JOC Article

Introduction of a Hydroxy Group at the Para Position and *N*-Iodophenylation of *N*-Arylamides Using Phenyliodine(III) Bis(Trifluoroacetate)

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The reaction of anilides with phenyliodine(III) bis(trifluoroacetate) (PIFA) in trifluoroacetic acid (TFA), TFA−$CHCl_3$, or hexafluoroisopropyl alcohol (HFIP) is described. When the acyl group of the anilide is highly electronegative, such as trifluoroacetyl, or the phenyl group is substituted with an electron-withdrawing group, the 4-iodophenyl group is transferred from PIFA to the amide nitrogen to afford acetyldiarylamines. On the other hand, when the acyl group contains an electron-donating function, such as 4-methoxyphenyl, or the phenyl group is substituted with an electron-donating group, a trifluoroacetoxy group is transferred to the para position of the anilide aromatic ring. This group is hydrolyzed during workup to produce the corresponding phenol.

Introduction

Hypervalent iodine reagents have been widely used for the oxidation of phenols and anilines.[1] In contrast, there have been relatively few reports concerning hypervalent iodine oxidation of *N*-arylamides. It was reported that acetanilide does not react appreciably with phenyliodine(III) diacetate (PIDA) at room temperature. However, acetanilides having electron-donating substituents, such as methoxy or methyl, at the para position react with PIDA in acetic acid to give high yields of *m*-acetoxy derivatives.[2] Nair et al. investigated the mechanism of this reaction and found that it involves an electrophilic displacement that results in direct transfer of an acetoxy group to the para position and subsequent intramolecular migration to the meta position.[3] Following these early reports, very little has been published regarding reaction of acetanilide and PIDA or phenyliodine(III) bis(trifluoroacetate) (PIFA). This is surprising in view of the extensive research that has been done with these reagents using other substrates.[1a,e] Recently Abramovitch et al. reported that treament of *N*-arylacetamide with $C_6F_5I(OCOCF_3)_2$ in toluene solution results in a complex mixture.[4] Although they made no attempt to isolate the individual components of this mixture owing to its complexity, they presumed one of the major products to be an *N*-arylated product formed by the attack of solvent toluene on the electron-deficient nitrogen.

PIFA is the most frequently used and easily available reagent in the family of hypervalent iodine compounds. We have investigated the reaction of acetanilide (**1a**) with PIFA and found that this reagent introduces a 4-iodophenyl group to the amide nitrogen to give acetyldiarylamines in the case of electron-poor amides and introduces a hydroxy group to the para position of the phenyl group in the case of electron-rich amides in synthetically useful yields (Scheme 1).

Results and Discussion

Introduction of a Hydroxy Group to the Para Position of Acetanilides Using PIFA. Treatment of **1a** with PIFA (1.2 molar equiv) in $CHCl_3$−trifluoroacetic acid (TFA) (10 equiv) for 1.5 h at room temperature gave 4-hydroxyphenylacetamide (**2a**) (64%) and *N*-(4-iodophenyl)-*N*-phenylacetamide (**3a**) (6%). From 4-methoxy-*N*-phenylbenzamide (**1d**) the corresponding *p*-hydroxy compound (**2d**) was exclusively obtained in 91% yield under similar conditions. This reaction was much influenced by the choice of solvent. Various solvents such as TFA, hexafluoroisopropyl alcohol (HFIP), CH_2Cl_2, $CHCl_3$, and benzene were examined. For hydroxylation of the aryl group, use of PIFA in TFA, or a combination of 10 equiv of TFA in $CHCl_3$, proved to be most effective. Several types of anilides have been examined. The results are presented in Table 1.

When the acyl group or the phenyl group contains an electron-donating function, a trifluoroacetoxy group is introduced to the para position of the phenyl group. Electron-donating substituents facilitate this reaction, as shown in Table 2 (entries 1, 2, 4−7).

N-(4-Methoxyphenyl)acetamide (**1i**) was submitted to refluxing with PIFA in TFA for 5 min, and the *o*-hydroxylated compound **2i**−**1** was obtained in 63% yield along with the *m*-hydroxy compound **2i**−**2** (8%) (entry

(1) (a) Varvoglis, A. *Tetrahedron* **1997**, *53*, 1179. (b) Prakash, O.; Saini, N.; Sharma, P. K. *Heterocycles* **1994**, *38*, 409. (c) Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431. (d) Varvoglis, A. *Synthesis* **1984**, 709. (e) Varvoglis, A. *Chem. Soc. Rev.* **1981**, *10*, 377.

(2) Barlin, G. B.; Riggs, N. V. *J. Chem. Soc.* **1954**, 3125.

(3) (a) Kokil, P. B.; Patil, S. D.; Ravindranathan, T.; Nair, P. M. *Tetrahedron Lett.* **1979**, 989. (b) Johnson, W. D.; Sherwood, J. E. *Aust. J. Chem.* **1972**, *25*, 1213. (c) Johnson, W. D.; Riggs, N. V. *Aust. J. Chem.* **1964**, *17*, 787.

