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Approach to the Synthesis of Indoline Derivatives from Diaryliodonium Salts

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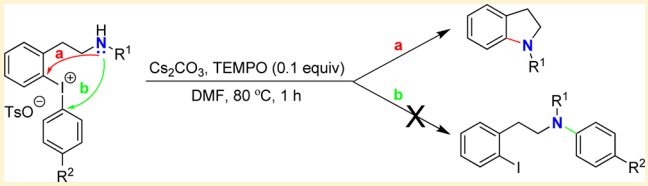
Supporting Information

ABSTRACT: An effective method of constructing the indoline moiety via intramolecular nucleophilic ring closure of a diaryliodonium salt is described. Diacetoxyiodoarene compounds (**1a−1e**) were converted into intermediate Koser's reagent and coupled with arylstannanes (**7−10**) to form diaryliodonium salts (**11a−14e**). Indoline compounds with different *N*-protecting groups, **15**, **16**, **17**, and **18**, were synthesized in higher yields by treating salts (**11a−14e**) with Cs_2CO_3 and TEMPO. Regardless of the electronic environment of five *para*-substituted iodoarenes and the natures of four *N*-protected arylstannane groups, the conversion proceeded well to afford corresponding indolines in yields of 72−84 and 70−84%, respectively.



INTRODUCTION

Indoline frameworks are an important part in numerous biologically active natural and non-natural products[1] and as organic dyes for dye-sensitized solar cells.[2] *N*-Protected indolines have been synthesized using different strategies (Figure 1), such

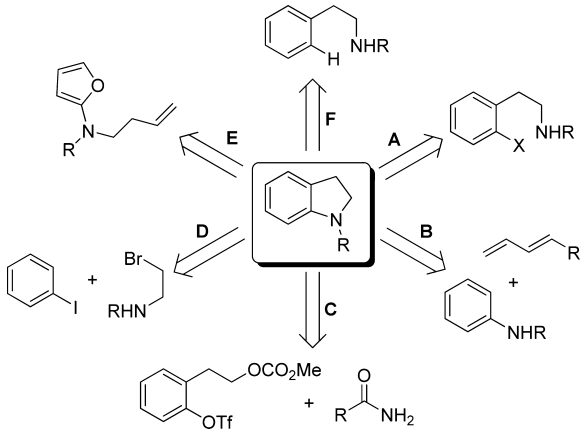


Figure 1. Strategies used to synthesize indolines.

as via the Pd- or Cu-catalyzed cyclization of amine, amide, or carbamate,[3] the radical cyclization of *O*-bromophenethylamine[4] (type A), Pd-catalyzed intermolecular 1,2-carboamination from *N*-aryl ureas and 1,3-dienes (type B),[5] Pd-catalyzed domino amidation from *O*-triflyloxy phenethyl carbonates using amide (type C),[6] Pd-catalyzed C−C/C−N coupling of bromoalkylamines (type D),[7] intramolecular Diels−Alder reaction of 2-aminofurans (type E),[8] and the Pd-catalyzed C−H activation of arylethylamines (type F).[9] A more versatile route for the synthesis of indoline was reported via aryne annulation[10] and via solid-phase organic synthesis (SPOS) using selenenyl bromide resin.[11]

The chiral indolines (*S*)-indoline-2-carboxylic acid or ester[12] are important chiral auxiliaries, chiral catalysts, and heterocyclic alkaloid natural products,[13] especially when added to the pharmacophore of a natural product. Kuwano and Kashiwabara synthesized (*S*)-indoline-2-carboxylic acid via the cyclization of 2-substituted or *N*-substituted anilines using metal-catalyzed, radical, and/or asymmetric processes.[14] Furthermore, the ruthenium-catalyzed asymmetric enantioselective hydrogenation of *N*-protected indoles was found to proceed to chiral indolines with high enantiomeric excesses. Recently, *N*-acyl indoline was prepared via unique one-pot cyclization of 2-aminophenethyl alcohol with carboxylic acids in the presence of PPh_3, CCl_4, and NEt_3 without metal.[15] A metal-free approach to the synthesis of indoline was also employed by Correa et al. in 2006.[16] In addition, the Cu-catalyzed C−N bond formation of diaryliodonium salts[17] and the hypervalent iodine reagent[18] by nucleophilic amination have been explored.

Herein, we describe a novel method of constructing the indoline core by metal-free intramolecular nucleophilic ring closing of diaryliodonium salts. Although aryliodonium salts exhibit a strong withdrawing effect at the $C-I^+$ bond,[19] metal-free nucleophilic indoline synthesis from a diaryliodonium salt has not been reported previously. Accordingly, we systematically explored the feasibility of this intramolecular coupling reaction and sought to determine its scope and limitations. Initially, we envisaged that an indoline moiety could be constructed by an intramolecular nucleophilic ring closure from the corresponding diaryliodonium salt without a metal catalyst (Figure 2).

Intramolecular aromatic nucleophilic substitution could proceed via two routes (a or b). The reaction through route a provides the desired indoline product via a 5-membered transition state, whereas route b would result in the acyclic

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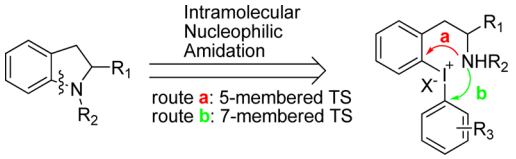


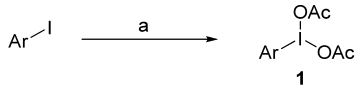
Figure 2. The envisioned synthetic route.

compound via a 7-membered transition state. However, because the 5-membered transition state is preferred, indoline products are expected to be formed exclusively.[20]

RESULTS AND DISCUSSION

Heterodiaryliodonium salts can be prepared in different ways. We chose to adopt a method based on coupling between arylstannanes and (diacetoxy)iodoarenes. To optimize this coupling reaction, diacetoxyiodoarenes with different *para*-substituents, **1a**, **1b**, **1c**, **1d**, and **1e**, were chosen. These were prepared by the oxidative acetoxylation of iodoarenes using sodium periodate in the presence of sodium acetate and acetic anhydride in acetic acid at 120 °C for 2 h (Scheme 1).[21]

Scheme 1. Synthesis of Diacetoxyiodoarene Compounds[a]



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1a: Ar = 4-fluorophenyl (72%)
1b: Ar = 4-chlorophenyl (65%)
1c: Ar = 4-bromophenyl (46%)
1d: Ar = 4-iodoanisolyl (70%)
1e: Ar = 4-toluenyl (75%)

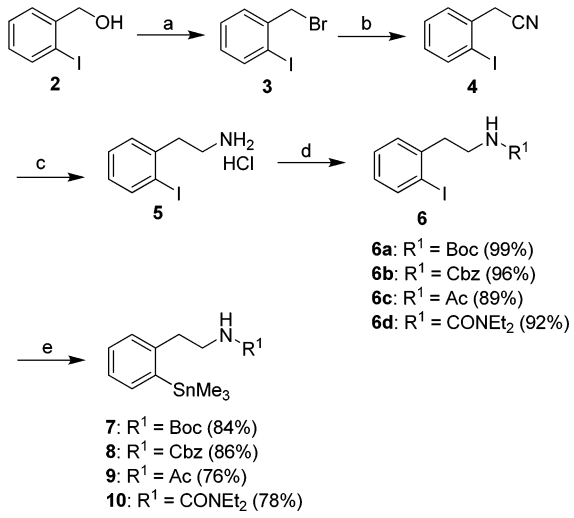
[a](a) $NaIO_4$, NaOAc, glacial AcOH, Ac_2O, 120 °C, 2 h.

The synthesis of the arylstannane intermediates began with the bromination of commercially available 2-iodobenzyl alcohol (**2**) with PBr_3 at 0 °C in THF to afford 2-iodobenzyl bromide (**3**) at a yield of 98% (Scheme 2). Compound **3** was treated with NaCN and heated to reflux for 4 h in ethanol to provide 2-iodobenzyl acetonitrile (**4**) at a yield of 88%. The reduction of compound **4** with BH_3−THF complex followed by acidification with hydrogen chloride afforded 2-iodobenzyl amine hydrochloride (**5**). The amino functionality of **5** was protected with Boc, Cbz, Ac, and $CONEt_2$ to provide 2-iodobenzyl amines **6a**, **6b**, **6c**, and **6d** at yield of 99, 96, 89, and 92%, respectively. Treating compounds **6a**, **6b**, **6c**, and **6d** with Sn_2Me_6 and heating at 120 °C for 1 h in the presence of $Pd(PPh_3)_4$ afforded the desired arylstannanes **7**, **8**, **9**, and **10** at yields of 84, 86, 76, and 78%, respectively.

