51−4.44 (m, 1H), 3.53 (dd, J = 10.8, 4.7 Hz, 1H), 3.44 (dd, J = 10.8, 6.5 Hz, 1H), 3.09 (dd, J = 13.2, 5.2 Hz, 1H), 2.74 (dd, J = 13.2, 9.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.2, 141.5, 139.4, 129.1, 128.5,

dx.doi.org/10.1021/jo501739j | J. Org. Chem. XXXX, XXX, XXX−XXX

127.9, 127.7, 127.5, 127.3, 74.9, 58.2, 42.2, 32.7. The NMR data were in agreement with reported results.[38]

*5-(Chloromethyl)-3,3-diphenyldihydrofuran-2(3H)-one (**10c**).* Compound **10c** was prepared according to the general procedure and isolated as a white solid (94.5 mg, 66% yield) after flash chromatography (petroleum ether:ethyl acetate = 80:1); mp = 107−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43−7.11 (m, 10H), 4.59−4.53 (m, 1H), 3.71 (d, J = 5.1 Hz, 2H), 3.03−2.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.6, 141.2, 140.4, 128.9, 128.4, 128.1, 127.9, 127.6, 79.6, 60.5, 44.3, 43.2. The NMR data were in agreement with reported results.[39]

*2-(Iodomethyl)-4,4-diphenyltetrahydrofuran (**11a**).* Compound **11a** was prepared according to the general procedure and isolated as a white solid (163.9 mg, 90% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); mp = 54−55 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29−6.94 (m, 10H), 4.61 (dd, J = 8.8, 0.8 Hz, 1H), 4.12 (d, J = 8.8 Hz, 1H), 4.06−3.94 (m, 1H), 3.19 (dd, J = 9.9, 5.0 Hz, 1H), 3.13 (dd, J = 9.9, 6.8 Hz, 1H), 2.66 (dd, J = 12.2, 5.9 Hz, 1H), 2.34 (dd, J = 12.3, 9.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.8, 145.0, 128.6, 128.5, 127.2, 127.0, 126.8, 126.6, 77.9, 77.5, 56.5, 45.3, 10.7; IR (KBr): 3024, 2941, 1597, 1490, 1444, 1263, 1198, 1040, 874, 767, 702, 665 cm^{-1}; HRMS-ESI (m/z): $[M+NH_4]^+$ calcd for $C_{17}H_{17}IO$, 382.0668; found: 382.0656.

*2-(Bromomethyl)-4,4-diphenyltetrahydrofuran (**11b**).* Compound **11b** was prepared according to the general procedure and isolated as an oil (136.2 mg, 86% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29−7.02 (m, 10H), 4.59 (d, J = 8.7 Hz, 1H), 4.20−4.13 (m, 1H), 4.10 (d, J = 8.8 Hz, 1H), 3.36 (dd, J = 10.2, 5.1 Hz, 1H), 3.31 (dd, J = 10.2, 6.1 Hz, 1H), 2.61 (dd, J = 12.3, 5.6 Hz, 1H), 2.43 (dd, J = 12.3, 9.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.7, 144.9, 128.6, 128.7, 127.2, 127.0, 126.8, 126.6, 77.8, 77.4, 56.2, 43.6, 36.0. The NMR data were in agreement with reported results.[40]

*2-(Chloromethyl)-4,4-diphenyltetrahydrofuran (**11c**).* Compound **11c** was prepared according to the general procedure and isolated as an oil (114.5 mg, 84% yield) after flash chromatography (petroleum ether:ethyl acetate = 50:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35−6.96 (m, 10H), 4.59 (d, J = 8.7 Hz, 1H), 4.22−4.15 (m, 1H), 4.10 (d, J = 8.8 Hz, 1H), 3.54−3.46 (m, 2H), 2.58 (dd, J = 12.3, 6.1 Hz, 1H), 2.48 (dd, J = 12.2, 9.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.6, 143.9, 127.5, 127.4, 126.0, 125.9, 125.6, 125.4, 76.9, 76.2, 54.9, 46.1, 41.3; IR (KBr): 3027, 2951, 1597, 1491, 1447, 1264 1062, 1004, 976, 878, 751, 701 cm^{-1}; HRMS-ESI (m/z): $[M+NH_4]^+$ calcd for $C_{17}H_{17}ClO$, 290.1312; found: 290.1305.