(4) Abramovitch, R. A.; Ye, X. *J. Org. Chem.* **1999**, *64*, 5904.

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SCHEME 1

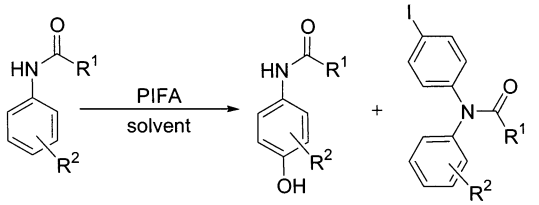
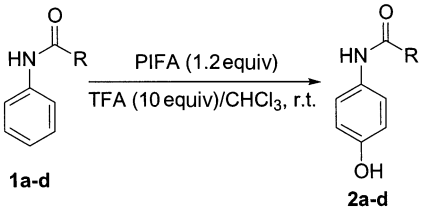
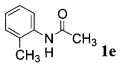
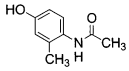
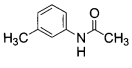
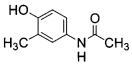
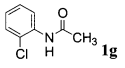
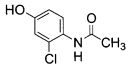
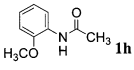
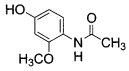
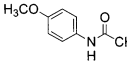
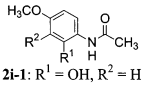
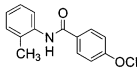
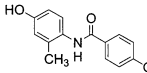
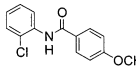
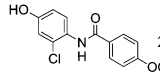
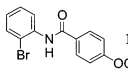
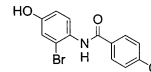
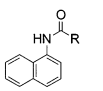
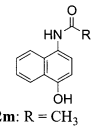


TABLE 1. *p*-Hydroxylation of Anilides Using PIFA



entry	starting material	R	time (min)	product (% yield)
1	**1a**	CH_3	90	**2a** (64)
2	**1b**	C_6H_5	30	**2b** (82)
3	**1c**	$C(CH_3)_3$	15	**2c** (70)
4	**1d**	C_6H_4-4-OCH_3	20	**2d** (91)

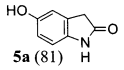
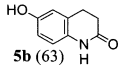
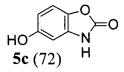
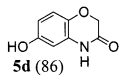
TABLE 2. Hydroxylation of Substituted Anilides Using PIFA

entry	starting material	method[a, b]	time (min)	product yield (%)
1	 **1e**	A	3	 **2e** (82)
2	 **1f**	B	40	 **2f** (69)
3	 **1g**	B	150	 **2g** (37)
4	 **1h**	A	3	 **2h** (72)
5	 **1i**	A	5	**2i-1** (63); **2i-2** (8)
6		C	10	**2i-1** (20); **2i-2** (41)
				 **2i-1**: R^1 = OH, R^2 = H; **2i-2**: R^1 = H, R^2 = OH
7	 **1j**	B	20	 **2j** (65)
8	 **1k**	B	120	 **2k** (56)
9	 **1l**	B	120	 **2l** (57)
10	 **1m**	B	30	**2m** (61)
11	**1n**	B	5	**2n** (67)
				 **2m**: R = CH_3; **2n**: R = C_6H_4-4-OCH_3

[a] PIFA (1.2 equiv). [b] A: TFA/reflux. B: TFA (10 equiv)/$CHCl_3$/rt. **C**: TFA/ice cooling.

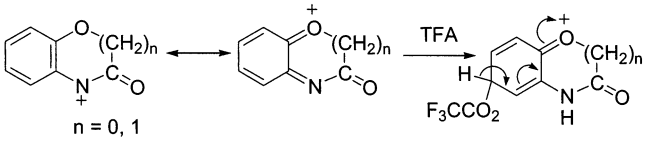
5). Under milder reaction conditions (ice cooling, 10 min), **2i**−**2** was obtained in 41% yield along with **2i**−**1** (20%) (entry 6). This indicates that a trifluoroacetoxy group attacks the ipso position first and subsequently migrates to the meta position, as was the case with the reaction of **1i** with PIDA in acetic acid.[3a]

TABLE 3. Hydroxylation of Benzannulated Lactams with PIFA

entry	starting material	method[a, b]	time (h)	product yield (%)
1	 **4a**	B	25	 **5a** (81)
2	 **4b**	B	33	 **5b** (63)
3	 **4c**	A	3[c]	 **5c** (72)
4	 **4d**	A	2[c]	 **5d** (86)

[a] PIFA (1.2 equiv). [b] A: TFA/reflux. B: TFA (10 equiv)/$CHCl_3$/rt. [c] Minutes.

