INTRAMOLECULAR BENZYLIC CYCLIZATION WITH NITRENIIUM IONS GENERATED FROM N-ACYLAMINOPHTHALIMIDES USING PHENYLIODINE(III) BIS(TRIFLUOROACETATE): FORMATION OF PHENYL SUBSTITUTED LACTAMS

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Abstract – N-Phthalimido-N-acylnitrenium ions generated from N-acylaminophthalimides using phenyliodine(III) bis(trifluoroacetate) in polyfluoro alcohols do not undergo intramolecular aromatic substitution reactions. Instead, intramolecular cyclization to the benzylic position occurs to afford lactams having a phenyl group substituted at the α-position to the ring nitrogen. These reactions proceed in moderate to good yields.

Nitrenium ions continue to receive increasing attention from synthetic, theoretical, and biological perspectives. However, synthetic applications of nitrenium ions remain limited, primarily because they exist only as short-lived reaction intermediates. We have been exploring strategies to increase the lifetime of the ion in order to enhance the synthetic value of this species.

In previous work, we have reported that N-methoxy- and N-allyloxy-N-acylnitrenium ions (I and II) can be generated from the corresponding N-chloro-N-methoxyamides and N-chloro-N-allyloxyamides, respectively, by the action of silver or zinc ion. We have also reported that I^4 and N-phthalimido-N-acylnitrenium ions (III)^5 can be generated directly from the corresponding N-methoxyamides and N-acylaminophthalimides, respectively, by the action of phenyliodine(III) bis(trifluoroacetate) (PIFA). These nitrenium ions are stabilized by adjacent methoxy, allyloxy and phthalimido groups, respectively, attached to the nitrogen, and are able to undergo intramolecular substitution reactions with a range of aromatic compounds. PIFA is the most frequently used and easily available reagent in the family of hypervalent iodine compounds, and Wardrop et al. recently utilized PIFA for the generation of I in the synthesis of biologically active compounds.^6

This paper is dedicated to Professor Dr. Ekkehard Winterfeldt on the occasion of his 75th birthday.
Herein, we report that III, having a pendant phenyl group suitably located in a molecule, do not undergo intramolecular aromatic substitution reactions, but instead intramolecular cyclization to the benzylic position occurs to give phenyl substituted lactams in moderate to good yields. Previously we had examined PIFA-mediated cyclization of N-methoxy-5-phenylpentanamide in hexafluoroisopropanol and obtained the benzannulated compound, 1-methoxy-3,4,5,6-tetrahydro-1-benzoazocin-2(1H)-one in 72% yield.7 We undertook preliminary experiments to examine intramolecular cyclization of N-(5-phenylpentanamido)phthalimide (1a) with PIFA in various solvents, anticipating a similar benzannulation to occur. However, treatment of 1a with PIFA for 18 h at room temperature afforded 5-phenyl-N-phthalimido-δ-lactam (2a), the product of cyclization to the benzylic position, in 46% yield in 2,2,3,3-tetrafluoro-1-propanol and in 36% yield in 2,2,2-trifluoroethanol. In contrast to the previous work, the reaction produced only small amounts of the benzannulated compound, 1-phthalimido-3,4,5,6-tetrahydro-1-benzoazocin-2(1H)-one (3). Thus, the nitrenium ion generated by PIFA attacks the benzylic position, presumably because formation of an eight-membered ring required for benzannulation is unfavorable. We believe that this is the first case wherein a nitrenium ion attack at an aliphatic carbon is preferred over aromatic substitution. We examined this unprecedented reaction further with substrates 1b-j. Initially, the effects of solvent on the reaction were studied. The results are presented in Table 1.

Table 1. Benzylic cyclization of 1a with PIFA in various solvents

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Product (2a) Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₂Cl₂</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>CHCl₃</td>
<td>trace</td>
</tr>
<tr>
<td>3</td>
<td>CF₃CH₂OH</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>(CF₃)₂CHOH</td>
<td>36 + trace⁺</td>
</tr>
<tr>
<td>5</td>
<td>CHF₂CF₂CH₂OH</td>
<td>46 + trace⁺</td>
</tr>
</tbody>
</table>
The yield of 2a is slightly better in 2,2,3,3-tetrafluoro-1-propanol than in 2,2,2-trifluoroethanol. In the case of long chain fluorinated solvents the reaction proceeds unsatisfactorily probably because of poor solubility of 1a in these solvents (entries 6 and 7). Generally reactions in poorly nucleophilic polar solvents gave good results, while use of other polar solvents such as dichloromethane and chloroform did not give satisfactory results. The combination of the phthalimido group and fluorinated solvents plays an important role for the stabilization of the acyl nitrenium ion and for its further reaction. Several N-(phenylpentanamido)phthalimides (1a-h) and the similar compounds (1i and 1j) reacted in a similar way and the results are presented in Table 2.

