Hydrazidohydroxylation of Styrenes with N-Acetylaminophthalimide Using Phenylioniode(III) Bis(trifluoroacetate) (PIFA)

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Abstract: Regioselective hydrazidohydroxylation of styrenes with N-acetylaminophthalimide using phenyliodine(III) bis(trifluoroacetate) was carried out to afford 1-aryl-2-(N-acetyl-N-phthalimido)aminoethyl trifluoroacetates in high yields. The procedure is operationally simple and removal of trifluoroacetyl and phthalimido groups was performed by treatment of the trifluoroacetate with hydrazine hydrate in good yield. A synthetic study and a mechanistic proposal for the hydrazidohydroxylation are presented.

Key words: hydrazidohydroxylation, styrene, N-acetylaminophthalimide, nitrenium ion, phenyliodine(III) bis(trifluoroacetate)

Divalent positively charged nitrogen species (nitrenium ions) which are stabilized by the neighboring groups have been widely applied in the field of synthetic organic chemistry.1

Previously, we have reported that nitrenium ions I (Figure 1) can be generated from the corresponding N-methoxy- or N-allyoxy-N-chloroamides by the action of silver2 or zinc3 ions or triethylamine4 or by direct oxidation of the corresponding amides with phenyliodine(III) bis(trifluoroacetate) (PIFA).5

More recently, hypervalent iodine compounds such as PIFA have been often utilized because these reagents have low toxicity, are readily available, are easy to handle, and are environmentally friendly.5 We recently reported a fundamentally new protocol for the construction of nitrogen heterocycles by the intramolecular electrophilic aromatic substitution with N-acyl-N-phthalimidonitrenium ions II generated from the corresponding N-acylaminophthalimides using PIFA.7 In an extension of this work, we have investigated the reaction of olefins 1 with N-
acetyliminophthalimide (2) using PIFA anticipating that hydrazide derivatives having a trifluoroacetate group on the adjacent carbon might be formed (Figure 2).

Initially, we examined the reaction of 4-chlorostyrene (1d) with 2 using PIFA in various solvents such as chloroform, acetonitrile, tetrahydrofuran, and 2,2,2-trifluoro-ethanol. Treatment of 1d and 2 (1.1 molar equiv) with PIFA (1.2 molar equiv) in chloroform at reflux for 30 minutes gave 2-(N-acetyl-N-phthalimido)-1-(4-chlorophenyl)aminoethyl trifluoroacetate (3d) in 85% yield. The structural determination of 3d was performed by the comparison of the chemical shifts of the benzyl proton of 3d and of the corresponding proton of the hydrolyzed 3d (5d). The signal of the benzyl proton of 5d appeared at considerably higher field (1 ppm) compared with the benzyl proton of 3d, which indicates that the oxygen function attached to the benzyl position. In acetonitrile or tetrahydrofuran the reaction mixture contained several unidentifiable products (TLC) and 3d was obtained in poor yield. In 2,2,2-trifluoroethanol PIFA reacted with 2 for one hour in the presence of 1a at room temperature to form the adduct, the iodophenyl group of which rearranged to the amide nitrogen to give N-acetyl-N-(4-iodophenyl)aminophthalimide (4) in 80% yield. A similar N-iodophenylation reaction of acetonilides using PIFA was reported previously. Accordingly, several styrenes reacted in chloroform, and the results are presented in Table 1.

Normally, the nitrenium ion IIa could attack both α- and β carbons of styrenes to afford two regioisomers. In practice, however, HPLC analysis of the reaction mixture revealed that the reaction is extremely regioselective and one regioisomer alone is obtained in the case of unsubstituted and α-methyl substituted styrenes in high yield (Table 1, entries 1–9). For β-methyl-substituted styrenes, two regioisomers were obtained (entry 10).

Next, we tried the hydrolysis of 3. Initially the hydrolysis was performed in 10% aqueous sodium bicarbonate solution at room temperature. However, no products were extracted from the aqueous solution, probably because the phthalimido ring opened in addition to the hydrolysis of trifluoroacetate. Next, a weakly acidic solvent (AcOH–H₂O = 2:1) was used for hydrolysis. To our surprise, the trifuloroacetate was removed from the aqueous solution, probably because the oxygen function attached to the benzyl position. Normally, the nitrenium ion could attack both α and β positions of this new intermediate to give the two regioisomers 5a and 5a', respectively. These regioisomers thus obtained were trifluoroacetylated with trifluoroacetic anhydride to give 3a, 3d, and 3g. The results are presented in Table 2.