SCHEME 2



Introduction of a Hydroxy Group to Benzannulated Lactams Using PIFA. Several benzannulated lactams **4a**−**d** were submitted to the same reaction. The results are presented in Table 3. A hydroxy group was introduced at the para position to the nitrogen of **4a,b** to give **5a,b** in high yields. In the case of compounds **4c,d**, participation of the phenolic oxygen atom is so strong that a hydroxyl group was incorporated into the meta position to the nitrogen via the route illustrated in Scheme 2.

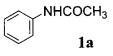
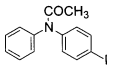
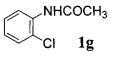
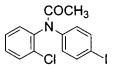
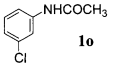
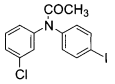
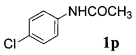
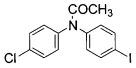
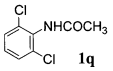
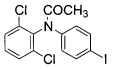
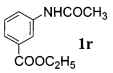
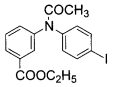
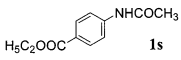
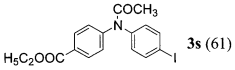
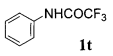
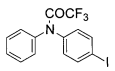
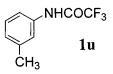
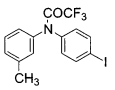
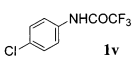
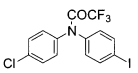
Previously we generated the same types of the intermediates from 4-methoxy-2*H*-1,4-benzoxazin-3-one with concentrated sulfuric acid in methanol and found that both meta and para positions to the oxygen were methoxylated.[5] In the present case only the *p*-hydroxylated product was obtained (86%) (Table 3, entry 4).

Synthesis of Acetyldiarylamines by *N*-Iodophenylation of Acetanilides Using PIFA. In addition to hydroxylation of the phenyl group, we also observed *N*-iodophenylation as a competing reaction. When the acyl group of the anilide is highly electronegative or the phenyl group is substituted with an electron-withdrawing group, the *p*-iodophenyl group of PIFA rearranged to the amide nitrogen predominantly to afford acetyldiarylamines. The *N*-iodophenylation reaction rate was remarkably increased using HFIP as solvent. Thus, stirring a mixture of **1a** and PIFA in HFIP for 10 min at room temperature produced **3a** in 75% yield (6% in $CHCl_3$−TFA). Under similar conditions, *p*-iodophenylated compound **3t** was obtained from trifluoroacetanilide (**1t**) in 83% yield. The results are presented in Table 4.

Several acetyldiarylamines having an iodo group on the para position were prepared in high yield, even in the case of sterically crowded 2,6-dichloroacetanilide (**1q**) (entry 5). Generally diarylamines are of substantial

(5) Sakamoto, T.; Hosoda, I.; Kikugawa, Y. *J. Heterocycl. Chem.* **1988**, *25*, 1279.

TABLE 4. *N*-Iodophenylation of *N*-Arylamides with PIFA

entry	starting material	method[a, b]	time (h)	product yield (%)
1	 **1a**	**C**	10[c]	 **3a** (75)
2	 **1g**	**D**	0.5	 **3g** (79)
3	 **1o**	**D**	1	 **3o** (79)
4	 **1p**	**D**	1	 **3p** (40)
5	 **1q**	**D**	2[c]	 **3q** (90)
6	 **1r**	**E**	20[c]	 **3r** (85)
7	 **1s**	**E**	5	 **3s** (61)
8	 **1t**	**C**	16	 **3t** (83)
9	 **1u**	**D**	6	 **3u** (82)
10	 **1v**	**C**	120	 **3v** (65)[d]

[a] PIFA (1.3 equiv). [b] C: HFIP-TFA (10:1)/rt. D: HFIP/rt. E: PIFA (2.0 equiv)/HFIP/reflux. [c] Minutes. [d] Recovery of **1v** (16%).

synthetic and industrial importance. They have been used as intermediates for synthesis of various nitrogen heterocyclic compounds.[6] A number of synthetic methods such as the classical copper-mediated Ullmann coupling, a copper-catalyzed arylation with triarylbismuth diacetates, and a recently reported soluble copper-catalyzed coupling exist for aromatic carbon−nitrogen bond formation.[7] The mild conditions of the recently developed palladium- and nickel-catalyzed aminations of aryl halides offer considerable advantages over classical methods.[8] Our new synthesis allows easy access to this important class of compounds. Furthermore, the iodo substituent can serve as a versatile functional group for synthesizing more complex molecules.[9]

Mechanistic Consideration. It is obvious from these results that PIFA interacts with anilides to produce an electron-deficient nitrogen that behaves as a nitrenium ion. We propose the following mechanism to account for the products arising from this unprecedented reaction (Scheme 3).