**Table 2.** Benzylic cyclization of N-(5-phenylpentanamido)phthalimides (1) with PIFA

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting Material</th>
<th>Reaction Time (h)</th>
<th>Product Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a (X = H)</td>
<td>18</td>
<td>2a (46)</td>
</tr>
<tr>
<td>2</td>
<td>1b (X = F)</td>
<td>5</td>
<td>2b (73)</td>
</tr>
<tr>
<td>3</td>
<td>1c (X = Cl)</td>
<td>18</td>
<td>2c (56)</td>
</tr>
<tr>
<td>4</td>
<td>1d (X = Br)</td>
<td>18</td>
<td>2d (71)</td>
</tr>
<tr>
<td>5</td>
<td>1e (X = I)</td>
<td>18</td>
<td>2e (72)</td>
</tr>
<tr>
<td>6</td>
<td>1f (X = OMe)</td>
<td>4</td>
<td>3 (10)</td>
</tr>
</tbody>
</table>

\[ \text{H}(\text{CF}_2)_6\text{CH}_2\text{OH} \] 2

\[ \text{CF}_3(\text{CF}_2)_2\text{OCF}(\text{CF}_3)\text{CH}_2\text{OH} \] 7

\(^a\) Yield of compound 3.
These results show that benzylic cyclization occurs in good yields with compounds having a 4-halogenophenyl group (Table 2, entries 1-5) and that seven membered spirodienones are formed from compounds having 4-alkoxyphenyl groups (Table 2, entries 6 and 7). Compound 1h, which has an electron-withdrawing cyano group in the para-position, did not give rise to either the benzannulated and spirobenzannulated products. Instead, the 4-iodophenyl group was transferred from PIFA to the amide nitrogen to afford the acyldiarylamine 5 in 70% yield.

The nitrenium ions formed from 1i and 1j, which have two reaction sites in a molecule, gave rise to both the benzannulated and the benzylic cyclization compounds.

As for the reaction mechanism it is assumed from the by-products that initially PIFA attacks the amide moiety of 1 to afford an electron deficient nitrogen that behaves as a nitrenium ion; however, the precise reaction mechanism, especially the reason for the benzylic carbon-nitrogen bond formation, remains unclear.

In summary, we have developed a new method for the synthesis of phenyl substituted lactams from N-acylaminophthalimides using PIFA in 2,2,3,3-tetrafluoro-1-propanol. PIFA reacts with the amide nitrogen to form an intermediate, which is decomposed to generate an electron deficient nitrogen ion (III). When the phenyl group is not suitably located in a molecule, the benzyl position is attacked by this electron deficient nitrogen to form phenyl substituted lactams in moderate to good yields.

**EXPERIMENTAL**

All the melting points were determined with a Yanagimoto hot-stage melting point apparatus and are uncorrected. $^1$H NMR (270 MHz) spectra and $^{13}$C NMR spectra (68 MHz) were measured on a JEOL JNM-EX270 spectrometer with tetramethylsilane (MeSi$_4$) as an internal reference. $^1$H NMR and $^{13}$C
NMR spectral data are reported in parts per million (δ) relative to MeSi4. IR spectra were recorded on a JASCO IR 810 spectrophotometer. MS spectra were obtained with a JEOL JMX-DX 300 spectrometer with a direct inlet system at 70 eV. Elemental analyses were performed in the Microanalytical Laboratory of this University.

All the starting materials 1a-j were prepared by the reaction of the corresponding acid chlorides with N-aminophthalimide in dry pyridine.5d 5-Arylpentanoic acids were synthesized by the literature method.9 2-Benzylbenzoic acid and 2-phenethylbenzoic acids were commercially available.