The described transformation can be rationalized as depicted in Scheme 1. Thus the trifluoroacetyl group of 3a is eliminated by the assistance of the adjacent acetamido nitrogen to form the aziridinium ion. The solvent water attacks both the α and β positions of this new intermediate to give the two regioisomers 5a and 5a', respectively.

![Scheme 1](image-url)  
Proable reaction mechanism for the hydrolysis of 3a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>Product (yield, %)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>3a (90)</td>
</tr>
<tr>
<td>2</td>
<td>1b</td>
<td>3b (92)</td>
</tr>
<tr>
<td>3</td>
<td>1c</td>
<td>3c (74)</td>
</tr>
<tr>
<td>4</td>
<td>1d</td>
<td>3d (85)</td>
</tr>
<tr>
<td>5</td>
<td>1e</td>
<td>3e (82)</td>
</tr>
<tr>
<td>6</td>
<td>1f</td>
<td>3f (74)</td>
</tr>
<tr>
<td>7</td>
<td>1g</td>
<td>3g (80)</td>
</tr>
<tr>
<td>8</td>
<td>1h</td>
<td>3h (68), 5h (10)</td>
</tr>
<tr>
<td>9</td>
<td>1i</td>
<td>3i (90)</td>
</tr>
<tr>
<td>10</td>
<td>1j</td>
<td>3j (32), 3j' (44)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>Product (yield, %)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>3a</td>
<td>5a (68), 5a' (22)</td>
</tr>
<tr>
<td>2</td>
<td>3d</td>
<td>5d (63), 5d' (11)</td>
</tr>
<tr>
<td>3</td>
<td>3g</td>
<td>5g (61), 5g' (29)</td>
</tr>
</tbody>
</table>

Table 1  Hydrazidohydroxylation of Styrenes with N-Acetyliminophthalimide Using PIFA

Table 2  Hydrolysis of the Trifluoroacetates of 3 in Acidic Conditions

* Reaction conditions: 1a–j (1 mmol), 2 (1.1 mmol), and PIFA (1.2 mmol) in CHCl₃ (10 mL); stirred for 0.5–1 h at reflux.

b Isolated yields of the pure products.

c A hydrolyzed product of 3h was detected in this case.
were used as authentic samples in the HPLC analysis. The phthaloyl and trifluoroacetyl groups of 3a were deprotected by the action of hydrazine hydrate as usual to give N-(2-hydroxy-2-phenylethyl)acetohydrazide (6) in 75% yield. Synthesis of hydrazinoethanols is rarely reported and this method will offer an alternative for their synthesis.

Taking the above-mentioned mechanism of hydrolysis into consideration, a plausible pathway for the original hydrazidohydroxylation reaction is shown in Scheme 2.

The hydrazidohydroxylation reaction proceeds in an electrophilic attack of 1a to the double bond, and subsequently without formation of aziridinium ions, the created carbocationic species can be captured by a free trifluoroacetate anion or quenched by the elimination of an adjacent hydrogen (entry 9) to afford the products.

In conclusion, we have achieved highly regioselective vicinal difunctionalization in a simple single-step reaction. Thus, the reaction of the nitrenium ion 1a with styrenes gave hydrazide derivatives having a trifluoroacetoxy group on the adjacent carbon in good yields. Further application of this methodology for the synthesis of lactams having a trifluoroacetoxy group in a molecule is underway.

All required fine chemicals were used directly without purification. CHCl₃ and THF used for the reactions were of commercial anhydrous grade. Silica gel (230–400 mesh) was used for column chromatography; while 250 μm silica gel plates were used for TLC analysis. The purities of several compounds were analyzed by high-performance liquid chromatography using Shimpack C₁₈ reverse phase column (4.6 mm x 150 mm), with flow rate 0.3 mL/min and a tunable UV detector set at 254 nm. A mixture of MeCN–H₂O (75:25) was used as mobile phase. ¹H NMR spectra were recorded at 270 or 500 MHz using TMS as reference. ¹³C NMR spectra were measured with a spectrometer at 67.8 or 125.7 MHz. Mass spectra were measured with a spectrometer.