Initially PIFA attacks the amide moiety of **1** to give the intermediate **A** or **B**. Cleavage of the N−I bond of **A** generates a nitrenium ion, the charge of which is preferentially located on nitrogen and the ortho and the para ring carbons. When the nitrenium ion is not stabilized by electron-withdrawing groups, such as a trifluoroacetyl, the iodophenyl group of **B** rearranges to the nitrogen intramolecularly to give **3** in high yield (Table 4). The intramolecular nature of this rearrangement is demonstrated by the fact that only the 4-iodophenyl compound is isolated when benzene or toluene is present in the solvent mixture. In addition, no 2-iodo compound is detected in the reaction mixture. The intermediate **A** is less plausible because an improbable 180° rotation of the iodophenyl group would be required for the transfer of this group to give **3**. HFIP is required as solvent in order to obtain a high yield of **3**. HFIP is known to have a high ionizing ability and low nucleophilicity and presumably stabilizes **B**, allowing the subsequent intramolecular migration reaction. In contrast, intermediate **A** bearing an electron-donating group may dissociate in $CHCl_3$ to give iodobenzene and **C**. The charge of **C** can be delocalized extensively at the para position and trapped by a trifluoroacetate anion derived from PIFA to give **D**. Hydrolysis of **D** during workup gives the product phenol **2** (Tables 1 and 2).

Conclusions

In summary, in the reaction of anilides with PIFA, an iodophenyl group of PIFA is introduced to the nitrogen of anilides derived from strong acids, such as TFA. On the other hand, when the carbonyl group of the anilide is derived from a weaker acid, a trifluoroacetyl group of PIFA is introduced to the para position of the phenyl group. Both reactions occur in synthetically useful yields. Since there are many natural products containing both a nitrogen and phenolic group, including some biologically important nitrogen heterocycles, the present protocol will offer a convenient aromatic hydroxylation method due to its operational simplicity and use of readily available reagents.

Experimantal Section

General Methods. Melting points are uncorrected. NMR spectra were recorded at 270 MHz (^{1}H) and 125 MHz (^{13}C) in $CDCl_3$ with TMS as the internal reference. Mass spectra were measured with a direct inlet system at 70 eV. Elemental analyses were performed in the Microanalytical Laboratory of Josai University.

Materials. Compounds **1a**, **1b**−**i**, **1m**, **1o**, **1p**, **2i**−**1**, **4a**, **4c**, and **4d** were obtained from commercial suppliers and used without further purification. Compounds **1c**, **1d**, **1j**, **1k**, **1q**−**v**, **2a**−**c**, **2f**−**h**, **2m**, **3a**, **4b**, and **5a**−**d** are known. Compounds **1l** and **1n** were prepared by acylation of the corresponding amines.

***N*-(2-Bromophenyl)-4-methoxybenzamide (1l):** colorless crystals; mp 148−150 °C (AcOEt/*n*-hexane); IR (KBr) 3280, 1650, 1610, 1530, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.89 (s, 3H), 7.00 (td, J = 8.0, 1.5 Hz, 1H), 7.01 (d, J = 8.9 Hz, 2H), 7.37 (td, J = 8.0, 1.5 Hz, 1H), 7.57 (dd, J = 8.0, 1.5 Hz, 1H), 7.91 (d, J = 8.9 Hz, 2H), 8.40 (br s, 1H), 8.55 (dd, J = 8.0, 1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 55.4, 113.7, 120.4, 126.1, 127.7,

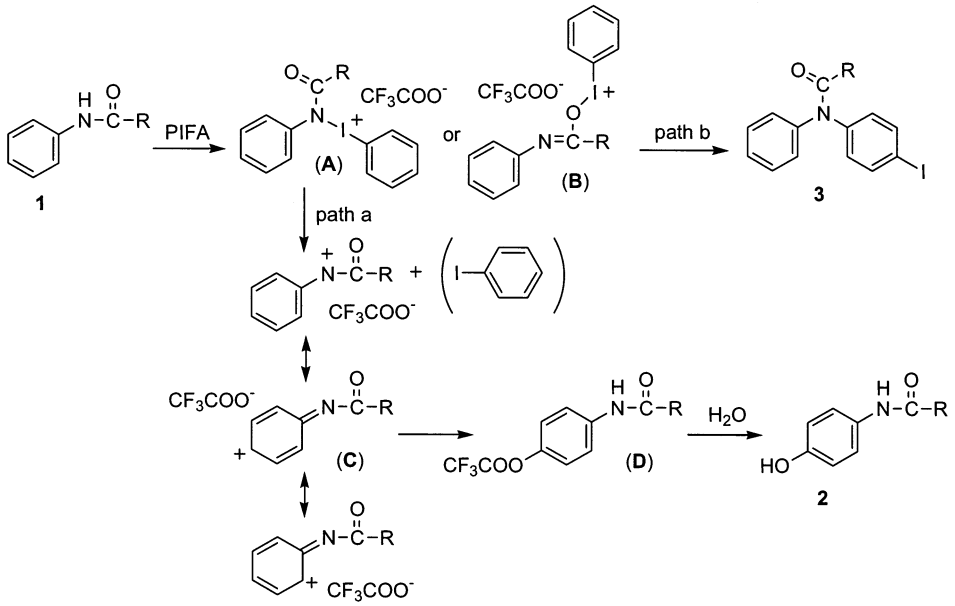
(6) Olah, G. A.; Ramaiah, P.; Wang, Q.; Prakash, G. K. S. *J. Org. Chem*. **1993**, *58*, 6900 and references therein.