**N-(1,3-Dioxoisooindolin-2-yl)-5-phenylpentanamide (1a).** Colorless crystals: mp 132-134 °C (AcOEt/n-hexane); IR (KBr) 3250, 1805, 1750, 1670, 1525, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.72-1.82 (m, 4H), 2.43 (t, J = 7.1 Hz, 2H), 2.67 (t, J = 6.8 Hz, 2H), 7.14-7.33 (m, 6H), 7.77-7.83 (m, 2H), 7.87-7.94 (m, 2H); EI-MS m/z 332 (M⁺, 0.6), 162 (100), 117 (16.7), 91 (39.8); FAB-MS m/z 333 (M⁺ + 1). Anal. Calcd for C₁₉H₁₈N₂O₃: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.74; H, 5.60; N, 8.68.

**N-(1,3-Dioxoisooindolin-2-yl)-5-(4-fluorophenyl)pentanamide (1b).** Colorless crystals: mp 132-133 °C (AcOEt/n-hexane); IR (KBr) 3170, 3000, 1790, 1750, 1670, 1510, 1220, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.61-1.87 (m, 4H), 2.43 (t, J = 7.0 Hz, 2H), 2.63 (t, J = 6.9 Hz, 2H), 6.90-7.01 (m, 2H), 7.08-7.19 (m, 2H), 7.37 (br s, 1H), 7.74-7.83 (m, 2H), 7.86-7.96 (m, 2H); EI-MS m/z 340 (M⁺, 0.4), 162 (100), 109 (48.6); FAB-MS m/z 341 (M⁺ + 1, 48.8). Anal. Calcd for C₁₉H₁₇FN₂O₃: C, 67.05; H, 5.03; N, 8.23. Found: C, 67.17; H, 5.12; N, 8.26.

**N-(1,3-Dioxoisooindolin-2-yl)-5-(4-chlorophenyl)pentanamide (1c).** Colorless crystals: mp 148-149 °C (AcOEt-n-hexane); IR (KBr) 3170, 3000, 1790, 1750, 1670, 1500, 1220, 870 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.65-1.85 (m, 4H), 2.43 (t, J = 6.8 Hz, 2H), 2.63 (t, J = 6.9 Hz, 2H), 7.14 (d, J = 8.7 Hz, 2H), 7.24 (d, J = 8.7 Hz, 2H), 7.43 (br s, 1H), 7.73-7.84 (m, 2H), 7.85-7.98 (m, 2H); EI-MS m/z 358 (M⁺ + 2, 0.1), 356 (M⁺, 0.3), 292 (2.1), 238 (7.5), 194 (8.7), 162 (100), 151 (12.5), 125 (28.7). Anal. Calcd for C₁₉H₁₇ClN₂O₃: C, 63.96; H, 4.80; N, 7.85. Found: C, 63.93; H, 4.85; N, 7.83.

**N-(1,3-Dioxoisooindolin-2-yl)-5-(4-bromophenyl)pentanamide (1d).** Colorless crystals: mp 165-167 °C (AcOEt-n-hexane); IR (KBr) 3260, 1800, 1755, 1675, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.65-1.85 (m, 4H), 2.43 (t, J = 6.9 Hz, 2H), 2.62 (t, J = 6.9 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.29 (br s, 1H), 7.74-7.84 (m, 2H), 7.86-7.96 (m, 2H); EI-MS m/z 402 (M⁺ + 2, 0.3), 400 (M⁺, 0.3), 292 (2.1), 238 (7.5), 171 (19.5), 169 (19.9), 162 (100), 104 (15.0). Anal. Calcd for C₁₉H₁₇BrN₂O₃: C, 56.87; H, 4.27; N, 6.98. Found: C, 57.06; H, 4.04; N, 6.97.

**N-(1,3-Dioxoisooindolin-2-yl)-5-(4-iodophenyl)pentanamide (1e).** Colorless crystals: mp 178-179 °C (CHCl₃-n-hexane); IR (KBr) 3250, 1800, 1750, 1670, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.67-1.87 (m, 4H), 2.43 (t, J = 7.0 Hz, 2H), 2.61 (t, J = 7.0 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 7.40 (br s, 1H), 7.60
(d, J = 8.4 Hz, 2H), 7.74-7.83 (m, 2H); EI-MS m/z 448 (M⁺, 3.1), 286 (50.2), 162 (100); FAB-MS m/z 449 (M⁺ + 1, 27.7). Anal Calcd for C₁₉H₁₇IN₂O₃: C, 50.91; H, 3.82; N, 6.25. Found: C, 50.95; H, 3.85; N, 6.28.