Scheme 2 Proposed reaction mechanism for hydrazidohydroxylation

<table>
<thead>
<tr>
<th>R</th>
<th>ν (cm⁻¹)</th>
<th>J (Hz)</th>
</tr>
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<tr>
<td>1H NMR (270 MHz, CDCl₃, rotamers):</td>
<td>δ = 1.98 (s, 2.4 H), 2.37 (s, 0.9 H), 3.92–4.32 (m, 2 H), 6.37–6.55 (m, 1 H), 7.26–7.43 (m, 5 H), 7.8–8.01 (m, 4 H),</td>
<td>J = 14.8, 3.1 Hz, 0.6 H), 3.82 (dd, J = 15.4, 2.4 Hz, 1 H),</td>
</tr>
<tr>
<td>¹³C NMR (125.7 MHz, DMSO-d₆, rotamers):</td>
<td>δ = 19.6, 20.2, 50.0, 53.9, 77.3, 77.5, 114.2 (q, J = 286.1 Hz), 123.7, 123.90, 123.91, 124.1, 126.6, 126.9, 128.76, 128.79, 129.2, 129.3, 129.5, 129.64, 129.7, 134.9, 135.2, 135.3, 155.52 (q, J = 41.7 Hz), 155.54 (q, J = 41.7 Hz), 164.7, 165.0, 165.1, 165.4, 168.5, 171.6, FABMS (3-nitrobenzyl alcohol + Na): m/z (%) = 443 (M⁺ + Na, 28.7). Anal. Calcd for C₂₀H₁₄ClF₃N₂O₅: C, 52.82; H, 3.10; N, 6.66. Found: C, 57.33; H, 3.48; N, 6.49.</td>
<td></td>
</tr>
<tr>
<td>IR (KBr):</td>
<td>1740, 1700, 1700, 1220, 1150 cm⁻¹.</td>
<td>1740, 1700, 1700, 1220, 1150 cm⁻¹.</td>
</tr>
<tr>
<td>1-(2-Chlorophenyl)-2-[N-(1,3-dioxoisooindolin-2-yl)acetamido]ethyl 2,2,2-Trifluoroacetate (3b)</td>
<td>White crystals; mp 127–130 °C (Et₂O–hexane). IR (KBr): 1740, 1700, 1700, 1220, 1150 cm⁻¹.</td>
<td>1-(2-Chlorophenyl)-2-[N-(1,3-dioxoisooindolin-2-yl)acetamido]ethyl 2,2,2-Trifluoroacetate (3c)</td>
</tr>
</tbody>
</table>

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1H NMR (500 MHz, DMSO-d<sub>6</sub>, rotamers): δ = 1.98 (s, 2 H), 2.30 (s, 0.3 H), 3.87 (dd, J = 15.4, 9.5 Hz, 1 H), 4.40 (dd, J = 15.4, 2.7 Hz, 1 H), 5.95 (dd, J = 9.5, 3.5 Hz, 0.1 H), 6.11 (dd, J = 9.5, 2.7 Hz, 0.9 H), 7.26–7.44 (m, 4 H), 7.81–8.01 (m, 4 H).

FABMS (3-nitrobenzyl alcohol + NaI): m/z (%) = 477 (M<sup>+</sup> + Na<sup>+</sup>, 26.7).

Anal. Caled for C<sub>22</sub>H<sub>17</sub>F<sub>3</sub>N<sub>2</sub>O<sub>5</sub>; C, 58.07; H, 3.46. Found: C, 58.15; H, 4.04; N, 6.39.

2-[1-(3-Dioxoisooindolin-2-yl)acetamido]-1-p-tolylethyl 2,2,2-Trifluoroacetate (3g)

White crystals; mp 95–97 °C (Et<sub>2</sub>O–hexane).

IR (KBr): 1790, 1750, 1700, 1230, 1150 cm<sup>-1</sup>.