(7) (a) Gujadhur, R.; Venkataraman, D.; Kintigh, J. T. *Tetrahedron Lett*. **2001**, *42*, 4791. (b) Combes, S.; Finet, J.-P. *Tetrahedron* **1998**, *54*, 4313.

(8) (a) Yang, B. H.; Buchwald, S. L.; *J. Organomet. Chem*. **1999**, *576*, 125. (b) Wolfe, J. P.; Wagaw, S.; Marcoux, J. F.; Buchwald, S. L. *Acc. Chem. Res*. **1998**, *31*, 805. (c) Hartwig, J. F. *Synlett* **1997**, 329.

(9) For some recent reports, see: (a) Huang, Y.-C.; Majumdar, K. K.; Cheng, C.-H. *J. Org. Chem*. **2002**, *67*, 1682. (b) Faucher, N.; Ambroise, Y.; Cintrat, J.-C.; Doris, E.; Pillon, F.; Rousseau, B. *J. Org. Chem*. **2002**, *67*, 932. (c) Kwong, F. Y.; Klapars, A.; Buchwald, S. L. *Org. Lett*. **2002**, *4*, 581. (d) Uozumi, Y.; Arii, T.; Watanabe, T. *J. Org. Chem*. **2001**, *66*, 5272. (e) Ali, M. H.; Buchwald, S. L. *J. Org. Chem*. **2001**, *66*, 2560.

SCHEME 3



128.0, 128.7, 129.6, 132.6, 136.7, 162.1, 164.7; EI-MS *m*/*z* 307 (M^+ + 2, 4.40), 305 (M^+, 4.34), 226 (27.4), 135 (100). Anal. Calcd for $C_{14}H_{12}BrNO_2$: C, 54.92; H, 3.95; N, 4.58. Found: C, 54.93; H, 3.69; N, 4.52.

4-Methoxy-*N*-(naphthalen-1-yl)benzamide (1n): colorless crystals; mp 203−204 °C (EtOH); IR (KBr) 3250, 1650, 1610, 1500, 1250, 1180, 800 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 3.91 (s, 3H), 7.09 (d, J = 9.0 Hz, 2H), 7.49−7.57 (m, 3H), 7.79−7.85 (m, 2H), 7.92−7.98 (m, 1H), 8.08−8.18 (m, 1H), 8.14 (d, J = 9.0 Hz, 2H), 9.50 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 55.4, 113.7, 123.4, 123.9, 125.5, 125.9, 126.0, 126.1, 126.6, 128.0, 129.3, 129.7, 133.8, 134.1, 162.0, 165.6; EI-MS *m*/*z* 277 (M^+, 31.6), 135 (100). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.80; H, 5.41; N, 5.01.

Typical Procedure for the Preparation of 2a. To **1a** (100 mg, 0.74 mmol) in TFA (844 mg, 7.4 mmol) and $CHCl_3$ (10 mL) was added PIFA (382 mg, 0.89 mmol). After stirring the reaction mixture for 90 min at room temperature, 5% $NaHCO_3$ (30 mL) was added under cooling. The aqueous layer was extracted with AcOEt (25 mL × 5), and the combined organic layer was washed with brine (30 mL), dried over Na_2SO_4, and concentrated. The crude products were chromatographed on a column of silica gel. First elution with AcOEt/*n*-hexane (1:1) afforded **3a** (14 mg, 6%). Further elution with the same solvent mixture afforded **2a** (72 mg, 64%).

***N*-(4-Hydroxyphenyl)-4-methoxybenzamide (2d):** colorless crystals; mp 226−230 °C (AcOEt); IR (KBr) 3320, 1650, 1610, 1520, 1360 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.83 (s, 3H), 6.72 (d, J = 8.7 Hz, 2H), 7.04 (d, J = 8.5 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.93 (d, J = 8.5 Hz, 2H), 9.21 (s, 1H), 9.85 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 55.3, 113.4, 114.8, 122.2, 127.1, 129.3, 130.7, 153.4, 161.5, 164.2; EI-MS *m*/*z* 243 (M^+, 20.7), 135(100). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 68.89; H, 5.18; N, 5.68.

***N*-(4-Hydroxy-2-methylphenyl)acetamide (2e):** colorless crystals; mp 129−130 °C (AcOEt/*n*-hexane); IR (KBr) 3300, 3250, 1630, 1560, 1480 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (s, 3H), 2.19 (s, 3H), 5.45 (br s, 1H), 6.60 (dd, J = 8.3, 3.0 Hz, 1H), 6.62 (d, J = 3.0 Hz, 1H), 6.84 (br s, 1H), 7.29 (d, J = 8.3 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 17.9, 22.9, 112.4, 116.4, 126.9, 127.8, 133.8, 154.8, 168.0; EI-MS *m*/*z* 165 (M^+, 54.7), 123 (100). Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.27; H, 6.81; N, 8.48.