The formation of diaryliodonium salts (**11**−**14**) from various organostannanes and diacetoxyiodoarenes were compared using the same reaction condition (Table 1).[22] First, diacetoxyiodoarene compounds were then converted to intermediate Koser's reagent derivatives with *p*-TsOH·H_2O, which were coupled with arylstannanes, to afford corresponding diaryliodonium salts (**11a**−**14e**). In short, all conversions proceeded efficiently to provide desired products in reasonable yields (65−75%) regardless of the electronic environments of the *para*-substituents on the diacetoxyiodoarenes and the nature of the arylstannane *N*-protecting group.

To find the optimal nucleophilic ring closing conditions, we chose a series of diaryliodonium salts that consisted of one fixed aryl group (2-(2-*N*-Boc-aminoethyl)phenyl) and one variable counterpart (various *para*-substituted phenyl, **11a**−**11e**) as

Scheme 2. Synthesis of Organostannane Intermediates[a]

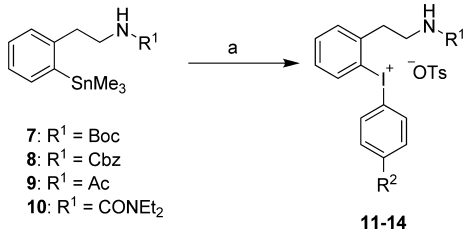


6a: R^1 = Boc (99%)
6b: R^1 = Cbz (96%)
6c: R^1 = Ac (89%)
6d: R^1 = $CONEt_2$ (92%)

7: R^1 = Boc (84%)
8: R^1 = Cbz (86%)
9: R^1 = Ac (76%)
10: R^1 = $CONEt_2$ (78%)

[a](a) PBr_3, THF, 0 °C, 30 min, 98%; (b) NaCN, EtOH, reflux, 4 h, 88%; (c) BH_3−THF, THF, reflux, 1 h, 65%; (d) for **6a**, $(Boc)_2O$, Et_3N, MeOH/THF (1:1), 80 °C, 1 h; for **6b**, Cbz-Cl, Et_3N, MeOH/THF (1:1), rt, 1 h; for **6c**, AcCl, Et_3N, MeOH/THF (1:1), rt, 1 h; for **6d**, diethylcarbamoyl chloride, Et_3N, DMF, rt, 8 h; (e) $Pd(PPh_3)_4$, Sn_2Me_6, toluene, N_2, 120 °C, 1 h.

Table 1. Synthesis of Diaryliodonium Salts (11−14)[a]



7: R^1 = Boc
8: R^1 = Cbz
9: R^1 = Ac
10: R^1 = $CONEt_2$

11-14

entry	SM	R^1	R^2	product	yield (%)[b]
1	**7**	Boc	F	**11a**	70
2	**7**	Boc	Cl	**11b**	72
3	**7**	Boc	Br	**11c**	65
4	**7**	Boc	OCH_3	**11d**	75
5	**7**	Boc	CH_3	**11e**	67
6	**8**	Cbz	F	**12a**	70
7	**8**	Cbz	Cl	**12b**	75
8	**8**	Cbz	Br	**12c**	72
9	**8**	Cbz	OCH_3	**12d**	67
10	**8**	Cbz	CH_3	**12e**	70
11	**9**	Ac	F	**13a**	70
12	**9**	Ac	Cl	**13b**	73
13	**9**	Ac	Br	**13c**	68
14	**9**	Ac	OCH_3	**13d**	72
15	**9**	Ac	CH_3	**13e**	65
16	**10**	$CONEt_2$	F	**14a**	73
17	**10**	$CONEt_2$	Cl	**14b**	69
18	**10**	$CONEt_2$	Br	**14c**	72
19	**10**	$CONEt_2$	OCH_3	**14d**	68
20	**10**	$CONEt_2$	CH_3	**14e**	74

[a](a) (i) **1a**−**e**, *p*-TsOH·H_2O, CH_3CN/CH_2Cl_2, rt, N_2, 1 h; (ii) **7**−**10**, CH_2Cl_2, rt, 24 h [b]All reactions were carried out on a 0.5 mmol scale of precursor.

model precursors for the *N*-Boc-indoline **15** (Table 2). First, compound **11a** was subjected to various reaction conditions to

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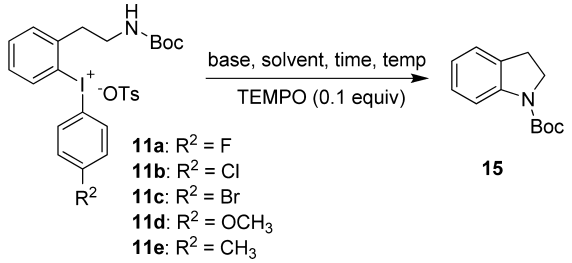
Table 2. Optimization of Reaction Conditions for the Synthesis of Indoline from Diaryliodonium Salts[a]



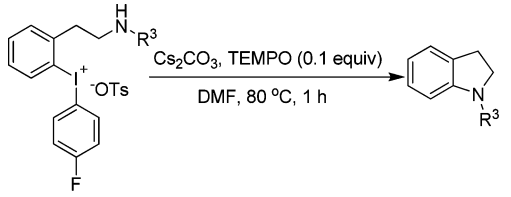
entry	SM	conditions	time (h)	temp (°C)	yield (%)[b]
1	**11a**	Cs_2CO_3, DMF	0.5	rt	56
2	**11a**	Cs_2CO_3, DMF	0.5	80	73
3	**11a**	Cs_2CO_3, DMF	3	rt	62
4	**11a**	Cs_2CO_3, DMF	1	80	84
5	**11a**	Cs_2CO_3, DMF	1	80	30[c]
6	**11a**	Cs_2CO_3, DMF	24	rt	65
7	**11a**	Cs_2CO_3, DMF	24	80	84
8	**11a**	Cs_2CO_3, DMF/H_2O	24	rt	25[d]
9	**11a**	Cs_2CO_3, TFE	24	80	23[d]
10	**11a**	Cs_2CO_3, CH_3CN	24	80	73
11	**11a**	K_2CO_3, DMF	3	80	62
12	**11a**	Na_2CO_3, DMF	3	80	67
13	**11a**	DBU, DMF	3	80	42
14	**11b**	Cs_2CO_3, DMF	1	80	80
15	**11c**	Cs_2CO_3, DMF	1	80	76
16	**11d**	Cs_2CO_3, DMF	1	80	72
17	**11e**	Cs_2CO_3, DMF	1	80	74

[a]Reactions were carried out using 0.5 mmol scale of precursor with 3.0 equiv of base in 1.0 mL of solvent in the presence of 0.1 equiv of TEMPO. [b]Isolated yields. [c]Reaction carried out without TEMPO. [d]Determined by NMR yield.

produce **15** (Table 2, entries 1−13). Since the free radical decomposition of iodonium salts is known to inhibit the reaction, TEMPO was added as a radical scavenger.[23] Initially, compound **11a** was treated with 3.0 equiv of Cs_2CO_3 and 0.1 equiv of TEMPO in DMF at rt and stirred for 30 min to afford **15** in a yield of 56% (Table 2, entry 1). When the reaction time was extended to 3 h, the yield was increased to 62% (Table 2, entry 3), but prolonged reaction did not have much beneficial effect (24 h, 65%; Table 2, entry 6). When the reaction was performed at a higher temperature (80 °C for 30 min), **15** was obtained at a yield of 73% (Table 2, entry 2), and when the reaction time was extended to 1 h, the yield increased (84%; Table 2, entry 4). However, longer reaction times did not improve yields (24 h, 84%; Table 2, entry 7). To enhance the solubilities of diaryliodonium salts, water was added as a cosolvent, but running the reaction in a 50% aqueous DMF system resulted in a poor yield (25%; Table 2, entry 8) and the presence of unreacted **11a**. Other solvents, that is, 2,2,2-trifluoroethanol and CH_3CN (Table 2, entries 9 and 10), and other bases, K_2CO_3, Na_2CO_3, and DBU, were also examined (Table 2, entries 11−13), but yields were not improved. Other diaryliodonium salts, **11b**, **11c**, **11d**, and **11e**, were also reacted under the optimal conditions (80 °C, 1 h) to produce **15** in yields of 80, 76, 72, and 74%, respectively (Table 2, entries 14−16). When the reaction was run without TEMPO, desired product **15** was formed much less (30%), and some unreacted starting material **11a** remained (Table 2, entry 5).

