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I(III)-Catalyzed Oxidative Cyclization−Migration Tandem Reactions of Unactivated Anilines

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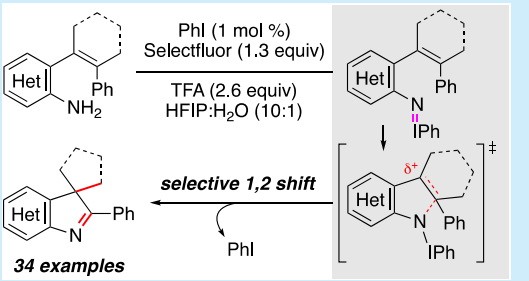
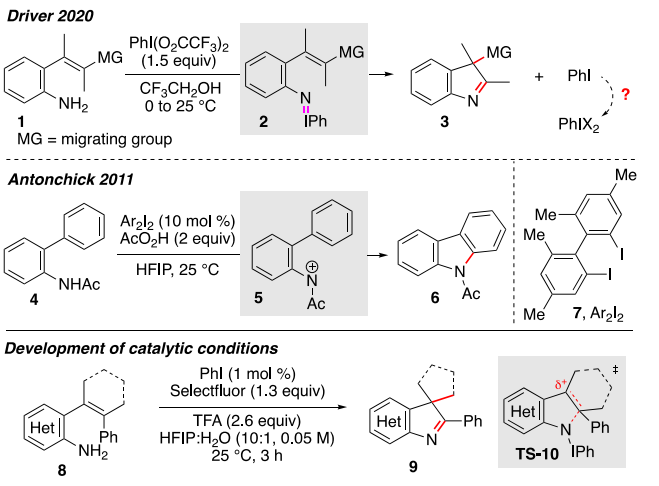
ABSTRACT: An I(III)-catalyzed oxidative cyclization−migration tandem reaction using Selectfluor as the oxidant was developed that converts unactivated anilines into 3*H*-indoles is reported herein. The reaction requires as little as 1 mol % of the iodocatalyst and is mild, tolerating pyridine and thiophene functional groups, and the dependence of the diastereoselectivity of the process on the identity of the iodoarene or iodoalkane precatalyst suggests that the catalyst is present for the stereochemical determining C−N bond forming step.



The ubiquitous nature of C−N bonds in nonplanar *N*-heterocycles and materials continues to spur the development of efficient processes that generate electrophilic nitrogen catalytic intermediates to trigger C−N bond formation.[1,2] While this intermediate can be accessed by oxidation, most methods require the presence of a strong electron-withdrawing *N*-substituent for a successful reaction outcome.[3] In contrast, catalytic reactions that construct C−NAr bonds employ an aryl azide or nitroarene as the N atom source require heat or superstoichiometric quantities of reductant to access the electrophilic *N*-aryl nitrogen intermediate.[4,5] Oxidative methods that generate the electrophilic *N*-aryl intermediate are less common[6] and require an *N*-electron-withdrawing substituent on the aniline. We discovered that electrophilic *N*-aryl nitrenoids could be generated from I(III)-mediated oxidation of unactivated 2-substituted anilines and trapped to afford benzazepinones or 3*H*-indoles.[7] At the conclusion of our study, we were curious if catalysis could be achieved by pairing iodobenzene with a superstoichiometric oxidant. Oxidative catalytic processes using an iodine catalyst have emerged recently as a powerful way to create new bonds through the dearomatization of electron-rich arenes.[8,9] While phenols and aromatic ethers are common substrates, the development of I(III)-catalyzed oxidative methods of anilines remains nascent and requires a strong electron-withdrawing group on nitrogen for C−N bond formation.[6] In 2011, Antonchick and co-workers reported that biaryl acetimides could be transformed into *N*-acetyl carbazoles using a diiodobiaryl catalyst and acetic peroxide as the oxidant (Scheme 1).[6a] Herein, we report that unactivated anilines can be converted into 3*H*-indoles, important bioactive scaffolds,[10] through an I(III)-catalyzed oxidative cascade reaction using Selectfluor as the terminal oxidant.

Scheme 1. Development of I(III)-Catalyzed C−N Bond Forming Reactions



To investigate if catalysis of an oxidative cyclization-migration reaction could be achieved, the reactivity of 2-aminostyrene **11a** toward a substoichiometric amount of iodobenzene and a terminal oxidant was examined (Table 1).[8h] This substrate is readily available from the cross-coupling of 2-aminophenylboronic acid and the vinyl triflate of derived from 2-phenylcyclohexanone. While we had only moderate success

