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Phenyliodine Bis(trifluoroacetate)-Mediated Oxidative C−C Bond Formation: Synthesis of 3-Hydroxy-2-oxindoles and Spirooxindoles from Anilides

Junwei Wang, Yucheng Yuan, Rui Xiong, Daisy Zhang-Negrerie, Yunfei Du,* and Kang Zhao*

Tianjin Key Laboratory for Modern Drug Delivery & High-Efficiency, School of Pharmaceutical Science and Technology, Tianjin University, Tianjin 300072, China

duyunfeier@tju.edu.cn; kangzhao@tju.edu.cn

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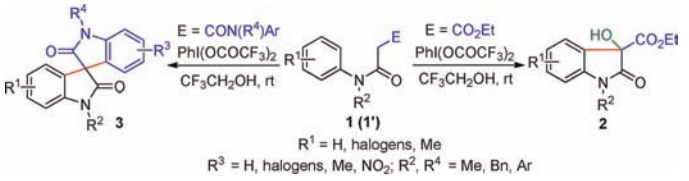
ABSTRACT



The reaction of phenyliodine bis(trifluoroacetate) (PIFA) with a series of anilides 1 (E = CO_2Et) in CF_3CH_2OH was found to give 3-hydroxy-2-oxindole derivatives 2, while that with various anilides 1′ (E = CON(R^4)Ar) afforded the C_2-symmetric or unsymmetric spirooxindoles 3. These processes feature a metal-free oxidative C(sp^2)−C(sp^3) bond formation, followed by oxidative hydroxylation or spirocyclization.

Over the past two decades, the chemistry of hypervalent iodine organic compounds has experienced prosperous development.[1] Especially, iodine(III) derivatives, such as phenyliodine(III) diacetate (PIDA) and phenyliodine(III) bis(trifluoroacetate) (PIFA), have been successfully applied to the construction of heterocycles via intramolecular C−N,[2] N−N,[3] or N−S[4] bond formation. In recent years, it was found that they could also be used in the formation of C−C bonds, without the need for a transition metal. While most of these reactions involve the intra- or intermolecular C(sp^2)−C(sp^2) bond formation that can lead to spirodienones[5] or biaryl compounds,[6] there are only a few examples that

(1) (a) Varvoglis, A. *Synthesis* **1984**, 709. (b) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123. (c) Pohnert, G. *J. Prakt. Chem.* **2000**, *342*, 731. (d) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **2002**, *102*, 2523. (e) Stang, P. J. *J. Org. Chem.* **2003**, *68*, 2997. (f) Moriarty, R. M. *J. Org. Chem.* **2005**, *70*, 2893. (g) Wirth, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3656. (h) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299. (i) Dohi, T.; Kita, Y. *Chem. Commun.* **2009**, 2073.

(2) (a) Wardrop, D. J.; Basak, A. *Org. Lett.* **2001**, *3*, 1053. (b) KikugawaY.; Nagashima, A.; Sakamoto, T.; Miyazawa, E.; Shiiya, M. *J. Org. Chem.* **2003**, *68*, 6739. (c) Correa, A.; Herrero, M. T.; Tellitu, I.; Domínguez, E.; Moreno, I.; SanMartín, R. *Tetrahedron* **2003**, *59*, 7103. (d) Correa, A.; Tellitu, I.; Domínguez, E.; Moreno, I.; SanMartín, R. *J. Org. Chem.* **2005**, *70*, 2256. (e) Du, Y.; Liu, R.; Linn, G.; Zhao, K. *Org. Lett.* **2006**, *8*, 5919. (f) Correa, A.; Tellitu, I.; Domínguez, E.; SanMartin, R. *J. Org. Chem.* **2006**, *71*, 8316. (g) Malamidou-Xenikaki, E.; Spyroudis, S.; Tsanakopoulou, M.; Hadjipavlou-Litina, D. *J. Org. Chem.* **2009**, *74*, 7315.