■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra for the obtained compounds and X-ray structure and crystal information file for compound **2v**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge the financial support from National Natural Science Foundation of China (NSFC 20972072, NSFC 21272121). G.-Q.L. acknowledges the support from The Ph.D. Student Innovative Research Program of Nankai University (68140001).

■ REFERENCES

(1) Pors, K.; Shnyder, S. D.; Teesdale-Spittle, P. H.; Hartley, J. A.; Zloh, M.; Searcey, M.; Patterson, L. H. *J. Med. Chem.* **2006**, *49*, 7013−7023.

(2) (a) Kemp, J. E. G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 7, p 469−513. (b) Qiu, J.; Silverman, R. B. *J. Med. Chem.* **2000**, *43*, 706−720.

(3) (a) Blackman, A. J.; Li, C.; Hockless, D. C. R.; Skelton, B. W.; White, A. H. *Tetrahedron* **1993**, *49*, 8645−8656. (b) Kim, W. G.; Kim, J. P.; Kim, C. J.; Lee, K. H.; Yoo, I. D. *J. Antibiot.* **1996**, *49*, 20−25. (c) Rahbæk, L.; Christophersen, C. *J. Nat. Prod.* **1997**, *60*, 175−177.

(4) (a) De Kimpe, N.; Boelens, M. *J. Chem. Soc., Chem. Comm.* **1993**, 916−918. (b) De Kimpe, N.; Boelens, M.; Piqueur, J.; Baele, J. *Tetrahedron Lett.* **1994**, *35*, 1925−1928. (c) Van Brabandt, W.; Van Landeghem, R.; De Kimpe, N. *Org. Lett.* **2006**, *8*, 1105−1108. (d) Minatti, A.; Muñiz, K. *Chem. Soc. Rev.* **2007**, *36*, 1142−1152. (e) D'Hooghe, M.; Aelterman, W.; De Kimpe, N. *Org. Biomol. Chem.* **2009**, *7*, 135−141. (f) Tan, C. K.; Yeung, Y.-Y. *Chem. Commun.* **2013**, *49*, 7985−7996.

(5) (a) Li, G. G.; Kotti, S.; Timmons, C. *Eur. J. Org. Chem.* **2007**, 2745−2758. (b) Chemler, S. R.; Bovino, M. T. *ACS Catal.* **2013**, *3*, 1076−1091.

(6) (a) Cai, Y. F.; Liu, X. H.; Hui, Y. H.; Jiang, J.; Wang, W. T.; Chen, W. L.; Lin, L. L.; Feng, X. M. *Angew. Chem., Int. Ed.* **2010**, *49*, 6160−6164. (b) Cai, Y. F.; Liu, X. H.; Jiang, J.; Chen, W. L.; Lin, L. L.; Feng, X. M. *J. Am. Chem. Soc.* **2011**, *133*, 5636−5639. (c) Huang, S. X.; Ding, K. L. *Angew. Chem., Int. Ed.* **2011**, *50*, 7734−7736.

(7) Horning, D. E.; M, M. J. *Can. J. Chem.* **1974**, *52*, 1321−1330.

(8) Yuan, X.; Liu, K.; Li, C. *J. Org. Chem.* **2008**, *73*, 6166−6171.

(9) Heuger, G.; Kalsow, S.; Göttlich, R. *Eur. J. Org. Chem.* **2002**, *2002*, 1848−1854.

(10) Sjöholm, Å.; Hemmerling, M.; Pradeille, N.; Somfai, P. *J. Chem. Soc., Perkin Trans. 1* **2001**, 891−899.