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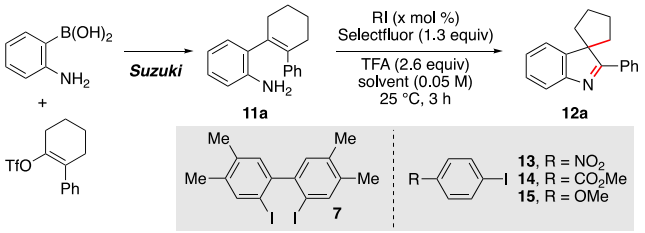
Table 1. Optimization of the I(III)-Catalyzed Oxidative Cyclization−Migration Reaction



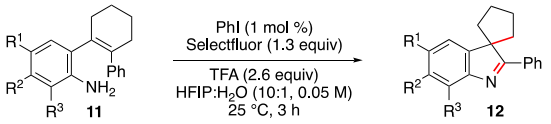
entry	RI	mol %	solvent	yield, %[a]
1	PhI	20	HFIP	42
2	PhI	20	HFIP/H_2O (100:1)	77
3	PhI	20	HFIP/H_2O (10:1)	100
4[c]	PhI	20	HFIP/H_2O (10:1)	90
5	PhI	5	HFIP/H_2O (10:1)	99
6	PhI	1	HFIP/H_2O (10:1)	99[b]
7	**7**	20	HFIP/H_2O (10:1)	91
8	**13**	20	HFIP/H_2O (10:1)	30
9	**14**	20	HFIP/H_2O (10:1)	73
10	**15**	20	HFIP/H_2O (10:1)	70
11	*n*-BuI	20	HFIP/H_2O (10:1)	100
12	I_2	20	HFIP/H_2O (10:1)	n.r.

[a]As determined using ^{1}H NMR spectroscopy using CH_2Br_2 as the internal standard. [b]98% isolated yield after silica gel chromatography. [c]$Me_3SiO_2CCF_3$ used instead of TFA.

using the combination of 20 mol % of PhI with mCPBA as the oxidant,[11] using Selectfluor as the oxidant resulted in 42% of 3*H*-indole **12a** (entry 1).[12,13] We found that a quantitative yield of **12a** could be obtained if water was added as a cosolvent (entries 2 and 3); increasing the amount of water over 50%, however, led to lower yields.[14] Our investigations also determined that trifluoracetic acid additive could be replaced with trimethylsilyltrifluoroacetate (entry 4).[15] To our delight, we found that the catalyst loading of PhI could be decreased to as little as 1 mol % without adversely affecting the yield (entries 5 and 6). The effect of changing the identity of the catalyst was also surveyed (entries 7−12). Biaryl **7** demonstrated that increasing the steric environment of the catalyst did not attenuate the yield of the oxidative cyclization process (entry 7). In contrast, changing the electronic nature of the ArI catalyst had a detrimental effect on the reaction outcome (entries 8−10): only 30% of **12a** was formed using 4-nitroiodobenzene as the catalyst. The yield rebounded using either 4-CO_2Me or 4-MeO iodoarene but was lower than when using iodobenzene. While alkyl iodine(III) species are established to decompose to I_2 or I−OH upon exposure to an oxidant,[16] we found 1-iodobutane afforded a quantitative yield of **12a** (entry 11), and no reaction was observed when I_2 was examined as a catalyst (entry 12).

Using the combination of 1 mol % of PhI and Selectfluor as the stoichiometric oxidant, we surveyed the effect of changing the electronic and steric nature of aniline **11** (Table 2). Irrespective of whether the *para*-R^1-substituent was an electron-releasing or electron-withdrawing group, nearly a quantitative yield of 3*H*-indole **12** was observed (entries 1−6). In contrast, the identity of the *meta*-R^2- substituent impacted the efficiency of the oxidative cyclization-migration reaction requiring 5 mol % of PhI for conversion to 3*H*-indole. While a moderate yield of **12g** (R^2 = OMe) was obtained (entry 7), changing its identity to a methyl, halide, or even trifluoromethyl group resulted in a significantly greater yield of the 3*H*-indole with the latter requiring only 1 mol % of PhI (entries 8−11). In contrast to our earlier reports using aryl azides or nitrostyrenes,[4b,5h] the steric environment around the N atom precursor can be increased with an additional *ortho*-substituent: high yields of 3*H*-indole was observed from anilines bearing an R^3-methoxy, methyl, or fluoro group using only 1 mol % of PhI (entries 12−14).

Table 2. Effect of Changing the Electronic Nature of the Aniline



entry	#	R^1	R^2	R^3	yield (%)[a]
1	**a**	H	H	H	98 (94)[b]
2	**b**	OMe	H	H	99
3	**c**	Me	H	H	99
4	**d**	Cl	H	H	85
5	**e**	F	H	H	97
6	**f**	OCF_3	H	H	91
7	**g**	H	OMe	H	50[c]
8	**h**	H	Me	H	88[c]
9	**i**	H	Cl	H	82[c]
10	**j**	H	F	H	76[c]
11	**k**	H	CF_3	H	91
12	**l**	H	H	OMe	86
13	**m**	H	H	Me	92
14	**n**	H	H	F	90

[a]Isolated after silica gel chromatography. [b]Reaction performed at 1.0 mmol scale with 20 mol % of PhI. [c]Reaction performed with 5 mol % of PhI.