The optimal conditions used to form **15** from **11a** were extended to diaryliodonium salts with different *N*-protecting groups, such as **12a**, **13a**, and **14a**, and afforded the corresponding *N*-protected indoline **16**, **17**, and **18** in yields of roughly 70% (Table 3). Diaryliodonium salts with a carbamate

Table 3. Synthesis of Indoline from Diaryliodonium Salts with Different *N*-Protecting Groups



11a-14a **15-18**

entry	R^3	SM	product	yield (%)
1	Boc	**11a**	**15**	84
2	Cbz	**12a**	**16**	80
3	Ac	**13a**	**17**	72
4	$CONEt_2$	**14a**	**18**	70

protecting group (Table 3, entries 1 and 2) afforded yields similar to **11a**, but salts with acetyl or urea protecting group provided lower yields (Table 3, entries 3 and 4).

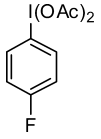
CONCLUSION

We described a simple and effective means of synthesizing the indoline moiety from diaryliodonium salts. In particular, *N*-Boc-indoline (**15**) was obtained in 84% yield from (2-*N*-Boc-aminoethylphenyl)(4-fluorophenyl)iodonium *p*-toluenesulfonate (**11a**) in the presence of 0.1 equiv of TEMPO and 3.0 equiv of Cs_2CO_3 at 80 °C in DMF for 1 h. Other *N*-protected indolines **16**, **17**, and **18** were synthesized under optimized conditions at yields of 80, 72 and 70%, respectively.

EXPERIMENTAL SECTION

General Procedure for Preparing Diacetoxyiodoarenes from Iodoarene.[21] A stirred suspension of $NaIO_4$ (2.20 g, 10.3 mmol) and AcONa (1.80 g, 22.0 mmol) in glacial AcOH (15 mL) and Ac_2O (1.5 mL) at rt was treated with the appropriate iodoarene (10.0 mmol). The reaction mixture was refluxed for the designated period. The reaction mixture was then poured into water (50 mL). The resulting mixture was filtered, and the residue was washed with 10% aq AcOH (2 × 10 mL) and dried under a stream of air. The remaining product was extracted from the filtrate with DCM and concentrated on rotary evaporator. Hexane was added to the obtained residue to collect the solid product. The product was filtered and washed with excess of hexane to provide corresponding iodoarene.

1-Diacetoxyiodo-4-fluorobenzene (1a).



White solid (2.38 g, 70%): mp 179−181 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 6 H), 7.14−7.25 (m, 2 H), 8.05−8.08 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 115.5, 118.5 (d, J = 22.7 Hz), 137.5 (d, J = 9.1 Hz), 164.3 (d, J = 252.4 Hz), 176.4. CAS registry number: 16308−15−9.

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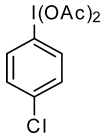
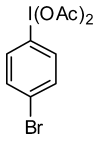
1-Diacetoxyiodo-4-chlorobenzene (1b).



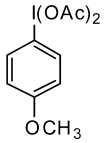
White solid (2.31 g, 65%): mp 112−115 °C (lit.[24] 109.8−113.2 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 6 H), 7.44 (d, J = 8.4 Hz, 2 H), 8.00 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 118.8, 131.2, 136.3, 138.4, 176.4. CAS registry number: 6973−73−5.

1-Diacetoxyiodo-4-bromobenzene (1c).



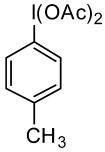
White solid (2.00 g, 50%): mp 120−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 6 H), 7.59 (d, J = 8.4 Hz, 2 H), 7.92 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2 119.6, 126.7, 134.1, 136.4, 176.4. CAS registry number: 41018−52−4.

4-Diacetoxyiodoanisole (1d).[25]



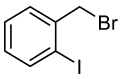
White solid (2.56 g, 73%): mp 93−96 °C (lit.[24] 92.4−96.0 °C; lit.°C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.98 (s, 6H), 3.84 (s, 3H), 6.95 (d, J = 9.2 Hz, 2H), 8.00 (d, J = 9.2 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.6, 29.5, 104.2, 127.9, 137.3, 141.7, 175.9. CAS registry number: 16308−14−8.

1-Diacetoxyiodo-4-methylbenzene (1e).



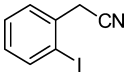
White solid (2.65 g, 79%): mp 108−110 °C (lit.[24] 106−110 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 6 H), 2.43 (s, 3H), 7.28 (d, J = 8.4 Hz, 2 H), 7.96 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.5, 21.7, 118.5, 131.9, 135.1, 142.8, 176.5. CAS registry number: 16308−16−0.

2-Iodobenzyl Bromide (3).



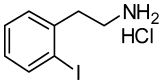
A stirred sample of commercially available 2-iodobenzyl alcohol **2** (5.00 g, 21.4 mmol) in THF (25 mL) at 0 °C under Ar was treated with PBr_3 (1.2 mL, 12.8 mmol). The reaction mixture was stirred at 0 °C for 30 min and concentrated under reduced pressure to provide the crude product. Flash column chromatography (SiO_2, 30% EtOAc/hexanes) afforded **3** (6.50 g, 98%) as a yellow solid: mp 56−60 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.60 (s, 2H), 6.93−7.02 (m, 1H), 7.26−7.37 (m, 1H), 7.47 (dd, J = 7.8, 1.8 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 38.7, 100.0, 128.8, 130.0, 130.4, 140.0, 140.2; MS ESI(GC) m/z 298 (M^+), 296 (M^+), 217 (100). Anal. Calcd for C_7H_6BrI: C, 28.31; H, 2.04. Found: C, 28.35; H, 1.84.

2-Iodobenzyl Cyanide (4).



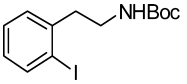
A sample of **3** (4.35 g, 14.7 mmol) in EtOH (40 mL) was treated with NaCN (2.16 g, 44.0 mmol) and refluxed for 4 h. After removal of organic solvent under reduced pressure, water (40 mL) was added to the residue. The resulting mixture was extracted with EtOAc (40 mL × 3), and the combined organic extracts were washed with saturated aq NaCl, dried (Na_2SO_4), and concentrated under reduced pressure. Flash column chromatography (SiO_2, 20% EtOAc/hexanes) provided **4** (4.00 g, 88%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 2H), 7.01−7.06 (m, 1H), 7.37−7.41 (m, 1H), 7.51−7.54 (m, 1H), 7.85 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.9, 99.0, 117.1, 128.99, 129.04, 129.8, 133.2, 139.8; MS ESI(GC) m/z 243 (M^+, 100). Anal. Calcd. For C_8H_6IN: C, 39.53; H, 2.49; N, 5.76. Found: C, 39.58; H, 2.48; N, 5.88.

2-(2-Iodophenyl)ethylamine Hydrochloride (5).



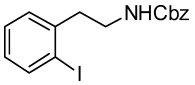
A stirred solution of **4** (3.04 g, 12.5 mmol) in anhydrous THF (12 mL) under Ar was treated with a solution of BH_3 in THF (1.0 M, 30 mL). The reaction mixture was refluxed for 1 h and then concentrated under reduced pressure. The residue was treated with ice-cold solution of HCl in CH_3OH (1.0 N, 20 mL), allowed to stand at 0 °C for 2 h, and filtered. The residue was washed with MeOH and dried under reduced pressure to afford the HCl salt **5** (2.30 g, 65%) as a white solid: mp 262−264 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.98−3.38 (m, 4H), 6.99−7.40 (m, 1H), 7.34−7.38 (m, 2H), 7.85 (d, J = 7.6 Hz, 1H), 8.35 (br s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 38.1, 39.0, 101.2, 129.3, 129.5, 130.4, 139.8, 140.5; MS ESI m/z 284 (M^+), 231 (100). Anal. Calcd. For $C_8H_{11}ClIN$: C, 33.89; H, 3.91; N, 4.94. Found: C, 33.83; H, 3.92; N, 4.99.