(11) (a) Szolcsányi, P.; Gracza, T.; Koman, M.; Prónayová, N.; Liptaj, T. *Tetrahedron: Asymmetry* **2000**, *11*, 2579−2597. (b) Manzoni, M. R.; Zabawa, T. P.; Kasi, D.; Chemler, S. R. *Organometallics* **2004**, *23*, 5618−5621. (c) Lei, A. W.; Lu, X. Y.; Liu, G. S. *Tetrahedron Lett.* **2004**, *45*, 1785−1788. (d) Szolcsányi, P.; Gracza, T. *Tetrahedron* **2006**, *62*, 8498−8502. (e) Michael, F. E.; Sibbald, P. A.; Cochran, B. M. *Org. Lett.* **2008**, *10*, 793−796. (f) Hovelmann, C. H.; Streuff, J.; Brelot, L.; Muñiz, K. *Chem. Commun.* **2008**, 2334−2336. (g) Yin, G. Y.; Wu, T.; Liu, G. S. *Chem.—Eur. J.* **2012**, *18*, 451−455.

(12) (a) Sherman, E. S.; Chemler, S. R.; Tan, T. B.; Gerlits, O. *Org. Lett.* **2004**, *6*, 1573−1575. (b) Sherman, E. S.; Fuller, P. H.; Kasi, D.; Chemler, S. R. *J. Org. Chem.* **2007**, *72*, 3896−3905.

(13) (a) Fuller, P. H.; Kim, J.-W.; Chemler, S. R. *J. Am. Chem. Soc.* **2008**, *130*, 17638−17639. (b) Paderes, M. C.; Belding, L.; Fanovic, B.; Dudding, T.; Keister, J. B.; Chemler, S. R. *Chem.—Eur. J.* **2012**, *18*, 1711−1726.

(14) (a) Zabawa, T. P.; Kasi, D.; Chemler, S. R. *J. Am. Chem. Soc.* **2005**, *127*, 11250−11251. (b) Sequeira, F. C.; Turnpenny, B. W.; Chemler, S. R. *Angew. Chem., Int. Ed.* **2010**, *49*, 6365−6368.

(15) Bovino, M. T.; Chemler, S. R. *Angew. Chem., Int. Ed.* **2012**, *51*, 3923−3927.

(16) (a) Zeng, W.; Chemler, S. R. *J. Am. Chem. Soc.* **2007**, *129*, 12948−12949. (b) Chemler, S. R. *Org. Biomol. Chem.* **2009**, *7*, 3009−3019. (c) Chemler, S. R. *J. Organomet. Chem.* **2011**, *696*, 150−158. (d) Chemler, S. R. *Science* **2013**, *341*, 624−625. (e) Turnpenny, B. W.; Chemler, S. R. *Chem. Sci.* **2014**, *5*, 1786−1793.

(17) (a) Liu, G. Q.; Li, W.; Li, Y. M. *Adv. Synth. Catal.* **2013**, *355*, 395−402. (b) Li, R.-L.; Liu, G.-Q.; Li, W.; Wang, Y.-M.; Li, L.; Duan, L.; Li, Y.-M. *Tetrahedron* **2013**, *69*, 5867−5873. (c) Liu, G.-Q.; Ding, Z.-Y.; Zhang, L.; Li, T.-T.; Li, L.; Duan, L.; Li, Y.-M. *Adv. Synth. Catal.* **2014**, *356*, 2303−2310.

(18) Li, W.; Liu, G.-Q.; Cui, B.; Zhang, L.; Li, T.-T.; Li, L.; Duan, L.; Li, Y.-M. *RSC Adv.* **2014**, *4*, 13509−13513.

(19) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155−4156.