The reaction scope was further explored using *N*-heteroaromatic substrates and by varying the identity of the *ortho*-alkenyl substituent using 20 mol % of PhI because lower catalyst loadings led to incomplete conversion unless otherwise noted (Scheme 2). We found that 2-, 3-, or 4-aminopyridines were smoothly transformed into 3*H*-indoles **17a−17c**. While thiophenes were incompatible in our stoichiometric reaction,[7] they were tolerated using the catalytic conditions. Surprisingly, neither ring contraction nor phenyl migration was observed from these electron-rich heteroarenes; instead cyclization only occurred to give **18d** and **18e** as the sole products.[17] Next, the effect of modifying the structure of the *ortho*-alkenyl substituent was investigated. While no diastereoselectivity was observed in **17f** with a homoallylic *tert*-butyl substituent using 1 mol % of PhI, substrates containing an *ortho*-heterocycle group could be transformed into spirocycles **17g** and **17h** although a higher catalyst loading was required; the latter showed that this reaction can access a structural motif prevalent in biologically active molecules and alkaloids.[2c] Aniline **16i** revealed that substrates bearing α-aryl substituents were effectively converted to **17i** using only 1 mol % of PhI. Our survey showed that the identity of the β-substituent controlled the reaction outcome. While ring contraction was observed with the β-methyl substituent to afford **17j**, when either a β-sulfone or β-carboxylate group was present, only a [1,2] shift of the electron-poor group was observed to afford **18k** and **18l**. To further probe this phenomenon, the electronic nature of the β-aryl substituent of the *ortho*-cyclohexenyl substituent was varied in **16m** and **16n**: while the electron-

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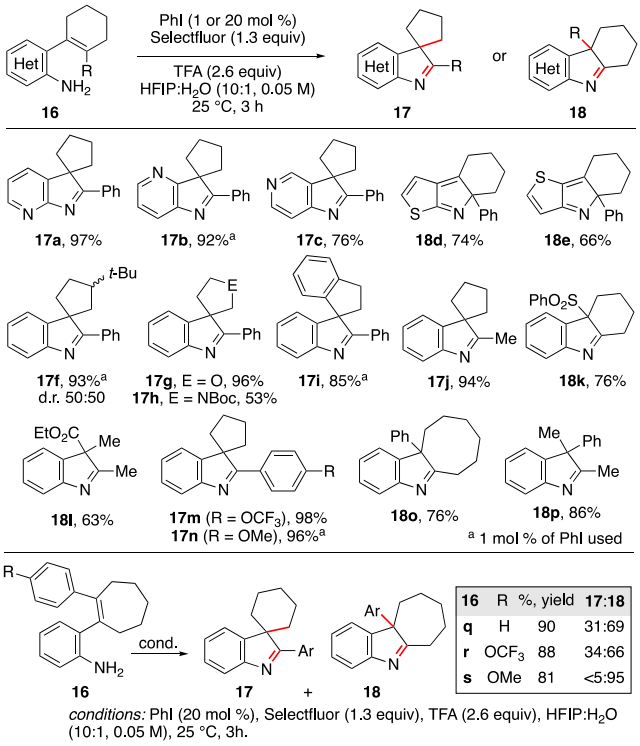
Scheme 2. Effect of Heteroarenes and *ortho*-Substituent Identity on the Reaction Outcome



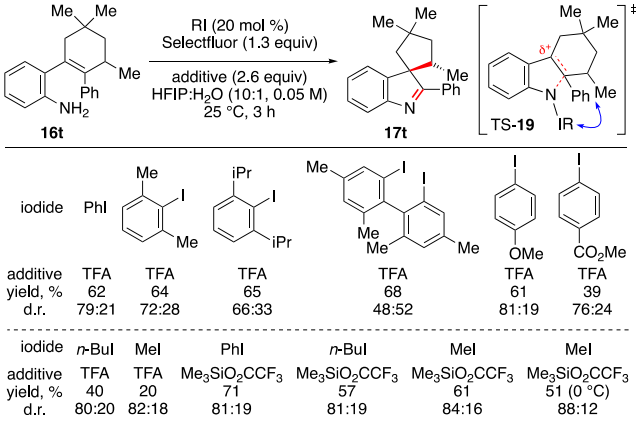
deficient **16m** required a higher catalyst loading, only ring contraction was observed. Increasing the size of the *ortho*-cycloalkenyl substituent in **16o** or acyclic **16p**, however, triggered a [1,2] phenyl shift to afford only **18o** or **18p**.