***t*-Butyl 2-Iodophenethylcarbamate (6a).**



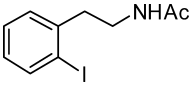
A stirred solution of **5** (1.00 g, 3.5 mmol) in 1:1 MeOH−THF (10 mL) was treated with Boc_2O (0.8 mL, 3.9 mmol) and Et_3N (0.7 mL, 5.3 mmol). The reaction mixture was refluxed for 1 h and then concentrated under reduced pressure. The residue was dissolved in EtOAc (100 mL), washed with water and saturated aq NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. Flash column chromatography (SiO_2, 30% EtOAc/hexanes) provided **6a** (1.3 g, 99%) as a white solid: mp 73−76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 9H), 2.91 (t, J = 7.2 Hz, 2H), 3.34−3.36 (m, 2H), 4.59 (s, 1H), 6.87−6.92 (m, 1H), 7.18−7.28 (m, 2H), 7.79 (d, J = 8.0 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.4, 40.4, 40.8, 79.2, 100.6, 128.2, 128.4, 130.1, 139.5, 141.6, 155.8; MS ESI m/z 370 ([M + Na]$^+$, 100). Anal. Calcd. For $C_{13}H_{18}INO_2$: C, 44.97; H, 5.23; N, 4.03. Found: C, 44.96; H, 5.14; N, 4.15.

Benzyl 2-(2-Iodophenyl)ethylcarbamate (6b).



A stirred solution of **5** (1.00 g, 3.5 mmol) in 1:1 MeOH−THF (10 mL) was treated with Cbz−Cl (0.6 mL, 3.8 mmol) and Et_3N (0.7 mL, 5.3 mmol). The reaction mixture was stirred at rt for 1 h and then concentrated under reduced pressure. The residue was dissolved in EtOAc (100 mL), washed with water and saturated aq NaCl, dried (Na_2SO_4), and concentrated under reduced pressure. Flash column chromatography (SiO_2, 30% EtOAc/hexanes) provided **6b** (1.28 g, 96%) as a white solid: mp 75−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.86 (t, J = 6.9 Hz, 2H), 3.33−3.39 (m, 2H), 4.74 (s, 1H), 5.01 (s, 2H), 6.81 (t, J = 7.4 Hz, 1H), 7.08−7.26 (m, 7H), 7.72 (d, J = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.8, 41.1, 66.8, 100.7, 128.23, 128.24, 128.51, 128.59, 128.62, 130.2, 136.7, 139.8, 141.5, 156.4; MS ESI m/z 404 ([M + Na]$^+$, 100). Anal. Calcd. For $C_{16}H_{16}INO_2$: C, 50.41; H, 4.23; N, 3.67. Found: C, 50.48; H, 4.18; N, 3.79.

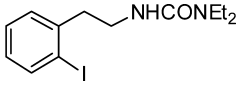
***N*-[2-(2-Iodophenyl)]ethylacetamide (6c).**



A stirred solution of **5** (1.00 g, 3.5 mmol) in THF (10 mL) was treated with acetyl chloride (0.3 mL, 3.8 mmol) and Et_3N (0.7 mL, 5.3 mmol). The reaction mixture was stirred at rt for 1 h and concentrated under reduced pressure. The residue was dissolved in EtOAc (100 mL), washed with water and saturated aqueous NaCl, dried (Na_2SO_4), and concentrated under reduced pressure. Flash column chromatography

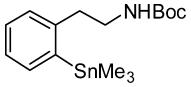
(SiO_2, 30% EtOAc/hexanes) provided **6c** (0.9 g, 89%) as a white solid: mp 71−74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (s, 3H), 2.92 (t, J = 6.8 Hz, 2H), 3.44−3.50 (m, 2H), 5.56 (s, 1H), 6.87−6.91 (m, 1H), 7.12−7.28 (m, 2H), 7.78−7.81 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.5, 39.7, 40.3, 100.8, 128.5, 128.6, 130.1 139.7, 141.7, 170.3; MS ESI m/z 312 ([M + Na]$^+$, 100). Anal. Calcd. For $C_{10}H_{12}INO$: C, 41.54; H, 4.18; N, 4.84. Found: C, 41.54; H, 4.17; N, 4.88.

1,1-Diethyl-3-[2-(2-iodophenyl)]ethylurea (6d).



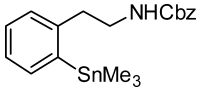
A stirred solution of **5** (1.00 g, 3.5 mmol) in DMF (10 mL) was treated with diethylcarbamoyl chloride (0.5 mL, 3.9 mmol) and Et_3N (0.7 mL, 5.3 mmol). The reaction mixture was stirred at rt for 8 h and diluted with EtOAc (100 mL). Resulting mixture was washed with water (20 mL × 3) and saturated aq NaCl, dried (Na_2SO_4), and concentrated under reduced pressure. Flash column chromatography (SiO_2, 50% EtOAc/hexanes) provided **6d** (1.11 g, 92%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, J = 1.6 Hz, 6H), 2.90−3.03 (m, 2H), 3.17−3.27 (m, 4H), 3.48−3.54 (m, 2H), 4.37 (s, 1H), 6.91−6.95 (m, 1H), 7.24−7.30 (m, 2H), 7.84 (d, J = 3.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 40.90, 40.92, 41.3, 100.8, 128.3, 128.5, 130.4, 139.6, 142.4, 157.3; MS ESI m/z 369 ([M + Na]$^+$, 100). Anal. Calcd. For $C_{13}H_{19}IN_2O$: C, 45.10; H, 5.53; N, 8.09. Found: C, 45.12; H, 5.54; N, 8.04.

Typical Procedure for the Preparation of Aryl Stannane (7−10).[25] *t*-Butyl 2-[2-(Trimethylstannyl)phenyl]ethylcarbamate (7).



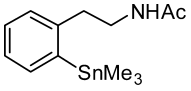
A solution of *N*-(*t*-butoxycarbonyl)-2-(2-iodophenyl)ethyl amine **6a** (770 mg, 2.21 mmol) in anhydrous toluene (12 mL) at rt under N_2 was treated with tetrakis(triphenylphospine)palladium(0) (229 mg, 0.31 mmol) and hexamethylditin (0.9 mL, 2.80 mmol). The reaction mixture was warmed at 120 °C for 1 h, cooled to rt, and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and subjected to flash column chromatography (SiO_2, 10% EtOAc/hexanes) to afford **7** (715 mg, 84%) as a white solid: mp 77−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.33 (s, 9H), 1.45 (s, 9H), 2.82 (t, J = 3.4 Hz, 2H), 3.38−3.39 (m, 2H), 4.55 (s, 1H), 7.19−7.32 (m, 3H), 7.44 (d, J = 7.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −8.15, 28.4, 39.1, 42.1,79.2, 125.9, 128.4, 128.8, 136.4, 142.4, 145.5, 155.7; MS ESI m/z 385 [M + H]$^+$, 249 (100). Anal. Calcd. For $C_{16}H_{27}NO_2Sn$: C, 50.03; H, 7.09; N, 3.65. Found: C, 50.03; H, 7.09; N, 3.65.

Benzyl 2-(Trimethylstannyl)phenylethylcarbamate (8).



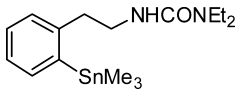
White solid, 726 mg, 86%: mp 73−76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.28 (s, 9H), 2.81 (t, J = 7.2 Hz, 2H), 3.39−3.44 (m, 2H), 4.7 (s, 1H), 5.06 (s, 2H), 7.14−7.32 (br m, 8H), 7.39 (d, J = 7.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −8.0, 39.1, 42.7, 66.9, 126.2, 128.3, 128.3, 128.6, 128.7, 129.0, 136.65, 136.71, 142.6, 145.3, 156.4; MS ESI m/z 442 ([M + Na]$^+$, 100). Anal. Calcd. For $C_{19}H_{25}NO_2Sn$: C, 54.58; H, 6.03; N, 3.35. Found: C, 54.55; H, 6.06; N, 3.34.