(20) (a) Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586−14587. (b) Alexanian, E. J.; Lee, C.;

Sorensen, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 7690−7691. (c) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 7179−7181. (d) Desai, L. V.; Sanford, M. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 5737−5740. (e) Muñiz, K.; Hövelmann, C. H.; Streuff, J. *J. Am. Chem. Soc.* **2008**, *130*, 763−773. (f) Wu, T.; Yin, G.; Liu, G. *J. Am. Chem. Soc.* **2009**, *131*, 16354−16355. (g) Chen, S.; Wu, T.; Liu, G.; Zhen, X. *Synlett* **2011**, 891−894.

(21) (a) Correa, A.; Tellitu, I.; Domínguez, E.; SanMartin, R. *J. Org. Chem.* **2006**, *71*, 8316−8319. (b) Fan, R.; Wen, F.; Qin, L.; Pu, D.; Wang, B. *Tetrahedron Lett.* **2007**, *48*, 7444−7447. (c) Wardrop, D. J.; Bowen, E. G.; Forslund, R. E.; Sussman, A. D.; Weerasekera, S. L. *J. Am. Chem. Soc.* **2009**, *132*, 1188−1189. (d) Lovick, H. M.; Michael, F. E. *J. Am. Chem. Soc.* **2010**, *132*, 1249−1251. (e) Tellitu, I.; Domínguez, E. *Trends Heterocyclic Chem.* **2011**, *15*, 23−32. (f) Wang, Q.; Zhong, W.; Wei, X.; Ning, M.; Meng, X.; Li, Z. *Org. Biomol. Chem.* **2012**, *10*, 8566−8569. (g) Farid, U.; Wirth, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 3462−3465. (h) Kong, W.; Feige, P.; de Haro, T.; Nevado, C. *Angew. Chem., Int. Ed.* **2013**, *52*, 2469−2473. (i) Muangkaew, C.; Katrun, P.; Kanchanarugee, P.; Pohmakotr, M.; Reutrakul, V.; Soorukram, D.; Jaipetch, T.; Kuhakarn, C. *Tetrahedron* **2013**, *69*, 8847−8856.

(22) For selected reviews on hypervalent iodine-promoted functionalization of alkenes, see: (a) Tellitu, I.; Domínguez, E. *Synlett* **2012**, *23*, 2165−2175. (b) Muñiz, K. *Pure Appl. Chem.* **2013**, *85*, 755−761. (c) Romero, R. M.; Woste, T. H.; Muñiz, K. *Chem.—Asian J.* **2014**, *9*, 972−983.

(23) (a) Lovell, P. J.; Bromidge, S. M.; Dabbs, S.; Duckworth, D. M.; Forbes, I. T.; Jennings, A. J.; King, F. D.; Middlemiss, D. N.; Rahman, S. K.; Saunders, D. V.; Collin, L. L.; Hagan, J. J.; Riley, G. J.; Thomas, D. R. *J. Med. Chem.* **2000**, *43*, 342−345. (b) Andriès, J.; Lemoine, L.; Mouchel-Blaisot, A.; Tang, S.; Verdurand, M.; Le Bars, D.; Zimmer, L.; Billard, T. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3730−3733.

(24) (a) Illuminati, G.; Mandolini, L. *Acc. Chem. Res.* **1981**, *14*, 95−102. (b) Kirby, A. J. In *Advances in Physical and Organic Chemistry*; Gold, V., Bethell, D., Eds.; Academic Press: New York, 1981; Vol. *17*, pp 183−278. (c) Denisova, T. G.; Denisov, E. T. *Russ. Chem. Bull.* **2002**, *51*, 949−960. (d) Ryu, J.-S.; Marks, T. J.; McDonald, F. E. *J. Org. Chem.* **2004**, *69*, 1038−1052. (e) Dzudza, A.; Marks, T. J. *Chem.—Eur. J.* **2010**, *16*, 3403−3422.