***N*-(3-Hydroxy-4-methoxyphenyl)acetamide (2i-2):** colorless crystals; mp 176−178 °C (benzene/*n*-hexane); IR (KBr) 3340, 1660, 1560, 1250, 1230 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.98 (s, 3H), 3.71 (s, 3H), 6.79 (d, J = 8.7 Hz, 1H), 6.89 (dd, J = 8.7, 1.8 Hz, 1H), 7.15 (d, J = 1.8 Hz, 1H), 8.99 (s, 1H), 9.65 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 23.9, 55.9, 107.6, 109.7, 112.5, 133.0, 143.5, 146.4, 167.6; EI-MS *m*/*z* 181 (M^+, 73.6), 124 (100). Anal. Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.48; H, 6.13; N, 7.72.

***N*-(4-Hydroxy-2-methylphenyl)-4-methoxybenzamide (2j):** colorless crystals; mp 223−225 °C (AcOEt); IR (KBr) 3270, 1630, 1620, 1520 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 2.20 (s, 3H), 3.88 (s, 3H), 6.66 (dd, J = 8.5, 2.4 Hz, 1H), 6.73 (d, J = 2.4 Hz, 1H), 7.03 (d, J = 8.9 Hz, 2H), 7.24 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 8.9 Hz, 2H), 8.22 (br s, 1H), 8.80 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 18.0, 55.4, 112.6, 113.5, 116.5, 126.8, 127.8, 128.2, 129.3, 135.4, 155.4, 161.6, 164.8; EI-MS *m*/*z* 257 (M^+, 25.8), 135(100). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.86; H, 5.60; N, 5.45.

***N*-(2-Chloro-4-hydroxyphenyl)-4-methoxybenzamide (2k):** colorless crystals; mp 200−201 °C (benzene); IR (KBr) 3280, 1640, 1620, 1550, 1520 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 3.89 (s, 3H), 6.85 (dd, J = 8.9, 2.8 Hz, 1H), 6.97 (d, J = 2.8 Hz, 1H), 7.06 (d, J = 8.9 Hz, 2H), 7.76 (d, J = 8.9 Hz, 1H), 8.01 (d, J = 8.9 Hz, 2H), 8.74 (s, 1H), 8.80 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 55.3, 113.5, 114.3, 115.6, 126.2, 126.3, 129.4, 129.9, 130.6, 156.2, 161.8, 164.8; EI-MS *m*/*z* 277 (M^+, 14.3), 242 (10.8), 135 (100). Anal. Calcd for $C_{14}H_{12}ClNO_3$: C, 60.55; H, 4.36; N, 5.04. Found: C, 60.39; H, 4.31; N, 5.02.

***N*-(2-Bromo-4-hydroxyphenyl)-4-methoxybenzamide (2l):** colorless crystals; mp 201−203 °C (AcOEt/*n*-hexane); IR (KBr) 3420, 3350, 1650, 1610, 1510 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 3.89 (s, 3H), 6.89 (dd, J = 8.7, 2.7 Hz, 1H), 7.06 (d, J = 8.9 Hz, 2H), 7.15 (d, J = 2.7 Hz, 1H), 7.74 (d, J = 8.7 Hz, 1H), 8.01 (d, J = 8.9 Hz, 2H), 8.74 (s, 1H), 8.76 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 55.4, 113.6, 114.9, 118.6, 121.6, 126.3, 127.9, 129.5, 130.1, 156.4, 161.9, 164.9; EI-MS *m*/*z* 323 (M^+ + 2, 7.23), 321 (M^+, 7.33), 242 (12.9), 135 (100). Anal. Calcd for $C_{14}H_{12}BrNO_3$: C, 52.20; H, 3.75; N, 4.35. Found: C, 51.98; H, 3.59; N, 4.15.

***N*-(4-Hydroxynaphthalen-1-yl)-4-methoxybenzamide (2n):** colorless crystals; mp 214−216 °C (AcOEt/*n*-hexane); IR (KBr) 3370, 3200, 1640, 1610, 1500, 1290, 1260, 1190, 770 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 3.91 (s, 3H), 6.93 (d, J = 7.9 Hz, 1H), 7.08 (d, J = 8.9 Hz, 2H), 7.43−7.54 (m, 3H), 7.94−8.01 (m, 1H), 8.12 (d, J = 8.9 Hz, 2H), 8.25−8.30 (m, 1H), 9.09 (s, 1H), 9.28 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 55.4, 107.3, 113.6, 122.3, 123.2, 124.6, 124.8, 125.1, 125.2, 126.1, 126.7, 129.5, 130.9, 151.8, 161.8, 165.6; EI-MS *m*/*z* 293 (M^+, 17.7),

135 (100). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.51; H, 5.06; N, 4.68.