2-(Trimethylstannylphenyl)ethylacetamide (9).



White solid, 660 mg, 76%: mp 74−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.34 (s, 9H), 1.97 (s, 3H), 2.85 (t, J = 7.0 Hz, 2H), 3.49−3.54 (m, 2H), 5.56 (s, 1H), 7.21−7.34 (m, 3H), 7.46 (d, J = 7.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.0, 23.5, 38.6, 41.1, 126.2, 128.5, 129.0, 136.7, 142.6, 145.5, 170.1; MS ESI m/z 350 ([M + Na]$^+$, 100). Anal. Calcd. For $C_{13}H_{21}NOSn$: C, 47.89; H, 6.49; N, 4.30. Found: C, 47.90; H, 6.35; N, 4.23.

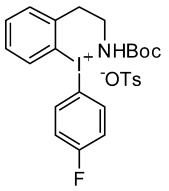
1,1-Diethyl-3-[2-(2-trimethylstannylphenyl)]ethylurea (10).



White solid, 664 mg, 78%: mp 81−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.31 (s, 9H), 1.08 (t, J = 2.8 Hz, 6H), 2.86 (t, J = 2.8 Hz, 2H), 3.21 (q, J = 2.8 Hz, 4H), 3.46−3.51 (m, 2H), 4.23 (s, 1H), 7.19−7.30 (br m, 3H), 7.45 (d, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −8.0, 13.9, 39.2, 41.3, 42.3, 126.0, 128.7, 128.8, 136.7, 142.6, 146.1, 157.2; MS ESI m/z 407 [M + Na]$^+$, 369 (100). Anal. Calcd. For $C_{16}H_{28}N_2OSn$: C, 50.16; H, 7.37; N, 7.31. Found: C, 50.10; H, 7.45; N, 7.47.

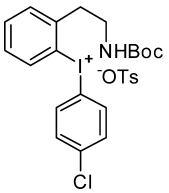
General Procedure for the Synthesis of Diaryl Iodonium Salts (11−14). A sample of diacetoxyiodoarene (0.5 mmol) in CH_2Cl_2 (1.0 mL) at rt under N_2 was treated with a solution of *p*-TsOH·H_2O (0.5 mmol) in CH_3CN (1.0 mL). The reaction mixture was stirred for 1 h and then treated with a solution of aryl stannane (**7**, **8**, **9**, or **10**) (0.5 mmol) in CH_2Cl_2 (1.0 mL). The reaction mixture was stirred for 24 h and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 10% MeOH/CH_2Cl_2) to provide corresponding salt that contained trace amount of tin impurity. To remove inorganic impurities, the salt was treated with Et_2O (20 mL), sonicated for 10 min, and filtered through a paper filter. The residue was dried under reduced pressure to afford pure salt as a white solid.

(2-(2-(*t*-Butoxycarbonylamino)ethyl)phenyl)(4-fluorophenyl)-iodonium *p*-Toluenesulfonate (11a).



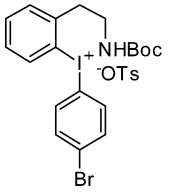
White solid (215 mg, 70%): mp 158−160 °C; ^{1}H NMR (400 MHz, CD_3OD-d_4) δ 1.42 (s, 9H), 2.36 (s, 3H), 3.07−3.10 (m, 2H), 3.29−3.31 (m, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.28−7.30 (m, 2H), 7.31−7.40 (m, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.63−7.65 (m, 1H), 7.69 (d, J = 8.0 Hz, 2H), 8.21−8.24 (m, 2H), 8.31 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3, 28.7, 40.2, 42.0, 80.3, 109.6, 120.5 (d, J = 23.4 Hz), 121.3, 127.0, 129.8, 131.5, 133.2, 134.6, 138.9, 139.0 (d, J = 8.6 Hz), 141.7, 143.2, 143.5, 158.5, 166.3 (d, J = 252.6 Hz); MS ESI m/z 442 (M$^+$), 164 (100). Anal. Calcd. For $C_{26}H_{29}FINO_5S$: C, 50.90; H, 4.76; N, 2.28; S, 5.23. Found: C, 50.88; H, 4.72; N, 2.39; S, 5.14.

(2-(2-(*t*-Butoxycarbonylaminoethyl)phenyl)(4-chlorophenyl)-iodonium *p*-Toluenesulfonate (11b).



White solid (226 mg, 72%): mp 163−165 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.39 (s, 9H), 2.28 (s, 3H), 2.97−3.01 (m, 2H), 3.13−3.18 (m, 2H), 7.10−7.15 (m, 3H), 7.35 (t, J = 7.2 Hz, 1H), 7.46 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 7.6 Hz, 1H), 7.58−7.64 (m, 3H), 8.22 (d, J = 8.8 Hz, 2H), 8.44 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.3, 23.4, 28.7, 41.2, 78.4, 114.5, 122.1, 126.0, 128.5, 130.5, 131.8, 132.2, 133.5, 137.2, 137.8, 138.1, 142.0, 146.2, 156.2, 175.0; MS ESI m/z 458 (M$^+$), 164 (100). Anal. Calcd. For $C_{26}H_{29}ClINO_5S$: C, 49.57; H, 4.64; N, 2.22; S, 5.09. Found: C, 49.47; H, 4.53; N, 2.25; S, 5.12.

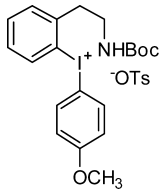
(2-(2-(*t*-Butoxycarbonylamino)ethyl)phenyl)(4-bromophenyl)-iodonium *p*-Toluenesulfonate (11c).



dx.doi.org/10.1021/jo300874m | J. Org. Chem. 2012, 77, 5705−5713

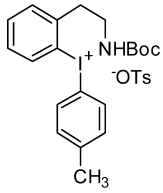
White solid (219 mg, 65%): mp 162−164 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.39 (s, 9H), 2.28 (s, 3H), 2.97−3.01 (m, 2H), 3.13−3.16 (m, 2H), 7.10−7.12 (m, 3H), 7.35−7.39 (m, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.51−7.53 (m, 1H), 7.64 (t, J = 7.2 Hz, 3H), 8.15 (d, J = 8.8 Hz, 2H), 8.44 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.3, 23.4, 28.7, 41.2, 78.4, 115.2, 122.0, 126.0, 126.6, 128.5, 130.5, 131.8, 133.5, 135.1, 137.3, 138.1, 142.0, 146.2, 156.2, 174.9; MS ESI, m/z 504 (M^+), 502 (M^+), 164 (100). Anal. Calcd. For $C_{26}H_{29}BrINO_5S$: C, 46.31; H, 4.33; N, 2.08; S, 4.75. Found: C, 46.38; H, 4.53; N, 2.01; S, 4.77.

(2-(2-(*t*-Butoxycarbonylamino)ethyl)phenyl)(4-methoxyphenyl)-iodonium *p*-Toluenesulfonate (11d).



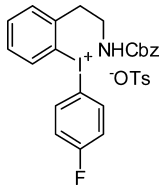
White solid (234 mg, 75%): mp 162−165 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.41 (s, 9H), 2.28 (s, 3H), 2.98−3.02 (m, 2H), 3.14−3.17 (m, 2H), 3.78 (s, 3H), 7.05 (d, J = 8.8 Hz, 2H), 7.10 (d, J = 7.6 Hz, 2H), 7.13−7.19 (m, 1H), 7.34 (t, J = 8.8 Hz, 1H), 7.46−7.51 (m, 3H), 7.60 (t, J = 7.2 Hz, 1H), 8.18 (d, J = 8.8 Hz, 2H), 8.41 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 20.8, 28.3, 38.4, 40.8, 55.7, 78.0, 105.1, 117.5, 121.9, 125.5, 128.0, 129.9, 131.1, 132.8, 136.1, 137.3, 137.6, 141.2, 145.8, 155.7, 161.9; MS ESI m/z 454 (M^+), 164 (100). Anal. Calcd. For $C_{27}H_{32}INO_6S$: C, 51.84; H, 5.16; N, 2.24; S, 5.13. Found: C, 51.92; H, 5.01; N, 2.00; S, 5.11.

(2-(2-(*t*-Butoxycarbonylamino)ethyl)phenyl)(*p*-tolyl)iodonium *p*-Toluenesulfonate (11e).