The reversal in the migration aptitude that was observed for anilines **11a** and **16o** spurred us to investigate this phenomenon further with *o*-cycloheptenyl-substituted substrates (Scheme 2).

Submission of **16q** to reaction conditions produced a 31:69 mixture of ring-contraction and aryl migration products. While reducing the electronic nature of the *β*-aryl group did not change the reaction outcome, only [1,2] aryl migration occurred with the electron-rich **16s**.

In an attempt to gain more insight into the potential stereoselectivity of the process, the reactivity of allylic-substituted **16t** was investigated (Scheme 3). Exposure of **16t** to 20 mol % of PhI and 1.3 equiv of Selectfluor produced **17t** as a 79:21 mixture of diastereomers. We were curious if changing the identity of the catalyst impacted the diastereoselectivity of the process. If the stereoselectivity of the process was affected, that would suggest the catalyst was present for the stereodetermining step.[8e,18] Contrary to our expectations, increasing the steric nature of the aryl iodide by adding *ortho*-methyl or *ortho*-isopropyl groups reduced the diastereoselectivity. This trend continued when the bulkier diodobiarene **7** was assayed to afford a nearly 1:1 mixture of diastereomers. The electronic nature of the iodoarene also affected the reaction outcome: a moderate improvement in the diastereoselectivity was observed using 4-MeO-iodoarene, whereas employing the electron-deficient 4-CO_2Me-iodoarene resulted in a reduced stereoselectivity and yield of 3*H*-indole **17t**. Iodoalkanes were also examined, and the diastereoselectivity inversely depended on the size and length of the alkyl chain.[11] While the best diastereoselectivity was obtained using

Scheme 3. Investigation of the Relationship between Diastereoselectivity and the Identity of the Iodine Catalyst



MeI, the yield of the transformation was significantly reduced.[19] To determine if the lowered yield was a result of the acidic reaction conditions, trimethylsilyl trifluoroacetate was examined as the additive, and the yield of **17t** was significantly improved without attenuation of the diastereoselectivity. Reducing the temperature of the reaction to 0 °C further improved the stereoselectivity to 88:12 using MeI and $Me_3SiO_2CCF_3$. Together these results suggest that the catalyst is present for the stereochemical defining C−N bond forming step (**TS-19**), and the inverse correlation of the steric nature with the selectivity implies that a shortened N−I bond is critical for achieving a selective reaction.

We discovered an oxidative catalytic process for generating electrophilic *N*-aryl nitrenoids from unactivated indoles to produce nonplanar *N*-heterocycles using the combination of an iodoarene or iodoalkane catalyst and Selectfluor as the oxidant. The compatibility of pyridine and thiofuran functionalities in this oxidative cyclization−migration reaction underscores the mildness of these conditions. The dependence of the diastereoselectivity with the identity of the catalyst indicates that it is present for the stereochemical defining C−N bond forming step. Our future studies will build on these results to probe the details of both the C−N and C−C bond forming steps as well as develop I(III)-catalyzed stereoselective oxidative reactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c03497.

Experimental details and spectral data (PDF)

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to the memory of Professor Kilian Muñiz.