(3) (a) Correa, A.; Tellitu, I.; Domínguez, E.; Moreno, I.; SanMartín, R. *J. Org. Chem.* **2006**, *71*, 3501. (b) Correa, A.; Tellitu, I.; Domínguez, E.; SanMartin, R. *Tetrahedron* **2006**, *62*, 11100. (c) Yasunari, M.; Kazuyuki, H.; Tomohiro, M.; Kosaku, H.; Hironao, S. *Heterocycles* **2009**, *79*, 669. (d) Wang, K.; Fu, X.; Liu, J.; Liang, Y.; Dong, D. *Org. Lett.* **2009**, *11*, 1015.

(4) (a) Correa, A.; Tellitu, I.; Domínguez, E.; SanMartin, R. *Org. Lett.* **2006**, *8*, 4811. (b) Huang, J.; Lu, Y.; Qiu, B.; Liang, Y.; Dong, D. *Synthesis* **2007**, 2791. (c) Brahemi, G.; Kona, F. R.; Fiasella, A.; Buac, D.; Soukupová, J.; Brancale, A.; Burger, A. M.; Westwell, A. D. *J. Med. Chem.* **2010**, *53*, 2757.

(5) Selected examples: (a) Kita, Y.; Tohma, H.; Inagaki, M.; Hatanaka, K.; Yakura, T. *J. Am. Chem. Soc.* **1992**, *114*, 2175. (b) Kita, Y.; Takada, T.; Gyoten, M.; Tohma, H.; Zenk, M. H.; Eichhorn, J. *J. Org. Chem.* **1996**, *61*, 5857. (c) Node, M.; Kodama, S.; Hamashima, Y.; Baba, T.; Hamamichi, N.; Nishide, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 3060. (d) Baxendale, I. R.; Deeley, J.; Griffiths-Jones, C. M.; Ley, S. V.; Saaby, S.; Tranmer, G. K. *Chem. Commun.* **2006**, 2566. (e) Zhang, Y.; Panek, J. S. *Org. Lett.* **2009**, *11*, 3366. (f) Li, Y.; Chen, H.; Shi, C.; Shi, D.; Ji, S. *J. Comb. Chem.* **2010**, *12*, 231.

(6) Selected examples: (a) Hamamoto, H.; Anilkumar, G.; Tohma, H.; Kita, Y. *Chem. Commun.* **2002**, 450. (b) Mirk, D.; Willner, A.; Fröhlich, R.; Waldvogel, S. R. *Adv. Synth. Catal.* **2004**, *346*, 675. (c) Dohi, T.; Morimoto, K.; Kiyono, Y.; Maruyama, A.; Tohma, H.; Kita, Y. *Chem. Commun.* **2005**, 2930. (d) Dohi, T.; Morimoto, K.; Maruyama, A.; Kita, Y. *Org. Lett.* **2006**, *8*, 2007. (e) Dohi, T.; Ito, M.; Morimoto, K.; Iwata, M.; Kita, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 1301. (f) Kita, Y.; Morimoto, K.; Ito, M.; Ogawa, C.; Goto, A.; Dohi, T. *J. Am. Chem. Soc.* **2009**, *131*, 1668.

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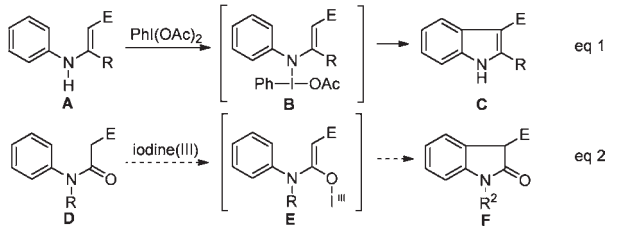
describe the metal-free, iodine(III) oxidant-mediated C(sp^2)−C(sp^2) formation in the construction of heterocycles.[7]