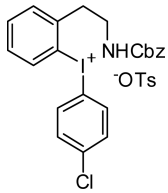
White solid (204 mg, 67%): mp 163−166 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.41 (s, 9H), 2.28 (s, 3H), 2.32 (s, 3H), 2.98−3.01 (m, 2H), 3.16−3.17 (m, 2H), 7.11(d, J = 7.6 Hz, 2H), 7.12−7.19 (m, 1H), 7.30−7.35 (m, 2H), 7.46−7.63 (br m, 5H), 8.11 (d, J = 8.0 Hz, 2H), 8.42 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 20.80, 20.82, 28.3, 38.5, 40.8, 77.9, 112.6, 121.5, 125.5, 128.1, 128.8, 129.9, 131.1, 131.4, 132.4, 132.8, 135.0, 137.5, 141.4, 142.5, 155.7; MS ESI m/z 438 (M^+), 164 (100). Anal. Calcd. For $C_{27}H_{32}INO_5S$: C, 53.20; H, 5.29; N, 2.30; S, 5.26. Found: C, 53.28; H, 5.38; N, 2.15; S, 5.29.

(2-(2-(Benzyloxycarbonylamino)ethyl)phenyl)(4-fluorophenyl)-iodonium *p*-Toluenesulfonate (12a).



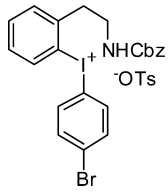
White solid (226 mg, 70%): mp 78−81 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 2.37 (s, 3H), 3.08−3.13 (m, 2H), 3.33−3.38 (m, 2H), 5.08 (s, 2H), 7.22−7.24 (m, 4H), 7.29−7.40 (m, 6H), 7.53−7.65 (m, 4H), 7.69 (d, J = 7.6 Hz, 2H), 8.18−8.26 (m, 2H), 8.32 (d, J = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 20.1, 38.8, 41.3, 66.3, 108.3, 119.4 (d, J = 23.7 Hz), 120.2, 125.8, 127.7, 127.9, 128.4, 128.7, 130.4, 131.9, 133.5, 137.2, 137.8, 137.9 (d, J = 9.1 Hz), 140.5, 141.9, 142.3, 157.7, 165.2 (d, J = 252.1 Hz); MS ESI m/z 476 (M^+), 91 (100). Anal. Calcd. For $C_{29}H_{27}FINO_5S$: C, 53.79; H, 4.20; N, 2.16; S, 4.95. Found: C, 53.82; H, 4.27; N, 2.11; S, 5.00.

(2-(2-(Benzyloxycarbonylamino)ethyl)phenyl)(4-chlorophenyl)-iodonium *p*-Toluenesulfonate (12b).



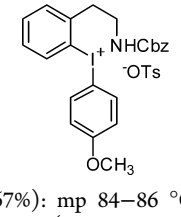
White solid (248 mg, 75%): mp 84−86 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 2.36 (s, 3H), 3.10 (t, J = 6.8 Hz, 2H), 3.34−3.36 (m, 2H), 5.07 (s, 2H), 7.20 (d, J = 7.6 Hz, 2H), 7.23−7.39 (m, 7H), 7.45 (d, J = 7.2 Hz, 2H), 7.54−7.69 (m, 4H), 8.11 (d, J = 7.2 Hz, 2H), 8.29 (d, J = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3, 40.0, 42.4, 67.5, 113.1, 121.2, 126.9, 128.8, 129.0, 129.5, 129.8, 131.6, 133.1, 133.2, 134.7, 137.7, 138.3, 139.0, 140.2, 141.7, 143.1, 143.5, 158.9; MS ESI m/z 492 (M^+), 91 (100). Anal. Calcd. For $C_{29}H_{27}ClINO_5S$: C, 52.46; H, 4.10; N, 2.11; S, 4.83. Found: C, 52.52; H, 4.36; N, 2.10; S, 4.79.

(2-(2-(Benzyloxycarbonylamino)ethyl)phenyl)(4-bromophenyl)-iodonium *p*-Toluenesulfonate (12c).



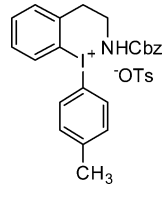
White solid (254 mg, 72%): mp 88−91 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 2.36 (s, 3H), 3.08−3.12 (m, 2H), 3.34−3.36 (m, 2H), 5.07 (s, 2H), 7.21 (d, J = 7.2 Hz, 2H), 7.33−7.38 (m, 6H), 7.55−7.72 (m, 6H) 8.02−8.04 (m, 2H), 8.29 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3, 40.0, 42.4, 67.5, 113.9, 121.1, 126.9, 128.5, 128.8, 129.1, 129.5, 129.8, 131.6, 133.1, 134.7, 136.2, 137.8, 138.3, 139.0, 141.7, 143.2, 143.5, 158.9; MS ESI m/z 538 (M^+), 536 (100). Anal. Calcd. For $C_{29}H_{27}BrINO_5S$: C, 49.17; H, 3.84; N, 1.98; S, 4.53. Found: C, 49.20; H, 3.98; N, 1.90; S, 4.76.

(2-(2-(Benzyloxycarbonylamino)ethyl)phenyl)(4-methoxyphenyl)-iodonium *p*-Toluenesulfonate (12d).



White solid (221 mg, 67%): mp 84−86 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 2.35 (s, 3H), 3.11 (t, J = 7.4 Hz, 2H), 3.35−3.39 (m, 2H), 3.81 (s, 3H), 5.08 (s, 2H), 6.99 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.28−7.39 (m, 6H), 7.50−7.55 (m, 1H), 7.56−7.62 (m, 1H), 7.69 (d, J = 7.6 Hz, 2H), 8.07 (d, J = 8.0 Hz, 2H), 8.24 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3, 39.9, 42.5, 56.3, 67.5, 104.2, 106.2, 118.8, 121.4, 127.0, 128.8, 129.0, 129.5, 129.8, 131.4, 132.9, 134.4, 138.3, 138.6, 141.8, 142.8, 143.4, 157.9, 164.4; MS ESI m/z 488 (M^+), 91 (100). Anal. Calcd. For $C_{30}H_{30}INO_6S$: C, 54.63; H, 4.58; N, 2.12; S, 4.86. Found: C, 54.53; H, 4.91; N, 1.92; S, 4.95.

(2-(2-(Benzyloxycarbonylamino)ethyl)phenyl)(*p*-tolyl)-iodonium *p*-Toluenesulfonate (12e).

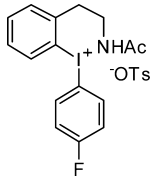


White solid (225 mg, 70%): mp 81−83 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 2.36 (s, 3H), 2.37 (s, 3H), 3.09−3.13 (m, 2H), 3.34−3.38

dx.doi.org/10.1021/jo300874m | J. Org. Chem. 2012, 77, 5705−5713

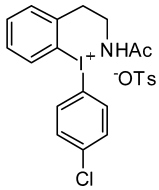
(m, 2H), 5.08 (s, 2H), 7.21 (d, J = 7.2 Hz, 2H), 7.29−7.33 (m, 8H), 7.51−7.54 (m, 1H), 7.56−7.61 (m, 1H), 7.69 (d, J = 7.6 Hz, 2H), 8.01 (d, J = 6.8 Hz, 2H), 8.25 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3 (2 CH_3−C), 40.0, 42.4, 67.5, 112.0, 121.0, 127.0, 128.8, 129.0, 129.5, 129.8, 131.4, 133.0, 133.9, 134.5, 136.2, 138.4, 138.8, 141.6, 143.0, 143.5, 145.0, 158.9; MS ESI m/z 472 (M^+), 91 (100). Anal. Calcd. For $C_{30}H_{30}INO_5S$: C, 55.99; H, 4.70; N, 2.18; S, 4.98. Found: C, 55.98; H, 4.89; N, 2.19; S, 4.97.

(2-(2-Acetamidoethyl)phenyl)(4-fluorophenyl)iodonium *p*-Toluenesulfonate (13a).