■ REFERENCES

(1) (a) Dauban, P.; Sanière, L.; Tarrade, A.; Dodd, R. H. Copper-catalyzed nitrogen transfer mediated by iodosylbenzene PhI = O. *J. Am. Chem. Soc.* **2001**, *123*, 7707−7708. (b) Liang, J.-L.; Yuan, S.-X.; Huang, J.-S.; Yu, W.-Y.; Che, C.-M. Highly diastereo- and enantioselective intramolecular amidation of saturated C−H bonds catalyzed by ruthenium porphyrins. *Angew. Chem., Int. Ed.* **2002**, *41*, 3465−3468. (c) Wehn, P. M.; Du Bois, J. Enantioselective Synthesis of the Bromopyrrole Alkaloids Manzacidin A and C by Stereospecific C−H Bond Oxidation. *J. Am. Chem. Soc.* **2002**, *124*, 12950−12951. (d) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. Expanding the scope of C−H amination through catalyst design. *J. Am. Chem. Soc.* **2004**, *126*, 15378−15379. (e) Omura, K.; Uchida, T.; Irie, R.; Katsuki, T. Design of a robust Ru(salen) complex: aziridination with improved turnover number using *N*-arylsulfonyl azides as precursors. *Chem. Commun.* **2004**, 2060−2061. (f) Lebel, H. n.; Huard, K.; Lectard, S. N-Tosyloxycarbamates as a source of metal nitrenes: rhodium-catalyzed C-H insertion and aziridination reactions. *J. Am. Chem. Soc.* **2005**, *127*, 14198−14199. (g) Liang, C.; Robert-Peillard, F.; Fruit, C.; Müller, P.; Dodd, R. H.; Dauban, P. Efficient diastereoselective intermolecular rhodium-catalyzed C−H amination. *Angew. Chem., Int. Ed.* **2006**, *45*, 4641−4644. (h) Reddy, R. P.; Davies, H. M. L. Dirhodium Tetracarboxylates Derived from Adamantylglycine as Chiral Catalysts for Enantioselective C−H Aminations. *Org. Lett.* **2006**, *8*, 5013−5016. (i) Milczek, E.; Boudet, N.; Blakey, S. Enantioselective C−H amination using cationic ruthenium(II)-pybox catalysts. *Angew. Chem., Int. Ed.* **2008**, *47*, 6825−6828. (j) Thornton, A. R.; Blakey, S. B. Catalytic metallonitrene/alkyne metathesis: a powerful cascade process for the synthesis of nitrogen-containing molecules. *J. Am. Chem. Soc.* **2008**, *130*, 5020−5021. (k) Stoll, A. H.; Blakey, S. B. Rhodium Catalyzed Allene Amination: Diastereoselective Synthesis of Aminocyclopropanes via a 2-Amidoallylcation Intermediate. *J. Am. Chem. Soc.* **2010**, *132*, 2108−2109. (l) Hennessy, E. T.; Betley, T. A. Complex N-Heterocycle Synthesis via Iron-Catalyzed, Direct C−H Bond Amination. *Science* **2013**, *340*, 591−595. (m) Dolan, N. S.; Scamp, R. J.; Yang, T.; Berry, J. F.; Schomaker, J. M. Catalyst-Controlled and Tunable, Chemoselective Silver-Catalyzed Intermolecular Nitrene Transfer: Experimental and Computational Studies. *J. Am. Chem. Soc.* **2016**, *138*, 14658−14667. (n) Jiang, H.; Lang, K.; Lu, H.; Wojtas, L.; Zhang, X. P. Intramolecular Radical Aziridination of Allylic Sulfamoyl Azides by Cobalt(II)-Based Metalloradical Catalysis: Effective Construction of Strained Heterobicyclic Structures. *Angew. Chem., Int. Ed.* **2016**, *55*, 11604−11608.

(2) (a) Kochanowska-Karamyan, A. J.; Hamann, M. T. Marine Indole Alkaloids: Potential New Drug Leads for the Control of Depression and Anxiety. *Chem. Rev.* **2010**, *110*, 4489−4497. (b) Schmidt, A. W.; Reddy, K. R.; Knölker, H.-J. Occurrence, Biogenesis, and Synthesis of Biologically Active Carbazole Alkaloids. *Chem. Rev.* **2012**, *112*, 3193−3328. (c) James, M. J.; O'Brien, P.; Taylor, R. J. K.; Unsworth, W. P. Synthesis of Spirocyclic Indolenines. *Chem. - Eur. J.* **2016**, *22*, 2856−2881.

(3) (a) Davies, H. M. L.; Du Bois, J.; Yu, J.-Q. C-H. Functionalization in organic synthesis. *Chem. Soc. Rev.* **2011**, *40*, 1855−1856. (b) Roizen, J. L.; Harvey, M. E.; Du Bois, J. Metal-Catalyzed Nitrogen-Atom Transfer Methods for the Oxidation of Aliphatic C−H Bonds. *Acc. Chem. Res.* **2012**, *45*, 911−922. (c) Scamp, R. J.; Rigoli, J. W.; Schomaker, J. M. Chemoselective silver-catalyzed nitrene insertion reactions. *Pure Appl. Chem.* **2014**, *86*, 381.

(4) For leading references on ArN_3, see: (a) Cenini, S.; Gallo, E.; Caselli, A.; Ragaini, F.; Fantauzzi, S.; Piangiolino, C. Coordination chemistry of organic azides and amination reactions catalyzed by transition metal complexes. *Coord. Chem. Rev.* **2006**, *250*, 1234−1253. (b) Shen, M.; Leslie, B. E.; Driver, T. G. Dirhodium(II)-Catalyzed Intramolecular C−H Amination of Aryl Azides. *Angew. Chem., Int. Ed.* **2008**, *47*, 5056−5059. (c) Driver, T. G. Recent Advances in Transition Metal-Catalyzed N-Atom Transfer Reactions of Azides. *Org. Biomol. Chem.* **2010**, *8*, 3831−3846. (d) Jenkins, D. M. Atom-Economical C2 + N1 Aziridination: Progress towards Catalytic Intermolecular Reactions Using Alkenes and Aryl Azides. *Synlett* **2012**, *23*, 1267−1270. (e) Ryu, J.; Shin, K.; Park, S. H.; Kim, J. Y.; Chang, S. Rhodium-Catalyzed Direct C−H Amination of Benzamides with Aryl Azides: A Synthetic Route to Diarylamines. *Angew. Chem., Int. Ed.* **2012**, *51*, 9904−9908. (f) Alt, I. T.; Guttroff, C.; Plietker, B. Iron-Catalyzed Intramolecular Aminations of C(sp3)−H Bonds in Alkylaryl Azides. *Angew. Chem., Int. Ed.* **2017**, *56*, 10582−10586.