N-(1,3-Dioxoisindolin-2-yl)-5-(4-methoxyphenyl)pentanamide (1f). Colorless crystals: mp 134-135 °C (AcOEt-n-hexane); IR (KBr) 3250, 1800, 1750, 1675, 1515, 1250, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.62-1.76 (m, 4H, CH), 2.42 (t, J = 6.9 Hz, 2H), 2.61 (t, J = 7.3 Hz, 2H), 3.78 (s, 3H), 6.82 (d, J = 8.5 Hz, 2H), 7.11 (d, J = 8.5 Hz, 2H), 7.35 (br s, 1H), 7.74-7.83 (m, 2H), 7.86-7.96 (m, 2H); EI-MS m/z 352 (M⁺, 11.0), 190 (100), 162 (15.4), 147 (46.1), 134 (47.5), 121 (61.2). Anal. Calcd for C₂₀H₂₀N₂O₄: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.05; H, 5.66; N, 7.84.

N-(1,3-Dioxoisindolin-2-yl)-5-(4-(2,2,2-trifluoroethoxy)phenyl)pentanamide (1g). Colorless crystals: mp 144-145 °C (AcOEt-n-hexane); IR (KBr) 3450, 1800, 1750, 1675, 1510, 1235 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.64-1.86 (m, 4H), 2.43 (t, J = 6.9 Hz, 2H), 2.62 (t, J = 6.8 Hz, 2H), 4.32 (q, J_H-F = 7.2 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.5 Hz, 2H), 7.35 (br s, 1H), 7.74-7.83 (m, 2H), 7.86-7.95 (m, 2H); EI-MS m/z 420 (M⁺, 0.6), 258 (100), 215 (40.4), 209 (49.3), 189 (56.2), 162 (31.1). Anal. Calcd for C₂₁H₁₉F₃N₂O₄: C, 60.00; H, 4.56; N, 6.66. Found: C, 59.77; H, 4.50; N, 6.76.

5-(4-Cyanophenyl)-N-(1,3-dioxoisindolin-2-yl)pentanamide (1h). Colorless crystals: mp 165-166 °C (AcOEt-n-hexane); IR (KBr) 3280, 1795, 1725, 1700, 1425, 1125, 715, 705 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.73-1.83 (m, 4H), 2.41-2.49 (m, 2H), 2.67-2.77 (m, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.42 (br s, 1H), 7.58 (d, J = 8.1 Hz, 2H), 7.77-7.83 (m, 2H), 7.89-7.94 (m, 2H); EI-MS m/z 347 (M⁺, 0.04), 162 (100), 116 (33.9); FAB-MS m/z 348 (M⁺ + 1, 48.5). Anal Calcd for C₂₀H₁₇IN₃O₃: C, 69.15; H, 4.93; N, 12.10. Found: C, 69.15; H, 5.00; N, 12.14.

2-Benzyl-N-(1,3-dioxoisindolin-2-yl)benzamide (1i). Colorless crystals: mp 198-201 °C (AcOEt-n-hexane); IR (KBr) 3280, 1795, 1725, 1700, 1425, 1125, 715, 705 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 4.27 (s, 2H), 7.17 (t, J = 7.6 Hz, 1H), 7.32-7.40 (m, 4H), 7.45 (td, J = 7.7, 1.3 Hz, 1H), 7.69 (d, J = 7.7 Hz, 2H), 7.91-8.02 (m, 4H); EI-MS m/z 356 (M⁺, 2.9), 195 (100), 165 (21.1). Anal. Calcd for C₂₂H₁₆N₂O₃: C, 74.15; H, 4.53; N, 7.86. Found: C, 74.15; H, 5.00; N, 7.85.

N-(1,3-Dioxoisindolin-2-yl)-2-phenethylbenzamide (1j). Colorless crystals: mp 189-192 °C (AcOEt); IR (KBr) 3290, 1795, 1730, 1705, 765, 715, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 3.02 (t, J = 7.5 Hz, 2H), 3.19 (t, J = 7.5 Hz, 2H), 7.11-7.34 (m, 8H), 7.44 (t, J = 7.2 Hz, 1H), 7.64 (d, J = 7.4 Hz, 1H), 7.78-7.88 (m, 2H), 7.91-7.99 (m, 2H); EI-MS m/z 370 (M⁺, 0.1), 209 (100), 131 (34.9); FAB-MS m/z 371 (M⁺ + 1). Anal. Calcd for C₂₃H₁₈N₂O₃: C, 74.58; H, 4.90; N, 7.56. Found: C, 74.59; H, 4.81; N, 7.53.