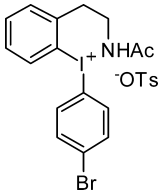
Pale yellow solid (194 mg, 70%): mp 170−173 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.94 (s, 3H), 2.37 (s, 3H), 3.12 (t, J = 7.6 Hz, 2H), 3.38−3.42 (m, 2H), 7.21−7.31 (m, 4H), 7.34−7.40 (m, 1H), 7.56−7.58 (m, 1H), 7.64 (d, 1H, J = 7.6 Hz), 7.69 (d, J = 6.8 Hz, 2H), 8.23−8.27 (m, 2H), 8.35 (d, J = 1.2 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3, 22.6, 39.5, 41.1, 109.5, 120.5 (d, J = 23.8 Hz), 121.4, 127.0, 129.8, 131.6, 133.0, 134.7, 139.0, 139.1 (d, J = 7.5 Hz), 141.8, 143.0, 143.4, 166.3 (d, J = 251.3 Hz), 173.7; MS ESI m/z 384 (M^+, 100). Anal. Calcd. For $C_{23}H_{23}FINO_4S$: C, 49.74; H, 4.17; N, 2.52; S, 5.77. Found: C, 49.67; H, 4.05; N, 2.47; S, 5.77.

(2-(2-Acetamidoethyl)phenyl)(4-chlorophenyl)iodonium *p*-Toluenesulfonate (13b).



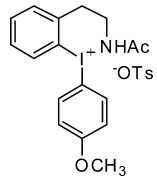
White solid (208 mg, 73%): mp 172−174 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.93 (s, 3H), 2.37 (s, 3H), 3.10−3.13 (m, 2H), 3.38−3.42 (m, 2H), 7.22 (d, J = 7.2 Hz, 2H), 7.24−7.37 (m, 1H), 7.51−7.54 (m, 2H), 7.57−7.59 (m, 1H), 7.64−7.70 (m, 3H), 8.14−8.17 (m, 2H), 8.34 (dd, J = 8.0, 1.2 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3, 22.6, 39.6, 41.1, 113.2, 121.3, 127.0, 129.8, 131.6, 133.0, 133.3, 134.7, 137.8, 139.1, 140.3, 141.7, 143.1, 143.4, 173.7; MS ESI m/z 400 (M^+), 399 (100). Anal. Calcd. For $C_{23}H_{23}ClINO_4S$: C, 48.31; H, 4.05; N, 2.45; S, 5.61. Found: C, 48.32; H, 3.85; N, 2.46; S, 5.66.

(2-(2-Acetamidoethyl)phenyl)(4-bromophenyl)iodonium *p*-Toluenesulfonate (13c).



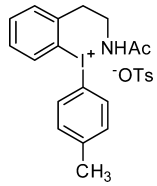
Pale yellow solid (209 mg, 68%): mp 178−181 °C (decomposed); ^{1}H NMR (400 MHz, CD_3OD) δ 1.93 (s, 3H), 2.37 (s, 3H), 3.11−3.13 (m, 2H), 3.38−3.40 (m, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.36−7.41 (m, 1H), 7.56−7.61 (m, 1H), 7.68−7.70 (m, 5H), 8.08 (d, J = 8.4 Hz, 2H), 8.34 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3, 22.6, 39.6, 41.1, 113.2, 121.3, 127.0, 129.8, 131.6, 133.0, 133.3, 134.8, 137.8, 139.1, 140.3, 141.7, 143.1, 143.4, 173.7; MS ESI m/z 446 (M^+), 444 (M^+), 162 (100). Anal. Calcxd. For $C_{23}H_{23}BrINO_4S$: C, 44.82; H, 3.76; N, 2.27; S, 5.20. Found: C, 44.75; H, 3.90; N, 2.39; S, 5.21.

(2-(2-Acetamidoethyl)phenyl)(4-methoxyphenyl)iodonium *p*-Toluenesulfonate (13d).



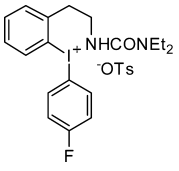
White solid (204 mg, 72%): mp 176−178 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.95 (s, 3H), 2.37 (s, 3H), 3.12−3.15 (m, 2H), 3.40−3.43 (m, 2H), 3.84 (s, 3H), 7.05 (d, J = 9.2 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.32−7.39 (m, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.61−7.66 (m, 1H), 7.70 (d, J = 8.0 Hz, 2H), 8.10 (d, J = 9.2 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3, 22.6, 39.5, 41.1, 56.3, 104.2, 118.9, 121.5, 127.0, 129.8, 131.4, 132.8, 134.4, 138.3, 138.8, 141.7, 142.8, 143.5, 164.4, 173.6; MS ESI m/z 396 (M^+, 100); HRMS FAB (Double focusing analyzer (DFA)) m/z calcd. for $C_{17}H_{19}INO_2^+$ [M − OTs]$^-$ 396.0455, found 396.0462.

(2-(2-Acetamidoethyl)phenyl)(*p*-tolyl)iodonium *p*-Toluenesulfonate (13e).



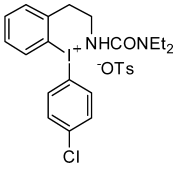
White solid (179 mg, 65%): mp 174−175 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.93 (s, 3H), 2.36 (s, 3H), 2.39 (s, 3H), 3.09−3.13 (m, 2H), 3.38−3.41 (m, 2H), 7.22−7.24 (m, 2H), 7.32−7.36 (m, 3H), 7.55 (d, J = 7.6 Hz, 1H), 7.62−7.70 (m, 3H), 8.03−8.06 (m, 2H), 8.30 (d, J = 6.8 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 21.3 (2 CH_3−C), 22.6, 39.5, 41.1, 112.1, 121.1, 127.0, 129.8, 131.5, 132.9, 133.9, 134.5, 136.2, 139.0, 141.7, 143.0, 143.5, 145.0, 173.6; MS ESI m/z 380 (M^+, 100). Anal. Calcd. For $C_{24}H_{26}INO_4S$: C, 52.27; H, 4.75; N, 2.54; S, 5.81. Found: C, 52.32; H, 4.58; N, 2.42; S, 5.77.

(2-(2-(3,3-Diethylureido)ethyl)phenyl)(4-fluorophenyl)-iodonium *p*-Toluenesulfonate (14a).



White solid (229 mg, 73%): mp 179−182 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.08 (t, J = 5.6 Hz, 6H), 2.37 (s, 3H), 3.15−3.17 (m, 2H), 3.26 (q, J = 5.6 Hz, 4H), 3.42−3.46 (m, 2H), 7.22−7.37 (m, 5H), 7.57 (dd, J = 6.0, 1.2 Hz, 1H), 7.58−7.63 (m, 1H), 7.70 (d, J = 6.4 Hz, 2H), 8.23−8.31 (m, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 14.0, 21.3, 40.7, 42.1, 42.2, 109.8, 120.5 (d, J = 23.8 Hz), 121.6, 127.0, 129.8, 131.4, 133.3, 134.5, 138.7, 139.1 (d, J = 8.8 Hz), 141.7, 143.4, 143.5, 159.6, 166.3 (d, J = 252.5 Hz); MS ESI m/z 441 (M^+), 219 (100). Anal. Calcd. For $C_{26}H_{30}FIN_2O_4S$: C, 50.98; H, 4.94; N, 4.57; S, 5.24. Found: C, 50.84; H, 5.00; N, 4.49; S, 5.33.

(2-(2-(3,3-Diethylureido)ethyl)phenyl)(4-chlorophenyl)-iodonium *p*-Toluenesulfonate (14b).

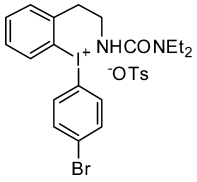


White solid (221 mg, 69%): mp 188−192 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.07 (t, J = 7.2, Hz, 6H), 2.36 (s, 3H), 3.13−3.17 (m, 2H), 3.24 (q, J = 7.2, Hz, 4H), 3.42−3.46 (m, 2H), 7.22 (d, J = 7.6 Hz, 2H), 7.31−7.37 (m, 1H), 7.52 (d, J = 7.6, Hz, 2H), 7.56−7.65 (m, 2H), 7.69 (d, J = 8.0 Hz, 2H), 8.15 (d, J = 8.0 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H); ^{13}C

dx.doi.org/10.1021/jo300874m | J. Org. Chem. 2012, 77, 5705−5713

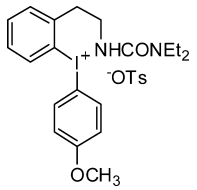
NMR (125 MHz, CD_3OD) δ 14.0, 21.3, 40.6, 42.0, 42.2, 113.4, 121.5, 127.0, 129.8, 131.4, 133.2, 133.3, 134.5, 137.8, 138.8, 140.2, 141.7, 143.4, 143.5, 159.6; MS ESI m/z 457 (M^+), 219 (100). Anal. Calcd. For $C_{26}H_{30}ClIN_2O_4S$: C, 49.65; H, 4.81; N, 4.45; S, 5.10. Found: C, 49.71; H, 4.68; N, 4.33; S, 5.23.