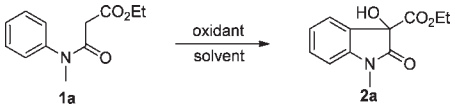
Scheme 1. Proposed Route to Access Oxindoles Based on the Previously Reported PIDA-Mediated Synthesis of Indoles



The oxindole skeleton is widely found in natural products and pharmaceutically active compounds.[8] Anilide derivatives have been vastly applied as substrates in the syntheses of oxindoles via transition-metal-catalyzed and -mediated processes through C−C bond formation between C(3)−C(3a).[9] The employment of PhI(OAc)$_2$ along with stoichiometric I_2 on *N*-alkyl-*N*-arylacrylamide derivatives has provided an alternative metal-free access to this important type of heterocycle, with concurrent introduction of two iodine atoms.[10] To the best of our knowledge, there are few examples describing the construction of oxindole rings from anilide derivatives via C(sp^2)−C(sp^3) bond formation by using iodine(III) reagents as the sole oxidant.[7d] We report herein a novel approach for constructing the naturally occurring and biologically important 3-hydroxy-2-oxindole[11] and spirooxindole[12] skeletons via PIFA-mediated tandem oxidation of anilide derivatives.

In our previous work, we successfully realized the formation of the indole framework (**C**) by PIDA-mediated oxidative ring closure of *N*-aryl enamine compounds (**A**), in which the NH was proposed to be oxidized by PIDA involving a N−I intermediate **B** (Scheme 1, eq 1).[7c] Inspired by this, we envisaged that the enol form tautomer of anilide derivatives **D** may very well undergo a similar process in the presence of an iodine(III) oxidant but via an O−I intermediate **E** to realize a C(sp^2)−C(sp^2) bond formation and give the oxindole compounds (Scheme 1, eq 2).

Table 1. Optimization of Reaction Conditions[a]



entry	oxidant	solvent	concn (mol/L)	t (°C)	time (h)	yield (%)[b]
1[c]	PIDA	DCE	0.20	60	6	23
2	PIDA	DCE	0.20	60	4	44
3	PIFA	DCE	0.20	60	3	55
4	PhIO	DCE	0.05	rt	24	22
5	PIFA	MeCN	0.20	60	5	60
6	PIFA	toluene	0.20	60	5	50
7	PIFA	EtOH	0.20	60	5	20
8	PIFA	EtOAc	0.20	60	5	45
9	PIFA	TFE	0.20	60	1	60
10	PIFA	TFE	0.20	rt	1	67
11	PIFA	TFE	0.10	rt	1	75
12	PIFA	TFE	0.05	rt	1	83
13[d]	PIFA	TFE	0.05	0−rt	1	50

[a] Reaction conditions: **1a** (1.0 mmol), oxidant (2.2 mmol) in solvent unless otherwise stated. [b] Isolated yields. [c] 1.3 equiv of PIDA was used. [d] $BF_3 \cdot Et_2O$ (10 mol %) was added.

Ethyl 3-(methyl (phenyl)amino)-3-oxo-propanoate **1a**, readily prepared via condensation of *N*-methylaniline with monoethyl malonate,[13] was chosen as the model substrate to probe the feasibility of the proposed conversion. We were pleased to find that the reaction of **1a** with PIDA, under the conditions for the conversion of **A** to **C**, successfully afforded 3-hydroxy-2-oxindole **2a** (Table 1, entry 1), which implies that not only the expected C−C bond formation occurred but also a second oxidative hydroxylation was also realized. Since at least 2 equiv of the oxidant were required for the process, the dosage of PIDA was increased from 1.3 to 2.2 equiv, and the yield was raised accordingly (Table 1, entry 2). Switching PIDA to other