Typical Procedure for the Preparation of 5c. To a solution of refluxing TFA (4 mL) containing **4c** (100 mg, 0.74 mmol) was added a TFA solution (2 mL) of PIFA (382 mg, 0.89 mmol) in one portion. After refluxing the reaction mixture for 3 min, the solvent was concentrated. To the residue was added 5% $NaHCO_3$ (30 mL) under cooling. The aqueous layer was extracted with AcOEt (50 mL × 2), and the combined organic layer was washed with brine (30 mL), dried over Na_2SO_4, and concentrated. Purification by column chromatography over silica gel (AcOEt/*n*-hexane = 1:1) afforded **5c** (81 mg, 72%).

Typical Procedure for the Preparation of 3g. To **1g** (100 mg, 0.59 mmol) in HFIP (5 mL) was added PIFA (330 mg, 0.77 mmol). After stirring the reaction mixture for 30 min at room temperature, HFIP was removed under reduced pressure. To the residue was added 5% $NaHCO_3$ (30 mL) under cooling. The aqueous layer was extracted with AcOEt (40 mL × 2), and the combined organic layer was washed with brine (30 mL), dried over Na_2SO_4, and concentrated. Purification by column chromatography over silica gel (AcOEt/*n*-hexane = 1:3) afforded **3g** (173 mg, 79%).

***N*-(2-Chlorophenyl)-*N*-(4-iodophenyl)acetamide (3g):** oil; IR (neat) 1690, 1490, 1370, 1320, 1310 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.01 (s, 3H), 7.09 (d, J = 8.6 Hz, 2H), 7.18−7.45 (m, 3H), 7.45−7.57 (m, 1H), 7.57−7.74 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 23.2, 90.5, 127.4, 128.3, 129.9, 130.8, 133.3, 137.6, 138.5, 139.7, 140.8, 169.8; EI-MS m/z 373 (M^+ + 2, 5.7), 371 (M^+, 16.9), 329 (100); HR-MS m/z for $C_{14}H_{11}ClINO$ calcd 370.9574, found 370.9557.

***N*-(3-Chlorophenyl)-*N*-(4-iodophenyl)acetamide (3o):** colorless crystals; mp 97−99 °C (*n*-hexane); IR (KBr) 1670, 1370, 1320 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.07 (s, 3H), 7.00 (d, J = 8.6 Hz, 2H), 7.14 (d, J = 7.4 Hz, 1H), 7.22−7.36 (m, 2H), 7.25 (t, J = 1.9 Hz, 1H), 7.67−7.76 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 23.3, 91.8, 125.7, 126.4, 127.1, 129.6, 130.7, 133.1, 138.2, 142.4, 144.0, 169.1; EI-MS m/z 373 (M^+ + 2, 10.4), 371 (M^+, 32.3), 329 (100). Anal. Calcd for $C_{14}H_{11}ClINO$: C, 45.25; H, 2.98; N, 3.77. Found: C, 45.22; H, 2.75; N, 3.63.

***N*-(4-Chlorophenyl)-*N*-(4-iodophenyl)acetamide (3p):** oil; IR (neat) 1680, 1490 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.06 (s, 3H), 6.99 (d, J = 8.6 Hz, 2H), 7.17 (d, J = 8.7 Hz, 2H), 7.29−7.40 (m, 2H), 7.62−7.74 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 23.8, 91.0, 127.9, 129.8, 131.8, 133.9, 138.3, 141.0, 142.3, 170.1; EI-MS m/z 373 (M^+ + 2, 9.80), 371 (M^+, 30.2), 329 (100); HR-MS m/z for $C_{14}H_{11}ClINO$ calcd 370.9574, found 370.9576.

***N*-(2,6-Dichlorophenyl)-*N*-(4-iodophenyl)acetamide (3q):** colorless crystals; mp 165−167 °C (benzene/*n*-hexane); IR (KBr) 1670, 1490, 1320, 1300 cm^{-1}; ^1H NMR (DMSO-d_6) δ (major/minor = 63:37) 1.88 (s, 1.9H), 2.15 (s, 1.1H), 7.03 (d, J = 8.0 Hz, 1.3H), 7.22 (d, J = 8.0 Hz, 0.7H), 7.37−7.50 (m, 0.4H), 7.50−7.85 (m, 4.6H); ^{13}C NMR (DMSO-d_6) δ (major) 22.8, 90.6, 126.4, 129.9, 131.6, 134.6, 136.7, 137.3, 139.3, 168.7; (minor) 22.0, 93.0, 128.7, 129.2, 130.4, 134.1, 137.6, 138.0, 140.3, 169.1; EI-MS m/z 409 (M^+ + 4, 3.42), 407 (M^+ + 2, 20.2), 405 (M^+, 31.1), 363 (100). Anal. Calcd for $C_{14}H_{10}Cl_2INO$: C, 41.41; H, 2.48; N, 3.45. Found: C, 41.67; H, 2.22; N, 3.25.