(5) For leading references on $ArNO_2$, see: (a) Bartoli, G.; Palmieri, G.; Bosco, M.; Dalpozzo, R. The reaction of vinyl Grignard reagents with 2-substituted nitroarenes: A new approach to the synthesis of 7-substituted indoles. *Tetrahedron Lett.* **1989**, *30*, 2129−2132. (b) Cenini, S.; Ragaini, F.; Tollari, S.; Paone, D. Allylic Amination of Cyclohexene Catalyzed by Ruthenium Complexes. A New Reaction Involving an Intermolecular C−H Functionalization. *J. Am. Chem. Soc.* **1996**, *118*, 11964−11965. (c) Akazome, M.; Kondo, T.; Watanabe, Y. Palladium complex-catalyzed reductive *N*-heterocyclization of nitroarenes: novel synthesis of indole and 2*H*-indazole derivatives. *J. Org. Chem.* **1994**, *59*, 3375−3380. (d) Söderberg, B. C.; Shriver, J. A. Palladium-Catalyzed Synthesis of Indoles by Reductive N-Heteroannulation of 2-Nitrostyrenes. *J. Org. Chem.* **1997**, *62*, 5838−5845. (e) Srivastava, R. S.; Nicholas, K. M. Iron-catalyzed allylic amination by nitroorganics. *Chem. Commun.* **1998**, 2705−2706. (f) Gao, H.; Xu, Q.-L.; Yousufuddin, M.; Ess, D. H.; Kürti, L. Rapid Synthesis of Fused *N*-Heterocycles by Transition-Metal-Free Electrophilic Amination of Arene C−H Bonds. *Angew. Chem., Int. Ed.* **2014**, *53*, 2701−2705. (g) Gui, J.; Pan, C.-M.; Jin, Y.; Qin, T.; Lo, J. C.; Lee, B. J.; Spergel, S. H.; Mertzman, M. E.; Pitts, W. J.; La Cruz, T. E.; Schmidt, M. A.; Darvatkar, N.; Natarajan, S. R.; Baran, P. S. Practical olefin hydroamination with nitroarenes. *Science* **2015**, *348*, 886−891. (h) Jana, N.; Zhou, F.; Driver, T. G. Promoting Reductive Tandem Reactions of Nitrostyrenes with $Mo(CO)_6$ and a Palladium Catalyst To Produce 3*H*-Indoles. *J. Am. Chem. Soc.* **2015**, *137*, 6738−6741. (i) Tong, S.; Xu, Z.; Mamboury, M.; Wang, Q.; Zhu, J. Aqueous Titanium Trichloride Promoted Reductive Cyclization of o-Nitrostyrenes to Indoles: Development and Application to the Synthesis of Rizatriptan and Aspidospermidine. *Angew. Chem., Int. Ed.* **2015**, *54*, 11809−11812. (j) Zhou, F.; Wang, D.-S.; Guan, X.; Driver, T. G. Nitroarenes as the Nitrogen Source in Intermolecular Palladium-Catalyzed Aryl C−H Bond Aminocarbonylation Reactions. *Angew. Chem., Int. Ed.* **2017**, *56*, 4530−4534.

(6) (a) Antonchick, A. P.; Samanta, R.; Kulikov, K.; Lategahn, J. Organocatalytic, Oxidative, Intramolecular C−H Bond Amination and Metal-free Cross-Amination of Unactivated Arenes at Ambient Temperature. *Angew. Chem., Int. Ed.* **2011**, *50*, 8605−8608. (b) Cho, S. H.; Yoon, J.; Chang, S. Intramolecular Oxidative C−N Bond Formation for the Synthesis of Carbazoles: Comparison of Reactivity between the Copper-Catalyzed and Metal-Free Conditions. *J. Am.*

Chem. Soc. **2011**, *133*, 5996−6005. (c) Fra, L.; Muñiz, K. Indole Synthesis through Sequential Electrophilic N−H and C−H Bond Activation Using Iodine(III) Reactivity. *Chem. - Eur. J.* **2016**, *22*, 4351−4354. (d) Bering, L.; Manna, S.; Antonchick, A. P. Sustainable, Oxidative, and Metal-Free Annulation. *Chem. - Eur. J.* **2017**, *23*, 10936−10946.

(7) Deng, T.; Mazumdar, W.; Ford, R. L.; Jana, N.; Izar, R.; Wink, D. J.; Driver, T. G. Oxidation of Nonactivated Anilines to Generate N-Aryl Nitrenoids. *J. Am. Chem. Soc.* **2020**, *142*, 4456−4463.