(7) Selected examples: (a) Kita, Y.; Tohma, H.; Hatanaka, K.; Takada, T.; Fujita, S.; Mitoh, S.; Sakurai, H.; Okas, S. *J. Am. Chem. Soc.* **1994**, *116*, 3684. (b) Arisawa, M.; Ramesh, N. G.; Nakajima, M.; Tohma, H.; Kita, Y. *J. Org. Chem.* **2001**, *66*, 59. (c) Yu, W.; Du, Y.; Zhao, K. *Org. Lett.* **2009**, *11*, 2417. (d) Liang, J.; Chen, J.; Du, F.; Zeng, X.; Li, L.; Zhang, H. *Org. Lett.* **2009**, *11*, 2820. (e) Ye, Y.; Zheng, C.; Fan, R. *Org. Lett.* **2009**, *11*, 3156.

(8) (a) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, 2209. (b) Trost, B.; Brennan, M. K. *Synthesis* **2009**, 3003. (c) Zhou, F.; Liu, Y. L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381. (d) Millemaggi, A.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2010**, 4527.

(9) For recent reviews, see: (a) Klein, J. E. M. N.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2011**, 6821. For selected examples, see: (b) Ashimori, A.; Bachand, B.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 6477. (c) Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, *66*, 3402. (d) Kündig, E. P.; Seidel, T. M.; Jia, Y.; Bernardinelli, G. *Angew. Chem., Int. Ed.* **2007**, *46*, 8484. (e) Marsden, S. P.; Watson, E. L.; Raw, S. A. *Org. Lett.* **2008**, *10*, 2905. (f) Ruck, R. T.; Huffman, M. A.; Kim, M. M.; Shevlin, M.; Kandur, W. V.; Davies, I. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 4711. (g) Jia, Y. X.; Kündig, E. P. *Angew. Chem., Int. Ed.* **2009**, *48*, 1636. (h) Ueda, S.; Okada, T.; Nagasawa, H. *Chem. Commun.* **2010**, *46*, 2462. (i) Zhu, J.; Zhang, W.; Zhang, L.; Liu, J.; Zheng, J.; Hu, J. *J. Org. Chem.* **2010**, *75*, 5505. (j) Klein, J. E. M. N.; Perry, A.; Pugh, D. S.; Taylor, R. J. K. *Org. Lett.* **2010**, *12*, 3446.

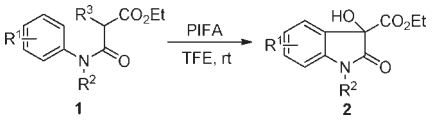
(10) Wei, H. L.; Piou, T.; Dufour, J.; Neuville, L.; Zhu, J. *Org. Lett.* **2011**, *13*, 2244.

(11) For recent reviews, see: (a) Peddibhotla, S. *Curr. Bioact. Compd.* **2009**, *5*, 20. For selected examples, see: (b) Tomita, D.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 6946. (c) Guo, Q.; Bhanushali, M.; Zhao, C. G. *Angew. Chem., Int. Ed.* **2010**, *49*, 9460. (d) Jia, Y. X.; Katayev, D.; Kündig, E. P. *Chem. Commun.* **2010**, *46*, 130. (e) Liu, Y. L.; Wang, B. L.; Cao, J. J.; Chen, L.; Zhang, Y. X.; Wang, C.; Zhou, J. *J. Am. Chem. Soc.* **2010**, *132*, 15176. (f) Gorokhovik, I.; Neuville, L.; Zhu, J. *Org. Lett.* **2011**, *13*, 5536.