3-[Acetyl(4-iodophenyl)amino]benzoic acid ethyl ester (3r): oil; IR (neat) 1720, 1680, 1490 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (t, J = 7.1 Hz, 3H), 2.07 (s, 3H), 4.37 (q, J = 7.1 Hz, 2H), 7.02 (d, J = 8.1 Hz, 2H), 7.41−7.51 (m, 2H), 7.69 (d, J = 8.1 Hz, 2H), 7.90 (s, 1H), 7.86−8.03 (m, 1H);^{13}C NMR ($CDCl_3$) δ 14.3, 23.8, 61.3, 91.2, 119.0, 127.7, 128.3, 129.2, 131.1, 132.4, 138.3, 142.4, 142.6, 165.5, 170.1; EI-MS m/z 409 (M^+, 44.7), 367 (100); HR-MS m/z for $C_{17}H_{16}INO_3$ calcd 409.0175, found 409.0159.

4-[Acetyl(4-iodophenyl)amino]benzoic acid ethyl ester (3s): oil; IR (neat) 1720, 1690, 1610, 1490, 1370, 1280 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (t, J = 7.1 Hz, 3H), 2.08 (s, 3H), 4.37 (q, J = 7.1 Hz, 2H), 7.00 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 8.6 Hz, 2H), 7.72 (d, J = 8.6 Hz, 2H), 8.04 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.3, 24.0, 61.2, 92.4, 118.6, 126.6, 129.6, 130.7, 138.7, 142.3, 146.4, 165.7, 170.0; EI-MS m/z 409 (M^+, 38.1), 367 (100); HR-MS m/z for $C_{17}H_{16}INO_3$ calcd 409.0175, found 409.0174.

Typical Procedure for the Preparation of 3t. To **1t** (100 mg, 0.53 mmol) in HFIP−TFA (10:1) (5 mL) was added PIFA (296 mg, 0.69 mmol). After stirring the reaction mixture for 16 h at room temperature, the solvent was concentrated. To the residue was added 5% $NaHCO_3$ (30 mL) under cooling. The aqueous layer was extracted with AcOEt (50 mL × 2), and the combined organic layer was washed with brine (30 mL), dried over Na_2SO_4, and concentrated. Purification by column chromatography over silica gel (AcOEt/*n*-hexane = 1:10) afforded **3t** (171 mg, 83%).

***N*-(4-Iodophenyl)-*N*-phenyl-2,2,2-trifluoroacetamide (3t):** colorless crystals; mp 62−63 °C (*n*-hexane); IR (KBr) 1710, 1600, 1500, 1400, 1240, 1220, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.05 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 9.7 Hz, 2H), 7.40−7.43 (m, 3H), 7.72 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 92.6, 116.4 (q, J = 288.6 Hz, CF_3), 126.0, 127.7, 128.6, 129.6, 138.6, 141.2, 156.7 (q, J = 36.6 Hz, CO); EI-MS m/z 391 (M^+, 100), 167 (75.9). Anal. Calcd for $C_{14}H_9F_3INO$: C, 42.99; H, 2.32; N, 3.58. Found: C, 42.84; H, 2.24; N, 3.55.

***N*-(3-Methylphenyl)-*N*-(4-iodophenyl)-2,2,2-trifluoroacetamide (3u):** oil; IR (neat) 1710, 1490, 1390, 1210, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.36 (s, 3H), 6.99−7.24 (m, 5H), 7.31 (t, J = 8.3 Hz, 1H), 7.71 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.2, 92.5, 116.4 (q, J = 288.8 Hz, CF_3), 122.9, 125.5, 127.7, 128.9, 129.3, 130.0, 138.5, 139.8, 141.1, 156.6 (q, J = 36.4 Hz, CO); EI-MS m/z 405 (M^+, 100), 298 (20.0), 186 (44.9), 181 (36.7), 181 (37.9); HR-MS for $C_{15}H_{11}F_3INO$ calcd 404.9837, found 404.9813.

***N*-(4-Chlorophenyl)-*N*-(4-iodophenyl)-2,2,2-trifluoroacetamide (3v):** oil; IR (neat) 1710, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.03 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 7.39 (d, J = 8.2 Hz, 2H), 7.74 (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 92.8, 116.3 (q, J = 288.6 Hz, CF_3), 127.6, 129.8, 133.5, 135.4, 137.5, 138.8, 141.0, 156.5 (q, J = 36.6 Hz, CO); EI-MS m/z 427 (M^+ + 2, 32.3), 425 (M^+, 100); HR-MS m/z for $C_{14}H_8ClF_3INO$ calcd 424.9291, found 424.9281.

Supporting Information Available: Experimental and literature melting points of known compounds **1c**, **1d**, **1j**, **1k**, **1q**−**v**, **2a**−**c**, **2f**−**h**, **2m**, **3a**, **4b**, and **5a**−**d**. This material is available free of charge via the Internet at http:// pubs.acs.org.

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