(8) (a) Dohi, T.; Maruyama, A.; Yoshimura, M.; Morimoto, K.; Tohma, H.; Kita, Y. Versatile Hypervalent-Iodine(III)-Catalyzed Oxidations with *m*-Chloroperbenzoic Acid as a Cooxidant. *Angew. Chem., Int. Ed.* **2005**, *44*, 6193−6196. (b) Dohi, T.; Maruyama, A.; Takenaga, N.; Senami, K.; Minamitsuji, Y.; Fujioka, H.; Caemmerer, S. B.; Kita, Y. A Chiral Hypervalent Iodine(III) Reagent for Enantioselective Dearomatization of Phenols. *Angew. Chem., Int. Ed.* **2008**, *47*, 3787−3790. (c) Uyanik, M.; Okamoto, H.; Yasui, T.; Ishihara, K. Quaternary Ammonium (Hypo)iodite Catalysis for Enantioselective Oxidative Cycloetherification. *Science* **2010**, *328*, 1376−1379. (d) Romero, R. M.; Wöste, T. H.; Muñiz, K. Vicinal Difunctionalization of Alkenes with Iodine(III) Reagents and Catalysts. *Chem. - Asian J.* **2014**, *9*, 972−983. (e) Haubenreisser, S.; Wöste, T. H.; Martínez, C.; Ishihara, K.; Muñiz, K. Structurally Defined Molecular Hypervalent Iodine Catalysts for Intermolecular Enantioselective Reactions. *Angew. Chem., Int. Ed.* **2016**, *55*, 413−417. (f) Uyanik, M.; Mutsuga, T.; Ishihara, K. 4,5-Dimethyl-2-Iodoxybenzenesulfonic Acid Catalyzed Site-Selective Oxidation of 2-Substituted Phenols to 1,2-Quinols. *Angew. Chem., Int. Ed.* **2017**, *56*, 3956−3960. (g) Mennie, K. M.; Banik, S. M.; Reichert, E. C.; Jacobsen, E. N. Catalytic Diastereo- and Enantioselective Fluoroamination of Alkenes. *J. Am. Chem. Soc.* **2018**, *140*, 4797−4802. (h) Zhang, D.-Y.; Zhang, Y.; Wu, H.; Gong, L.-Z. Organoiodine-Catalyzed Enantioselective Alkoxylation/Oxidative Rearrangement of Allylic Alcohols. *Angew. Chem., Int. Ed.* **2019**, *58*, 7450−7453.

(9) For recent reviews, see: (a) Singh, F. V.; Wirth, T. Hypervalent Iodine-Catalyzed Oxidative Functionalizations Including Stereoselective Reactions. *Chem. - Asian J.* **2014**, *9*, 950−971. (b) Yoshimura, A.; Zhdankin, V. V. Advances in Synthetic Applications of Hypervalent Iodine Compounds. *Chem. Rev.* **2016**, *116*, 3328−3435. (c) Muñiz, K. Aminations with Hypervalent Iodine. In *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; Springer International Publishing: Switzerland, 2016; Vol. *373*; pp 105−134. (d) Parra, A. Chiral Hypervalent Iodines: Active Players in Asymmetric Synthesis. *Chem. Rev.* **2019**, *119*, 12033−12088.

(10) Compare: (a) Lerchner, A.; Carreira, E. M. Synthesis of (±)-Strychnofoline via a Highly Convergent Selective Annulation Reaction. *Chem. - Eur. J.* **2006**, *12*, 8208−8219. (b) Indoles, Part Four, The Monoterpenoid Indole Alkaloids. In *Chemistry of Heterocyclic Compounds*; Saxton, J. E., Ed.; John Wiley & Sons: Hoboken, NJ, 2008. (c) Wang, S.; Sun, W.; Zhao, Y.; McEachern, D.; Meaux, I.; Barrière, C.; Stuckey, J. A.; Meagher, J. L.; Bai, L.; Liu, L.; Hoffman-Luca, C. G.; Lu, J.; Shangary, S.; Yu, S.; Bernard, D.; Aguilar, A.; Dos-Santos, O.; Besret, L.; Guerif, S.; Pannier, P.; Gorge-Bernat, D.; Debussche, L. SAR405838: An Optimized Inhibitor of MDM2−p53 Interaction That Induces Complete and Durable Tumor Regression. *Cancer Res.* **2014**, *74*, 5855−5865. (d) Gollner, A.; Rudolph, D.; Arnhof, H.; Bauer, M.; Blake, S. M.; Boehmelt, G.; Cockroft, X.-L.; Dahmann, G.; Ettmayer, P.; Gerstberger, T.; Karolyi-Oezguer, J.; Kessler, D.; Kofink, C.; Ramharter, J.; Rinnenthal, J.; Savchenko, A.; Schnitzer, R.; Weinstabl, H.; Weyer-Czernilofsky, U.; Wunberg, T.; McConnell, D. B. Discovery of Novel Spiro[3H-indole-3,2′-pyrrolidin]-2(1H)-one Compounds as Chemically Stable and Orally Active Inhibitors of the MDM2−p53 Interaction. *J. Med. Chem.* **2016**, *59*, 10147−10162.