(12) For selected examples, see: (a) Trost, B. M.; Cramer, N.; Silverman, S. M. *J. Am. Chem. Soc.* **2007**, *129*, 12396. (b) Bencivenni, G.; Wu, L. Y.; Mazzanti, A.; Giannichi, B.; Pesciaioli, F.; Song, M. P.; Bartoli, G.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2009**, *48*, 7200. (c) Deppermann, N.; Thomanek, H.; Prenzel, A. H. G. P.; Maison, W. *J. Org. Chem.* **2010**, *75*, 5994. (d) Wang, L. L.; Peng, L.; Bai, J. F.; Jia, L. N.; Luo, X. Y.; Huang, Q. C.; Xu, X. Y.; Wang, L. X. *Chem. Commun.* **2011**, *47*, 5593. (e) Hande, S. M.; Nakajima, M.; Kamisaki, H.; Tsukano, C.; Takemoto, Y. *Org. Lett.* **2011**, *13*, 1828.

(13) Wee, A. G. H.; McLeod, D. D. *Heterocycles* **2000**, *53*, 637.

Table 2. Synthesis of 3-Substituted-3-hydroxy-2-oxindoles by PIFA[a]



1 2

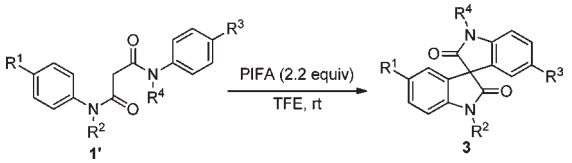
entry	anilide 1	product 2	yield (%)[b]
1	**1a** (R^1 = H)	**2a** (R^1 = H)	83
2	**1b** (R^1 = 4-Cl)	**2b** (R^1 = 5-Cl)	90
3	**1c** (R^1 = 3-F)	**2c** (R^1 = 6-F)	70
4	**1d** (R^1 = 4-Me)	**2d** (R^1 = 5-Me)	56
5	**1e** (R^1 = 3,4-Me)	**2e** (R^1 = 5,6-Me) **2e'** (R^1 = 4,5-Me)	69[c]
6	**1f** (R^2 = H)	**2f** (R^2 = H)	65
7	**1g** (R^2 = 4-Br)	**2g** (R^2 = 5-Br)	80
8	**1h**	**2h**	65
9	**1i**	**2i**	68
10	**1j**	**2j** (R^3 = Me, R^4 = Ph) **2j'** (R^3 = H, R^4 = Tol)	55[d]
11	**1k**	**2k**	0
12	**1l**	**2a**	0
13[e]	**1m**	**2a**	65

[a] General conditions: **1** (1.0 equiv), PIFA (2.2 equiv) in TFE at rt unless otherwise stated. [b] Isolated yields. [c] **2e** was obtained in 42% yield, with the other isomer being isolated in 27% yield. [d] The two regioisomers were inseparable, **2j**/**2j'** = 3:1. [e] **1m** (1.0 equiv), PIFA (1.2 equiv) in TFE, rt.

iodine(III) oxidants, namely, PIFA and PhI=O, shows that PIFA afforded the best yield (Table 1, entries 2–4). Solvent screening experiments revealed that the reaction in trifluoroethanol (TFE) gave the best yield in the shortest time, even at rt (Table 1, entries 5–10). Further study showed that when the concentration of **1a** was lowered from 0.20 to 0.10 and 0.05 mol/L, the yield gradually improved due to less byproducts being formed during the reactions (Table 1, entries 10–12). Attempts to further increase the yield by the use of $BF_3 \cdot Et_2O$ were unsuccessful.

Under the optimal reaction conditions (Table 1, entry 12), we explored the scope and limitations of this newly developed method by using various substituted anilides, bearing a terminal ethoxycarbonyl functionality. Anilides with weak electron-withdrawing groups (Cl, F) at the *para* or *meta* position of the phenyl ring reacted smoothly to afford the expected oxindoles **2b**–**c** in desirable yields, while the yields for substrates bearing electron-donating methyl group(s) were relatively lower (**2d**–**e**). In the case of a substrate bearing 3,4-dimethyl substituents, two regioisomeric products were formed. The substrates can also be extended to *N*-benzylated and *N*-arylated substrates, with no obvious effect on the yields (Table 2, entries 6–10), except for substrate **1j**, where two inseparable regioisomers were formed. The structure of **2c** was further established by X-ray crystallography (see Supporting Information), which unambiguously confirmed the structure of the obtained 3-hydroxy-2-oxindole compounds.