Reaction of N-(1,3-Dioxoisindolin-2-yl)-5-(4-bromophenyl)pentanamide (1d) with PIFA in 2,2,3,3-Tetrafluoro-1-propanol. A Typical Experimental Procedure for Table 2
PIFA (161 mg, 0.37 mmol) was added to a solution of 1d (100 mg, 0.25 mmol) in 2,2,3,3-tetrafluoro-1-propanol (20 mL). The reaction mixture was stirred at room temperature for 22 h under argon atmosphere. After the reaction, the mixture was evaporated and the residue was diluted with EtOAc (40 mL). The organic layer was washed with 10% Na₂CO₃ aq. (15 mL x 2), brine, and dried over Na₂SO₄. After removal of solvent, the residue was purified by column chromatography, eluting with EtOAc/toluene (1:10), to give 2d (71 mg, 71%).

2-(2-Oxo-6-phenylpiperidin-1-yl)isoindoline-1,3-dione (2a). Colorless crystals: mp 170-173 °C (AcOEt/n-hexane); IR (KBr) 1795, 1740, 1680, 1380, 715, 705 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 2.00-2.20 (m, 3H), 2.29-2.39 (m, 1H), 2.72-2.81 (m, 2H), 5.08-5.19 (m, 1H), 7.19-7.32 (m, 3H), 7.43 (d, J = 6.4 Hz, 2H), 7.64-7.74 (m, 3H), 7.76-7.82 (m, 1H); EI-MS m/z 320 (M⁺, 0.3), 251 (7.1), 173 (82.1), 145 (100), 130 (41.6), 104 (25.9); FAB-MS m/z 321 (M⁺ + 1). Anal. Calcd for C₁₉H₁₆N₂O₃: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.22; H, 4.77; N, 8.74.

2-(2-(4-Fluorophenyl)-6-oxopiperidin-1-yl)isoindoline-1,3-dione (2b). Colorless crystals: mp 220-222 °C (CHCl₃-n-hexane); IR (KBr) 2950, 1790, 1730, 1680, 700 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 2.00-2.16 (m, 3H), 2.26-2.37 (m, 1H), 2.75 (t, J = 5.9 Hz, 2H), 5.06-5.15 (m, 1H), 6.92-7.01 (m, 2H), 7.37-7.45 (m, 2H), 7.66-7.83 (m, 4H); EI-MS m/z 338 (M⁺, 0.1), 192 (43.7), 191 (48.0), 163 (100), 148 (42.8); FAB-MS m/z 339 (M⁺ + 1, 80.6). Anal. Calcd for C₁₉H₁₅FN₂O₃: C, 67.45; H, 4.47; N, 8.28. Found: C, 67.72; H, 4.61; N, 8.34.

2-(2-(4-Chlorophenyl)-6-oxopiperidin-1-yl)isoindole-1,3-dione (2c). Colorless crystals: mp 217-219 °C (AcOEt/n-hexane); IR (KBr) 1795, 1735, 1685, 1380, 1190, 880, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.96-2.14 (m, 3H), 2.23-2.38 (m, 1H), 2.74 (t, J = 5.5 Hz, 2H), 5.06-5.14 (m, 1H), 7.26 (d, J = 8.5 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.64-7.83 (m, 4H); EI-MS m/z 357 (M⁺ + 2 + H, 2.5), 355 (M⁺ + H, 7.6), 319 (8.3), 308 (14.9), 208 (40.6), 179 (77.2), 172 (100); FAB-MS m/z 355 (M⁺ + 1, 67.5). Anal. Calcd for C₁₉H₁₅ClN₂O₃: C, 64.32; H, 4.26; N, 7.90. Found: C, 64.35; H, 4.02; N, 7.93.