(11) Please refer to the Supporting Information for more details.

(12) For leading reports on the use of Selectfluor to oxidize aryl iodides, see: (a) Ye, C.; Twamley, B.; Shreeve, J. n. M. Straightforward Syntheses of Hypervalent Iodine(III) Reagents Mediated by Selectfluor. *Org. Lett.* **2005**, *7*, 3961−3964. (b) Sarie, J. C.; Thiehoff, C.; Mudd, R. J.; Daniliuc, C. G.; Kehr, G.; Gilmour, R. Deconstructing the Catalytic, Vicinal Difluorination of Alkenes: HF-Free Synthesis and Structural Study of p-TolIF2. *J. Org. Chem.* **2017**, *82*, 11792−11798.

(13) The unique reactivity of Selectfluor has been exploited in the development of environmentally sustainable processes. For example, see: (a) (review) Yang, L.; Dong, T.; Revankar, H. M.; Zhang, C.-P. Recent progress on fluorination in aqueous media. *Green Chem.* **2017**, *19*, 3951−3992. (b) Tian, Q.; Chen, B.; Zhang, G. Silver-initiated radical ring expansion/fluorination of ethynyl cyclobutanols: efficient synthesis of monofluoroethenyl cyclopentanones. *Green Chem.* **2016**, *18*, 6236−6240. (c) Liang, D.; Li, Y.; Gao, S.; Li, R.; Li, X.; Wang, B.; Yang, H. Amide-assisted radical strategy: metal-free direct fluorination of arenes in aqueous media. *Green Chem.* **2017**, *19*, 3344−3349. (d) Xie, L.-Y.; Qu, J.; Peng, S.; Liu, K.-J.; Wang, Z.; Ding, M.-H.; Wang, Y.; Cao, Z.; He, W.-M. Selectfluor-mediated regioselective nucleophilic functionalization of *N*-heterocycles under metal- and base-free conditions. *Green Chem.* **2018**, *20*, 760−764.

(14) In the absence of PhI, 3*H*-indole **12a** was obtained in only 22% yield.

(15) For leading reports on the use of $Me_3SiO_2CCF_3$ in I(III)-mediated oxidations, see: (a) Hu, B.; Miller, W. H.; Neumann, K. D.; Linstad, E. J.; DiMagno, S. G. An Alternative to the Sandmeyer Approach to Aryl Iodides. *Chem. - Eur. J.* **2015**, *21*, 6394−6398. (b) Qin, L.; Hu, B.; Neumann, K. D.; Linstad, E. J.; McCauley, K.; Veness, J.; Kempinger, J. J.; DiMagno, S. G. A Mild and General One-Pot Synthesis of Densely Functionalized Diaryliodonium Salts. *Eur. J. Org. Chem.* **2015**, *2015*, 5919−5924.

(16) Bosnidou, A. E.; Muñiz, K. Alkyliodines in High Oxidation State: Enhanced Synthetic Possibilities and Accelerated Catalyst Turn-Over. *Chem. - Eur. J.* **2019**, *25*, 13654−13664.

(17) The results of Shirinian and co-workers suggest that the 5*H*-thieno[3,2-*b*]pyrrole isomer is the thermodynamic product; see: Shimkin, A. A.; Shirinian, V. Z.; Nikalin, D. M.; Krayushkin, M. M.; Pivina, T. S.; Troitsky, N. A.; Vorontsova, L. G.; Starikova, Z. A. Isomerization of 3*H*- to 2*H*-[1]Benzothieno[3,2-*b*]pyrroles and Synthesis of the First Merocyanine Dyes Based on Them. *Eur. J. Org. Chem.* **2006**, *2006*, 2087−2092.

(18) For leading reports into the mechanism of iodine-mediated oxidative transformations, see: (a) Richardson, R. D.; Desaize, M.; Wirth, T. Hypervalent Iodine-Mediated Aziridination of Alkenes: Mechanistic Insights and Requirements for Catalysis. *Chem. - Eur. J.* **2007**, *13*, 6745−6754. (b) Harned, A. M. Concerning the mechanism of iodine(iii)-mediated oxidative dearomatization of phenols. *Org. Biomol. Chem.* **2018**, *16*, 2324−2329.

(19) While these data suggest that the alkyl group is present for the stereochemical determining C−N bond forming step, it is possible that an inorganic iodine species is the catalyst; see ref 16.

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