(25) (a) Yadav, J. S.; Subba Reddy, B. V.; Narasimha Chary, D.; Chandrakanth, D. *Tetrahedron Lett.* **2009**, *50*, 1136−1138. (b) Qiu, S.; Xu, T.; Zhou, J.; Guo, Y.; Liu, G. *J. Am. Chem. Soc.* **2010**, *132*, 2856−2857. (c) Wu, T.; Cheng, J.; Chen, P.; Liu, G. *Chem. Commun.* **2013**, *49*, 8707−8709. (d) Li, Z.; Song, L.; Li, C. *J. Am. Chem. Soc.* **2013**, *135*, 4640−4643.

(26) Suzuki, S.; Kamo, T.; Fukushi, K.; Hiramatsu, T.; Tokunaga, E.; Dohi, T.; Kita, Y.; Shibata, N. *Chem. Sci.* **2014**, *5*, 2754−2760.

(27) During the preparation of this manuscript, Zhang reported iodosobenzene-mediated intramolecular aminofluorination using $BF_3{\bullet}OEt_2$ as fluorine source: Cui, J.; Jia, Q.; Feng, R.-Z.; Liu, S.-S.; He, T.; Zhang, C. *Org. Lett.* **2014**, *16*, 1442−1445.

(28) (a) Martinez, H.; Rebeyrol, A.; Nelms, T. B.; Dolbier, W. R., Jr *J. Fluor. Chem.* **2012**, *135*, 167−175. (b) Huang, H.-T.; Lacy, T. C.; Błachut, B.; Ortiz, G. X.; Wang, Q. *Org. Lett.* **2013**, *15*, 1818−1821.

(29) Lambert, J. B.; Beadle, B. M.; Kuang, K. *J. Org. Chem.* **1999**, *64*, 9241−9246.

(30) (a) Braddock, D. C.; Cansell, G.; Hermitage, S. A. *Synlett* **2004**, 461−464. (b) Hamamoto, H.; Hattori, S.; Takemaru, K.; Miki, Y. *Synlett* **2011**, 1563−1566. (c) Zhou, Z.; He, X. *Synthesis* **2011**, 207−209.

(31) (a) Moriyama, K.; Izumisawa, Y.; Togo, H. *J. Org. Chem.* **2011**, *76*, 7249−7255. (b) Kim, H. J.; Cho, S. H.; Chang, S. *Org. Lett.* **2012**, *14*, 1424−1427.

(32) De Mico, A.; Margarita, R.; Parlanti, L.; Vescovi, A.; Piancatelli, G. *J. Org. Chem.* **1997**, *62*, 6974−6977.

(33) The structure of **8** was determined by comparison with reported results: Zhang, J.; Meng, L.; Li, C.; Xiao, G. *Chin. J. Chem.* **2013**, *31*, 1508−1512.

(34) (a) Jarvest, R. L.; Breen, A. L.; Edge, C. M.; Chaikin, M. A.; Jennings, L. J.; Truneh, A.; Sweet, R. W.; Hertzberg, R. P. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 2851−2856. (b) Ahungena, A.; Canney, D. J. *Med. Chem. Res.* **1996**, *6*, 618−634.

(35) Chávez, P.; Kirsch, J.; Hövelmann, C. H.; Streuff, J.; Martínez-Belmonte, M.; Escudero-Adán, E. C.; Martin, E.; Muñiz, K. *Chem. Sci.* **2012**, *3*, 2375−2382.

(36) The NMR data were in agreement with reported results: Hayakawa, J.; Kuzuhara, M.; Minakata, S. *Org. Biomol. Chem.* **2010**, *8*, 1424−1430.

(37) Higgs, D. E.; Nelen, M. I.; Detty, M. R. *Org. Lett.* **2001**, *3*, 349−352.

(38) Drake, M. D.; Bateman, M. A.; Detty, M. R. *Organometallics* **2003**, *22*, 4158−4162.

(39) Easton, N. R.; Fish, V. B. *J. Org. Chem.* **1953**, *18*, 1071−1074.

(40) Monkovic, I.; Perron, Y. G.; Martel, R.; Simpson, W. J.; Gylys, J. A. *J. Med. Chem.* **1973**, *16*, 403−407.