(2-(2-(3,3-Diethylureido)ethyl)phenyl)(4-bromophenyl)-iodonium *p*-Toluenesulfonate (14c).



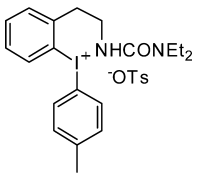
White solid (248 mg, 72%): mp 184−186 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.07 (t, J = 7.2, m Hz, 6H), 2.36 (s, 3H), 3.14 (t, J = 7.2 Hz, 2H), 3.24 (q, J = 7.2 Hz, 4H), 3.42−3.46 (m, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.32−7.38 (m, 1H), 7.56−7.59 (m, 1H), 7.62−7.70 (m, 5H), 8.08 (d, J = 8.0 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 14.0, 21.3, 40.7, 42.0, 42.2, 114.2, 121.4, 127.0, 128.4, 129.8, 131.4, 133.4, 134.5, 136.2, 137.8, 138.8, 141.7, 143.48, 143.52, 159.6; MS ESI m/z 503 (M^+), 501 (M^+), 219 (100). Anal. Calcd. For $C_{26}H_{30}BrIN_2O_4S$: C, 46.37; H, 4.49; N, 4.16; S, 4.76. Found: C, 46.26; H, 4.41; N, 4.21; S, 4.71.

(2-(2-(3,3-Diethylureido)ethyl)phenyl)(4-methoxyphenyl)-iodonium *p*-Toluenesulfonate (14d).



White solid (217 mg, 68%): mp 178−183 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.08 (t, J = 6.8 Hz, 6H), 2.36 (s, 3H), 3.14−3.17 (m, 2H), 3.25 (q, J = 6.8 Hz, 4H), 3.43−3.46 (m, 2H), 3.83 (s, 3H), 7.04 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.28−7.35 (m, 1H), 7.52−7.57 (m, 1H), 7.58−7.63 (m, 1H), 7.69 (d, J = 8.0 Hz, 2H), 8.10 (d, J = 8.8 Hz, 2H), 8.23 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 14.0, 21.3, 40.6, 42.1, 42.2, 56.3, 104.5, 118.8, 121.7, 127.0, 129.8, 131.3, 133.2, 134.2, 138.3, 138.4, 141.7, 143.2, 143.5, 159.6, 164.4; MS ESI m/z 453 (M^+), 219 (100); HRMS FAB (DFA) calcd. for $C_{20}H_{26}IN_2O_2^+$ [M − OTs^-]$^+$ 453.1033, found 453.1041.

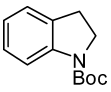
(2-(2-(3,3-Diethylureido)ethyl)phenyl)(*p*-tolyl)iodonium *p*-Toluenesulfonate (14e).



White solid (230 mg, 74%): mp 188−192 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 1.09 (t, J = 7.2 Hz, 6H), 2.38 (s, 3H), 2.40 (s, 3H), 3.15−3.18 (m, 2H), 3.26 (q, 7.2 Hz, 4H), 3.44−3.48 (m, 2H), 7.23 (d, J = 7.6 Hz, 2H), 7.33 (d, J = 8.0 Hz, 3H), 7.55−7.64 (m, 2H), 7.71 (d, J = 8.0 Hz, 2H), 8.05 (d, J = 8.4 Hz, 2H), 8.26 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 14.0, 21.3 (2 CH_3−C), 40.6, 42.1, 42.2, 112.2, 121.2 127.0, 129.8, 131.3, 133.2, 133.8, 134.3, 136.2, 138.6, 141.7, 143.4, 143.5, 144.9, 159.6; MS ESI m/z 437 (M^+), 219 (100). Anal. Calcd. For $C_{27}H_{33}IN_2O_4S$: C, 53.29; H, 5.47; N, 4.60; S, 5.27. Found: C, 53.17; H, 5.21; N, 4.61; S, 5.32.

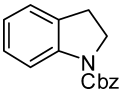
General Procedure for Metal-Free Synthesis of *N*-Protected Indoline. A solution of diaryliodonium salt (0.5 mmol) in DMF (1 mL) was treated with Cs_2CO_3 (3.0 equiv) and TEMPO (0.1 equiv) at rt. After the reaction mixture was warmed to 80 °C under Ar for 1 h, the mixture was cooled to rt and treated with water (5 mL). The resulting mixture was extracted with EtOAc (10 mL × 3). The combined organic extracts were washed with saturated aq NaCl, dried (Na_2SO_4), and concentrated under reduced pressure to provide crude product. Flash column chromatography (SiO_2, EtOAc/hexanes) afforded the corresponding *N*-protected indoline.

***N*-*t*-Butoxycarbonylindoline (15).**



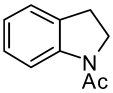
White solid (91 mg, 84%): mp 45−48 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.50 (s, 9H), 3.05 (t, J = 8.8 Hz, 2H), 3.89 (t, J = 8.8 Hz, 2H), 6.90 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 8.4, Hz, 1H), 7.18 (d, J = 7.6 Hz, 1H), 7.67 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.4, 28.7, 47.9, 80.7, 114.7, 122.7, 125.5, 127.7, 132.0, 143.1, 152.4; MS ESI(GC) m/z 219 (M^+), 117 (100). Anal. Calcd. For $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.20; H, 7.92; N, 6.39.

***N*-Benzyloxycarbonylindoline (16).**



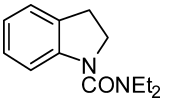
Brown solid (102 mg, 80%): mp 62−65 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.09 (t, J = 8.8 Hz, 2H), 3.99 (t, J = 8.0 Hz, 2H), 5.23 (s, 2H), 6.95 (t, J = 7.6 Hz, 1H), 7.15 (t, J = 8.0 Hz, 1H), 7.21 (d, J = 7.2 Hz, 1H), 7.32−7.45 (m, 5H), 7.73 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 27.7, 47.5, 66.9, 114.9, 122.7, 124.8, 127.6, 128.1, 128.2, 128.7, 131.0, 133.3, 142.7, 153.0. 27.7, 47.9, 66.9, 114.7, 123.2, 125.6, 127.8, 128.4, 128.7, 129.2, 132.0, 137.3, 142.9, 153.0; MS ESI(GC) m/z 253 (M^+), 91(100). Anal. Calcd. For $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.89; H, 6.02; N, 5.45.

***N*-Acetylindoline (17).**



Brown solid (58 mg, 72%): mp 96−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 3.20 (t, J = 6.8 Hz, 2H), 4.05 (t, J = 6.8 Hz, 2H), 7.00 (d, J = 6.0 Hz, 1H), 7.03−7.18 (m, 2H), 8.20 (d, J = 6.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.4, 28.1, 48.9, 117.1, 123.7, 124.6, 127.7, 131.2, 143.0, 168.9; MS ESI m/z 184 ([M + Na]$^+$, 100); HRMS EI (DFA) m/z calcd. for $C_{10}H_{11}NO$ [M^+] 161.0841, found 161.0840.

***N,N*-Diethylindoline-1-carboxamide (18).**



Yellow oil (76 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (t, J = 7.2 Hz, 6H), 3.02 (t, J = 8.0 Hz, 2H), 3.34 (q, J = 7.2 Hz, 4H), 3.88 (d, J = 8.0 Hz, 2H), 6.82−6.90 (m, 1H), 6.95 (d, J = 8.0 Hz, 1H), 7.09−7.17 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 28.3, 42.0, 50.5, 113.0, 121.3, 125.0, 127.1, 131.5, 144.9, 159.8; MS ESI m/z 241 ([M + Na]$^+$, 100); HRMS EI (DFA) calcd. for $C_{13}H_{18}N_2O$ [M^+] 218.1419, found 218.1420.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of compounds. 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.

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