1H NMR (500 MHz, DMSO-d<sub>6</sub>, rotamers): δ = 1.98 (s, 1.7 H), 2.30, 2.31, 2.34 (s each, 4.3 H), 3.72 (dd, J = 14.8, 2.9 Hz, 0.5 H), 3.83 (dd, J = 15.9, 3.1 Hz, 0.5 H), 4.56–4.65 (m, 1 H), 6.06–6.11 (m, 1 H), 7.22 (d, J = 10.0 Hz, 1 H), 7.25 (d, J = 10.0 Hz, 1 H), 7.34 (d, J = 10.0 Hz, 1 H), 7.45 (d, J = 10.0 Hz, 1 H) 7.95–8.08 (m, 4 H).

13C NMR (125.7 MHz, DMSO-d<sub>6</sub>, rotamers): δ = 19.6, 20.2, 20.9, 50.0, 53.9, 77.3, 77.5, 114.2 (q, J = 285.7 Hz), 123.7, 123.8, 123.8, 123.8, 123.8, 123.8, 123.8, 123.8, 127.0, 129.5, 129.5, 129.5, 129.5, 130.7, 130.7, 130.8, 130.8, 131.3, 135.4, 135.5, 135.5, 135.5, 135.5, 135.5, 135.5, 138.1, 155.5 (q, J = 40.2 Hz), 155.8 (q, J = 41.7 Hz), 164.7, 165.0, 165.1, 165.3, 168.5, 171.6.

FABMS (3-nitrobenzyl alcohol + NaI): m/z (%) = 475 (M<sup>+</sup> + Na<sup>+</sup>, 19.8).

Anal. Caled for C<sub>23</sub>H<sub>18</sub>F<sub>3</sub>N<sub>2</sub>O<sub>7</sub>; C, 55.24; H, 3.58; N, 5.86. Found: C, 54.94; H, 3.68; N, 5.81.

Methyl 4-[2-[1-(3-Dioxoisooindolin-2-yl)acetamido]-1-hydroxyethyl]benzoate (5h)

White crystals; mp 136–138 °C (Et<sub>2</sub>O–hexane).

IR (KBr): 3050, 1740, 1630, 1380, 1280 cm<sup>-1</sup>.

1H NMR (500 MHz, DMSO-d<sub>6</sub>, rotamers): δ = 1.91 (s, 1.6 H), 2.15 (s, 1.4 H), 3.58–3.61 (m, 0.7 H), 3.72 (dd, J = 15.3, 5.0 Hz, 0.8 Hz), 3.84 (s, 3 H), 3.97 (dd, J = 15.3, 5.0 Hz, 0.5 H), 4.07 (dd, J = 14.4, 5.0 Hz, 0.5 H), 4.80 (dd, J = 8.0, 5.0 Hz, 0.5 H), 4.92 (dd, J = 8.0, 5.0 Hz, 0.5 H), 7.50 (d, J = 8.2 Hz, 1 H), 7.65 (d, J = 8.2 Hz, 1 H), 7.89 (d, J = 8.2 Hz, 1 H), 7.95–8.01 (m, 4 H).

13C NMR (125.7 MHz, DMSO-d<sub>6</sub>, rotamers): δ = 19.9, 20.6, 52.0, 52.1, 52.2, 57.8, 70.5, 70.8, 123.67, 123.71, 123.9, 124.0, 126.4, 126.6, 128.5, 128.6, 129.0, 129.0, 129.4, 129.5, 129.5, 132.0, 135.2, 135.3, 148.29, 148.31, 164.5, 164.9, 165.1, 165.2, 166.07, 166.11, 169.1, 171.7.

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N-(1,3-Dioxoisindolin-2-yl)-N-(2-phenylallyl)acetamide (3i)
White crystals: mp 112–115 °C (Et₂O–hexane).

IR (KBr): 1800, 1740, 1690 cm⁻¹.

1H NMR (500 MHz, DMSO-d₆, rotamers): δ = 1.91 (s, 2.1 H), 2.24 (s, 0.9 H), 4.73 (s, 1.4 H), 4.87 (s, 0.6 H), 5.28 (s, 0.7 H), 5.48 (s, 0.7 H), 5.55 (s, 0.3 H), 5.69 (s, 0.3 H), 7.23–7.57 (m, 5 H), 7.93–8.04 (m, 4 H).