2-(2-(4-Bromophenyl)-6-oxopiperidin-1-yl)isoindole-1,3-dione (2d). Colorless crystals: mp 195-196 °C (AcOEt/n-hexane); IR (KBr) 1795, 1735, 1685, 1380, 1290, 885, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.95-2.16 (m, 3H), 2.22-2.40 (m, 1H), 2.74 (t, J = 5.4 Hz, 2H), 5.10-5.18 (m, 1H), 7.32 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 7.66-7.85 (m, 4H); EI-MS m/z 401 (M⁺ + 2 + H, 1.5), 399 (M⁺ + H, 1.9) 254 (27.4), 252 (30.1), 225 (50.5), 223 (50.9), 172 (100); FAB-MS m/z 399 (M⁺ + 1, 38.9). Anal. Calcd for C₁₉H₁₅BrN₂O₃: C, 57.16; H, 3.79; N, 7.02. Found: C, 57.20; H, 3.68; N, 6.94.

2-(2-(4-Iodophenyl)-6-oxopiperidin-1-yl)isoindole-1,3-dione (2e). Colorless crystals: mp 190-193 °C (CHCl₃-AcOEt-n-hexane); IR (KBr) 2950, 1790, 1730, 1690, 720 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.95-2.12 (m, 3H), 2.25-2.39 (m, 1H), 2.74 (t, J = 5.4 Hz, 2H), 5.00-5.13 (m, 1H), 7.25 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.69-7.87 (m, 4H); EI-MS m/z 446 (M⁺ , 0.5), 300 (49.4), 271 (74.8), 172 279
Anal. Calcd for C_{19}H_{15}IN_{2}O_{3}: C, 51.14; H, 3.39; N, 6.28. Found: C, 51.30; H, 3.44; N, 6.20.

3'-Phenyl-3'H,2,2'-biisoindolyl-1,1',3-trione (2i). Colorless crystals: mp 218-221 °C (AcOEt/n-hexane); IR (KBr) 1805, 1740, 1715, 710 cm⁻¹; ¹H NMR (500 MHz, Acetone-d₆) δ 6.12 (s, 1H), 7.34-7.39 (m, 4H), 7.47-7.51 (m, 1H), 7.65 (t, J = 7.4 Hz, 1H), 7.73 (dt, J = 7.4, 1.2 Hz, 2H), 7.87-7.90 (m, 1H), 7.92-7.99 (m, 4H); EI-MS m/z 354 (M⁺, 25.9), 208 (100), 195 (54.5), 165 (53.1).

Anal. Calcd for C_{22}H_{14}N_{2}O_{3}: C, 74.57; H, 3.98; N, 7.91. Found: C, 74.43; H, 3.83; N, 7.87.

2-(1-Oxo-3-phenyl-3,4-dihydroisoquinolin-2(1H)-yl)isoindoline-1,3-dione (2j) Colorless crystals: mp 173-175 °C (benzene/n-hexane); IR (KBr) 1790, 1735, 1690, 1300, 725, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 3.34 (dd, J = 16.0, 4.3 Hz, 1H), 3.59 (dd, J = 16.0, 11.7 Hz, 1H), 5.50 (dd, J = 11.7, 4.3 Hz, 1H), 7.72-7.32 (m, 4H), 7.38-7.50 (m, 3H), 7.54 (dd, J = 11.7, 4.3 Hz, 1H), 7.76-7.72 (m, 2H), 7.73-7.80 (m, 2H), 8.16 (dd, J = 7.6, 1.3 Hz, 1H); EI-MS m/z 368 (M⁺, 1.7), 221 (100), 118 (89.7). Anal. Calcd for C_{23}H_{16}N_{2}O_{3}: C, 74.99; H, 4.38; N, 7.60. Found: C, 74.99; H, 4.28; N, 7.58.

2-(2-Oxo-3,4,5,6-tetrahydrobenzo[b]azocin-1(2H)-yl)isoindoline-1,3-dione (3). Colorless crystals: mp 278-282 °C (EtOH); IR (KBr) 1795, 1740, 1685, 715 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.38-1.55 (m, 2H), 1.77-2.10 (m, 2H), 2.25 (d, J = 11.9 Hz, 1H), 2.53 (q, J = 7.2 Hz, 1H), 2.95 (q, J = 7.2 Hz, 1H), 3.34 (t, J = 13.0 Hz, 1H), 7.19-7.25 (m, 1H), 7.33 (d, J = 3.7 Hz, 2H), 7.51 (d, J = 7.7 Hz, 1H), 7.76-7.87 (m, 3H), 7.94-7.99 (m, 2H); EI-MS m/z 320 (M⁺, 100), 174 (33.1), 104 (35.1). Anal. Calcd for C_{19}H_{16}N_{2}O_{3}: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.00; H, 4.90; N, 8.61.