Table 3. Synthesis of Spirooxindoles by PIFA[a]



1' 3

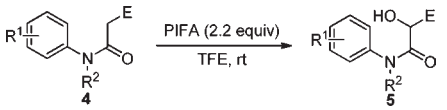
entry	R^1	R^2	R^3	R^4	product **3**	yield (%)[b]
1	H	Me	H	Me	**3a**	75
2	Cl	Me	Cl	Me	**3b**	60
3	H	Bn	H	Bn	**3c**	65
4	H	Ph	H	Ph	**3d**	63
5	H	Me	H	Bn	**3e**	53
6	H	Me	Me	Me	**3f**	50
7	H	Me	Cl	Me	**3g**	60
8	H	Me	NO_2	Me	**3h**	40

[a] General conditions: See Table 2. [b] Isolated yields.

In order to understand the reaction in more detail, anilides **1k**–**1m** were examined for the oxidative cyclization. Unfortunately, however, no cyclized product was detected when either anilide **1k** or **1l** was treated with PIFA under the optimal conditions whereas precyclized oxindole **1m** gave the hydroxylated oxindole **2a** in 65% yield (Table 2, entries 11–13). The unsuccessful cyclization of **1l** and the successful hydroxylation of **1m** clearly indicate the reaction process adopts a sequence of oxdidative C(sp^2)–C(sp^3) bond formation with the subsequent oxidative hydroxylation.

To our delight, when the ethoxycarbonyl group in the substrate was switched to an arylaminocarbonyl group, the corresponding N^1,N^3-diphenylmalonamides **1'** were conveniently converted to the spirooxindoles **3** under the described conditions (Table 3). This result clearly indicates that the oxidative spirocyclization was realized after the expected C–C bond formation. The C_2-symmetric spirooxindoles **3b**–**d** can be achieved by introducing a halogen atom to the phenyl rings or using the *N*-benzylated and *N*-arylated substrates. Furthermore, the C_2-unsymmetric spirooxindoles **3e**–**h** can also be realized by installing different substituents to the N-atom or phenyl ring. It is worth noting that the presence of a strong electron-withdrawing nitro group was also applicable to the method. In

Table 4. Oxidative Hydroxylation of **4**[a]



entry	R^1	R^2	E	product **5**	yield (%)[b]
1	4-NO_2	Me	CO_2Et	**5a**	90
2	2-Br	Me	CO_2Et	**5b**	75
3	H	Bn	COMe	**5c**	80
4	H	Me	CON(*n*-Pr)$_2$	**5d**	53

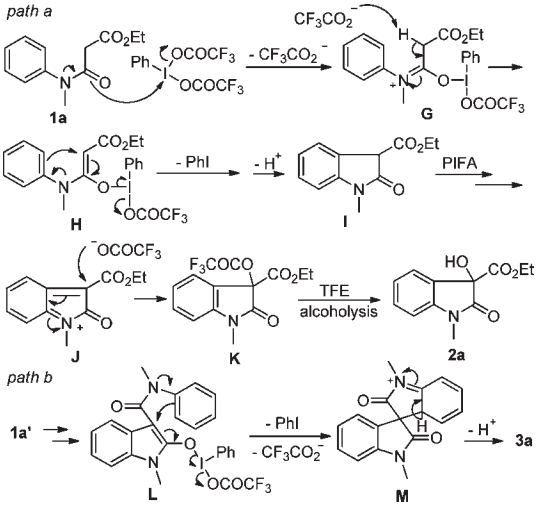
[a] General conditions: See Table 2. [b] Isolated yields.

all of the above cases, no corresponding 3-hydroxy-2-oxindole compound was detected during the process.