13C NMR (125.7 MHz, DMSO-d₆, rotamers): δ = 15.4, 15.8, 20.1, 20.2, 20.3, 20.7, 49.6, 54.3, 115.7, 117.5, 122.5, 123.7, 123.8, 123.9, 124.0, 124.1, 128.3, 128.4, 128.6, 129.5, 129.6, 129.7, 129.3, 134.6, 135.3, 135.38, 135.42, 135.5, 138.0, 138.5, 138.9, 139.4, 141.1, 164.3, 164.4, 164.5, 164.7, 169.0, 169.1, 170.2, 171.4.

FABMS (3-nitrobenzyl alcohol + Na⁺): m/z (%) = 405 (M⁺ + Na, 100).


FABMS (3-nitrobenzyl alcohol + Na⁺): m/z (%) = 457 (M⁺ + Na, 52.0).

Anal. Calcd for C₉₄H₁₃F₃N₂O₁₂: C, 58.07; H, 3.94; N, 6.45. Found: C, 57.99; H, 3.94; N, 6.35.

N-(1,3-Dioxoisindolin-2-yl)-N-(2-hydroxy-2-phenethyl)acetamide (5a) and N-(1,3-Dioxoisindolin-2-yl)-N-(2-hydroxy-1-phenylethyl)acetamide (5a′)
A mixture of 3a (71 mg, 0.169 mmol) in AcOH-H₂O (2:1, 9 mL) was heated at 70 °C for 0.5 h. After the reaction was complete, the mixture was diluted with EtOAc (50 mL). The organic layer was washed with brine (2 × 30 mL) and dried (Na₂SO₄). After removal of the solvent in vacuo, the mixture was purified by column chromatography on silica gel using 50% EtOAc–hexane to give the products 5a (37 mg, 68%) and 5a′ (12 mg, 22%) (Table 2).

5a
White crystals; mp 122–123 °C (EtOAc–hexane).

IR (KBr): 3420, 1800, 1740, 1690 cm⁻¹.

1H NMR (270 MHz, CDCl₃, + D₂O, rotamers): δ = 2.02 (s, 1.8 H), 2.38 (s, 1.2 H), 3.59–3.79 (m, 1 H), 3.95 (dd, J = 14.8, 9.7 Hz, 0.4 H), 4.13 (dd, J = 14.8, 2.1 Hz, 0.6 H), 4.84 (dd, J = 14.8, 2.7 Hz, 0.4 H), 5.02 (d, J = 9.4 Hz, 0.6 H) 7.19–7.42 (m, 5 H), 7.82–8.02 (m, 4 H).

13C NMR (125.7 MHz, DMSO-d₆, rotamers): δ = 19.0, 20.5, 52.2, 58.2, 70.7, 71.3, 123.6, 123.7, 123.9, 124.0, 124.1, 126.3, 126.7, 127.3, 127.32, 128.7, 128.11, 129.3, 129.4, 129.58, 129.61, 135.21, 135.23, 135.3, 142.8, 143.0, 164.5, 165.0, 166.0, 165.4, 169.0, 171.7.

EIMS: m/z (%) = 324 (M⁺, 0.1), 175 (100), 148 (56), 130 (46).

Anal. Calcd for C₂₁H₁₇F₃N₂O₅: C, 66.66; H, 4.97; N, 6.84. Found: C, 66.60; H, 5.00; N, 8.60.

5a′
White crystals; mp 151–152 °C (EtOAc–hexane).

IR (KBr): 3340, 1790, 1750, 1720 cm⁻¹.

1H NMR (270 MHz, CDCl₃, + D₂O, rotamers): δ = 2.12 (s, 3.3 H), 3.36 (dd, J = 13.2, 4.1 Hz, 1 H), 3.51 (dd, J = 13.5, 9.1 Hz, 1 H), 5.9 (dd, J = 8.9, 3.9 Hz, 1 H), 7.25–7.38 (m, 5 H), 7.71–7.86 (m, 4 H).

13C NMR (125.7 MHz, DMSO-d₆, rotamers): δ = 20.7, 54.2, 74.5, 123.0, 126.7, 127.8, 130.0, 134.5, 139.0, 166.7, 169.5.