7-(1,3-Dioxo-1,3-dihydroisoindol-2-yl)-7-aza-spiro[5.6]dodeca-1,4-diene-3,8-dione (4). Colorless crystals: mp 197-198 °C (AcOEt/n-hexane); IR (KBr) 1790, 1740, 1670, 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.94-2.13 (m, 4H), 2.24-2.38 (m, 2H), 2.80-2.94 (m, 2H), 6.17 (d, J = 10.1 Hz, 2H), 7.24 (d, J = 10.1 Hz, 2H), 7.71-7.89 (m, 4H); EI-MS m/z 336 (M⁺, 100), 174 (33.1), 104 (35.1). Anal. Calcd for C_{19}H_{16}N_{2}O_{4}: C, 67.85; H, 4.79; N, 8.33. Found: C, 67.75; H, 4.75; N, 8.05.

5-(4-Cyanophenyl)-N-(1,3-dioxoisooindolin-2-yl)-N-(4-iodophenyl)pentanamide (5). Colorless crystals: mp 173-174 °C (toluene); IR (KBr) 2230, 1750, 1740, 1690, 1670 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.62-1.74 (m, 4H), 2.32 (t, J = 6.5 Hz, 2H), 2.64 (t, J = 6.5 Hz, 2H), 7.24 (d, J = 10.1 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.74-7.92 (m, 6H); EI-MS m/z 549 (M⁺, 1.6), 364 (100), 116 (26.5); FAB-MS m/z 550 (M⁺ + 1, 20.0). Anal. Calcd for C_{26}H_{20}IN_{3}O_{3}: C, 56.84; H, 3.67; N, 8.76. Found: C, 57.05; H, 3.54; N, 8.57.

2-(6-Oxo-6,11-dihydro-dibenzo[b,e]azepin-5-yl)-isoindole-1,3-dione (6). Colorless crystals: mp 235-237 °C (AcOEt/n-hexane); IR (KBr) 1800, 1745, 1665, 1315, 710 cm⁻¹; ¹H NMR (500 MHz, Acetone-d₆) δ 3.98 (d, J = 13.1 Hz, 1H), 4.64 (d, J = 13.1 Hz, 1H), 7.22-7.28 (m, 4H), 7.37 (dt, J = 7.9, 1.3 Hz, 1H), 7.40-7.43 (m, 1H), 7.47-7.50 (m, 2H), 7.54 (dt, J = 7.9, 1.3 Hz, 1H), 7.76 (dd, J = 7.9, 1.2
(Hz, 1H), 7.97-8.15 (m, 2H); EI-MS \( m/z \) 354 (M\(^+\), 64.6), 208 (100), 179 (43.9). Anal. Calcd for C\(_{22}\)H\(_{14}\)N\(_2\)O\(_3\): C, 74.57; H, 3.98; N, 7.91. Found: C, 74.39; H, 3.96; N, 7.88.

2-(6-Oxo-11,12-dihydro-6\(H\)-dibenzo[\(b,f\]]azocin-5-yl)-isoindole-1,3-dione (7). Colorless crystals: mp 224-227 °C (AcOEt/n-hexane); IR (KBr) 1800, 1745, 1690, 1320, 710 cm\(^{-1}\); \(^1\)H NMR (270 MHz, CDCl\(_3\)) \( \delta \) 2.96-3.15 (m, 2H), 3.34-3.79 (m, 1H), 4.05-4.18 (m, 1H), 7.02-7.29 (m, 6H), 7.39 (dd, \( J = 9.6, 1.5 \) Hz, 1H), 7.57 (d, \( J = 7.6 \) Hz, 1H), 7.76-7.94 (m, 2H), 7.96-8.04 (m, 2H); EI-MS \( m/z \) 368 (M\(^+\), 63.3), 356 (17.3), 222 (100), 204 (29.8), 193 (78.1). Anal. Calcd for C\(_{23}\)H\(_{16}\)N\(_2\)O\(_3\): C, 74.99; H, 4.38; N, 7.60. Found: C, 75.03; H, 4.34; N, 7.56.

REFERENCES