However, when the substrate in **1a** is a *para*-methoxy group on the phenyl ring, no desired 3-hydroxy-2-oxindole product was obtained (not shown). Surprisingly, for anilide with a *para*-NO_2 or an *ortho*-Br substituent, uncyclized hydroxylated products (**5a**, **5b**) were formed as illustrated in Table 4.[14] Furthermore, when the ethoxycarbonyl group was changed to the acetyl group or alkylaminocarbonyl group, hydroxylated products **5c** and **5d** were formed respectively (Table 4). No cyclized products were detected when these hydroxylated products (**5a**–**d**) were heated at reflux, even in the presence of a Lewis acid ($BF_3 \cdot Et_2O$) or Brönsted acid (TFA). These results further imply that the formation of cyclized 3-hydroxy-2-oxindole does not go through the hydroxylated intermediate. Disappointingly, when the ethoxycarbonyl group in **1a** was replaced with a cyano group, the corresponding substrate was inert under the identical conditions, even at reflux temperature (not shown).

Based on the experimental results, a plausible mechanistic sequence is proposed for this PIFA-mediated tandem oxidation process (Scheme 2). First, the nucleophilic attack on the iodine center by the carbonyl oxygen in **1a** affords intermediate **G**, with the release of a trifluoroacetate anion. Then the capture of the acidic α-proton by the generated trifluoroacetate transforms the imine salt **G** into enamine **H**. Next, the electrocyclic ring closure,[7c] along with the concomitant cleavage of the I–O bond, occurs in **H**, with subsequent aromatization by the loss of a proton to afford the oxindole **I**. Consistent with the experimental result, the unsuccessful cyclization of **4a** might result from the delocalization of the electron pair on the amino group into the nitro group through resonance, thus preventing this step from taking place and resulting in the uncyclized product (**5a**). Further oxidation of **I** by PIFA adopts a

Scheme 2. Proposed Mechanism



similar sequence as described above to give the intermediate **J**. The nucleophilic attack of the trifluoroacetate anion on the sp^2 carbon center that is connected with the ethoxycarbonyl group regenerates the oxindole **K**, which realizes the trifluoroacetoxylation of oxindole **I**. Finally, the alcoholysis[15] of the trifluoroacetic ester group affords the hydroxylated oxindole **2a** (Scheme 2, path a). As to the spirolization observed in the conversion of **1′** to **3**, we propose a second intramolecular ring-closure reaction takes place between the phenyl ring in the side chain in **L**, assisted by the adjacent amino group, and the electron-deficient sp^2 carbon, along with the cleavage of the O–I bond. The formed intermediate **G** undergoes further proton loss to furnish the spirooxindole **3a** (Scheme 2, path b).[16]

In summary, we have shown a novel metal-free synthesis of 3-hydroxy-2-oxindoles and spirooxindoles via a PIFA-mediated cascade oxidation of anilide derivatives that bear an appropriate α-alkoxycarbonyl or α-arylaminocarbonyl group. These processes feature the oxidative cross-coupling of an sp^2 carbon with a side-chained sp^3 carbon, followed by further oxidative hydroxylation or spirocyclization. Ongoing studies are in progress to find proper oxidative conditions for the other unsuccessful anilide derivatives using such an iodine(III)-mediated C–C bond strategy.

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Supporting Information Available. Experimental procedures and spectral data for all new compounds and X-ray structural data of **2c** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

(14) For recent acetoxylation of anilide using PIDA, see: Liu, W. B.; Chen, C.; Zhang, Q.; Zhu, Z. B. *Beilstein J. Org. Chem.* **2011**, *7*, 1436.

(15) Control experiments indicate that H_2O is not necessary for the process.

(16) This spirocyclization proccess may also adopt an intramolecular Friedel–Crafts reaction; for such an example, see: England, D. B.; Merey, G.; Padwa, A. *Org. Lett.* **2007**, *9*, 3805.