FABMS (3-nitrobenzyl alcohol): m/z (%) = 325 (M⁺ + H, 26.1), 307 (100), 265 (32.2), 154 (46.2), 136 (38.9).

Anal. Calcd for C₂₁H₁₃F₃N₂O₅: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.28; H, 5.01; H: 8.57.

Deprotection of the Phthaloyl and Trifluoroacetyl Groups in 3a, d, d′, g, g′; N-(2-Hydroxy-2-phenethyl)acetohydrazide (6); Typical Procedure
A mixture of 3a (519 mg, 1.235 mmol) and 80% hydrazine monohydrate (386 mg, 6.168 mmol) in EtOH (5 mL) was stirred for 0.5 h at reflux. After the reaction was complete, the mixture was evaporated and the residue was diluted with EtOAc (30 mL). The mixture was filtered off and the filtrate was evaporated again. The residue was purified by column chromatography on silica gel using EtOAc to give the product 6 (176 mg, 74%); white crystals; mp 128–130 °C (EtOAc–hexane).

IR (KBr): 3230, 3200, 1655, 1620 cm⁻¹.

1H NMR (500 MHz, DMSO-d₆, + D₂O, rotamers): δ = 1.79 (s, 0.9 H), 2.04 (s, 2.1 H), 2.34 (dd, J = 14.5, 4.8 Hz, 0.3 H), 3.47 (dd, J = 9.4 Hz, 0.7 H), 7.19–7.42 (m, 5 H), 7.82–8.02 (m, 4 H).

Hydrazidohydroxylation of Styrenes
N-(1,3-Dioxoisooindolin-2-yl)-N-(2-hydroxy-1-p-tolyethy)acetamide (5g)

White crystals; mp 126–127 °C (EtOAc–hexane).

IR (KBr): 3450, 1790, 1750, 1720, 1400 cm⁻¹.

1H NMR (500 MHz, DMSO-d₆, rotamers): δ = 1.91 (s, 3 H), 2.24 (s, 3 H) 3.20 (dd, J = 14.0, 9.0 Hz, 1 H), 3.35 (dd, J = 15.0, 10.0 Hz, 1 H), 5.67 (dd, J = 10.0, 5.0 Hz, 1 H), 7.13 (d, J = 7.9 Hz, 2 H), 7.21 (d, J = 7.9 Hz, 2 H), 7.87 (s, 4 H).

13C NMR (125.7 MHz, DMSO-d₆): δ = 20.2, 20.4, 53.9, 74.0, 122.5, 126.0, 129.7, 134.1, 135.6, 136.7, 166.1, 169.0.

EIMS: m/z (%) = 338 (M⁺, 0.8), 278 (86), 175 (100), 130 (31.2). Anal. Calcd for C₁₉H₁₈N₂O₄: C, 67.45; H, 5.36; N, 8.28. Found: C, 67.54; H, 5.35; N, 8.36.

Trifluoroacetylation of 5a’, 5d’, 5g’; 2-[N-(1,3-Dioxoisooindolin-2-yl)acetamido]-2-phenylethyl 2,2,2-Trifluoroacetate (3a’)

Typical Procedure

Trifluoroacetic anhydride (0.1 mL, 0.525 mmol) was added to a solution of 5a’ (34 mg, 0.105 mmol) in pyridine (0.1 mL, 0.525 mmol) and THF (2.4 mL) at 0 °C. After stirring for 5 min, the reaction was quenched with 1% HCl (4 mL) and the mixture was extracted with Et₂O (2 ´ 20 mL). The combined organic solvents were washed with brine (15 mL), dried (Na₂SO₄), and concentrated. The residue was purified by short column chromatography on silica gel using 60% EtOAc–hexane to give the product 3a’ (31 mg, 70%); colorless crystals; mp 121–123 °C (EtOAc–hexane); HPLC: tR = 21.08.

IR (KBr): 3420, 1810, 1750, 1720, 1240, 1200 cm⁻¹.

1H NMR (270 MHz, CDCl₃, rotamers): δ = 1.95 (s, 2.6 H), 2.06 (s, 0.4 H), 4.05 (dd, J = 14.9, 9.6 Hz, 1 H), 4.25 (dd, J = 14.9, 3.2 Hz, 1 H), 5.94 (dd, J = 9.6, 3.1 Hz, 1 H), 7.26–7.37 (m, 5 H), 7.84–8.01 (m, 4 H).

13C NMR (125.7 MHz, DMSO-d₆, rotamers): δ = 20.5, 20.7, 53.4, 54.8, 71.1, 71.8, 115.2 (q, J = 288.4 Hz), 116.3 (q, J = 288.1 Hz), 124.2, 124.4, 124.5, 126.1, 126.2, 128.3, 128.5, 128.6, 129.0, 129.2, 129.4, 135.7, 135.8, 136.9, 137.3, 143.0, 157.4 (q, J = 34.4 Hz), 158.7 (q, J = 34.4 Hz), 163.7, 163.9, 169.2, 169.4.

FABMS (3-nitrobenzyl alcohol): m/z (%) = 421 (M⁺ + H, 3.3), 361 (100).


2-(4-Chlorophenyl)-2-hydroxyethyl-N-(1,3-dioxoisooindolin-2-yl)acetamide (5h)

White crystals; mp 94–95 °C (Et₂O–hexane).

IR (KBr): 1800, 1760, 1720, 1230, 1200 cm⁻¹.

1H NMR (500 MHz, DMSO-d₆, rotamers): δ = 1.91 (s, 3 H), 2.24 (s, 3 H) 3.20 (dd, J = 14.4, 3.7 Hz, 1 H), 4.41 (dd, J = 14.4, 10.1 Hz, 1 H), 5.87 (dd, J = 9.9, 3.9 Hz, 1 H), 7.42–7.46 (m, 4 H), 8.02–8.12 (m, 4 H).

13C NMR (125.7 MHz, DMSO-d₆): δ = 20.6, 52.9, 71.1, 114.9 (q, J = 288.8 Hz), 124.3, 124.4, 128.3, 128.4, 128.9, 129.0, 132.9, 135.8, 136.2, 157.2 (q, J = 36.5 Hz) 163.6, 163.8, 169.3.

FABMS (3-nitrobenzyl alcohol): m/z (%) = 455 (M⁺ + H, 3.2), 395 (40.3).

Anal. Calcd for C₂₀H₁₆ClN₂O₅: C, 52.82; H, 3.10; N, 6.16. Found: C, 52.94; H, 3.22; N, 6.31.

2-[N-(1,3-Dioxoisooindolin-2-yl)acetamido]-2-p-tolyethyl 2,2,2-Trifluoroacetate (3g)

White crystals; mp 94–95 °C (EtOAc–hexane).

IR (KBr): 1800, 1760, 1720, 1240, 1200 cm⁻¹.
Hydrazidohydroxylation of Styrenes

$^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 2.0$ (s, 3 H), 2.27 (s, 3 H), 3.88 (dd, $J = 3.6$, 10.2 Hz, 1 H), 7.17 (d, $J = 8.1$ Hz, 2 H), 7.29 (d, $J = 8.1$ Hz, 2 H), 8.01–8.11 (m, 4 H).

$^{13}$C NMR (125.7 Hz, DMSO-$d_6$): $\delta = 20.7$, 53.3, 71.6, 115.2 (q, $J = 297.7$ Hz), 124.4, 124.5, 126.4, 129.0, 129.1, 129.2, 134.3, 135.8, 137.7, 157.3 (q, $J = 36.2$ Hz), 163.7, 163.9, 169.4.

FABMS (3-nitrobenzylalcohol + NaI): $m/z$ (%) = 457 (M$^+$ + Na, 100).

Anal. Calcd for C$_{21}$H$_{17}$F$_3$N$_2$O$_5$: C, 58.07; H, 3.94; N, 6.45. Found: C, 58.16; H, 4.09; N, 6.46.

References


(3) Kikugawa, Y.; Shimada, M.; Matsumoto, K. *Heterocycles* 1994, 37, 293.


(11) In the intramolecular cyclization of an $N$-acylnitrenium ion and the olefin fragment in a molecule, Tellitu and Domínguez reported that the created carbocationic species are stabilized by the formation of aziridinium ion intermediates. See references 6j, l and m.


graphical abstract?????