Supporting Information

For

A straightforward and general access to α-phthalimido-α'-substituted propan-2-ones

Vittorio Pace*[a,b] and Wolfgang Holzer[b]

[a]Organic and Pharmaceutical Chemistry Department, Faculty of Pharmacy, Complutense University of Madrid, Plaza de Ramón y Cajal s/n, 28040 Madrid, Spain.

[b]Department of Drug and Natural Product Synthesis, University of Vienna, Althanstrasse 14, 1090 Vienna, Austria.

*Corresponding Author: Email: vpace@farm.ucm.es; Fax: +43-1-4277-55623; Tel: +43-1-4277-9556.

Materials and Instrumentation.

^{1}H NMR, ^{13}C NMR and ^{19}F NMR were recorded on a Bruker AC-250 spectrometer at 250 MHz, at 62.5 MHz and at 235 MHz respectively, from CDCl3 solutions at 25 °C. The center of the (residual) solvent signal was used as an internal standard which was related to TMS with δ 7.26 ppm (^{1}H) and δ 77.0 ppm (^{13}C). Spin-spin coupling constants (*J*) are given in Hz. IR absorption spectra were recorded as NaCl pellets on a Shimadzu FT-IR 8400S (E41107). Spectra analyses were performed with the software Shimadzu IRsolution (Version 1.21, 2005). Elementary microanalyses were carried out using a Leco® CHNS 932 equipment. Column chromatography purifications were conducted on silica gel 60 (40-63 μm). Melting points are uncorrected. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using ethyl acetate / hexanes mixture as the eluent unless otherwise specified. TLC was carried out on aluminium sheets precoated with silica gel 60F254 (Macherey-Nagel, Merk); the spots were visualised under UV light (λ = 254 nm) and/or KMnO4 (aq.) was used as revealing system. All chemicals were purchased from Sigma Aldrich, Acros and Alfa Aesar and solvents were purified by distillation immediately before use according standard procedures.

Preparation of aminoalcohols 3a-e via formal addition of HX acid. (General Procedure A)

To a solution of 2,3-epoxypropylphthalimide (**2**) (1.0 equiv.), in chloroform (10 mL) cooled at 0°C, a concentrated solution of hydrohalic acid (2.0 equiv.) was added dropwise. The mixture was allowed to react during 0.5-6 h (Table 1) and, therefore it was washed with saturated aqueous NaCl and extracted twice with dichloromethane. Organic phases were dried over anhydrous sodium sulfate, filtered and after removal of the organic solvents in vacuo pure compounds were obtained without needing of further purification.

2-(3-chloro-2-hydroxypropyl)-1*H*-isoindole-1,3(2*H*)-dione (**3a**).

By following the General Procedure A, starting from 1 (4.00 mmol, 820 mg) and HCl 37% (6 mL), compound **3a** was obtained in quantitative yield (958 mg) as a white solid, mp 95°C (lit.[1], 95°C)

IR (NaCl) 3313, 1772, 907, 730, 653 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 3.01 (bs, 1H), 3.70 (dd, *J* = 5.2 Hz, *J* = 11.3 Hz, 2H), 4.04 (dd, *J* = 14.1 Hz, *J* = 23.3 Hz, 2H), 4.21-4.30 (m, 1H), 3.98-4.11 (m, 1H), 7.78 (dd, *J* = 3.0 Hz, *J* = 5.1 Hz, 2H), 7.90 (dd, *J* = 3.0 Hz, *J* = 5.2 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 41.6, 47.3, 69.8, 123.6, 131.9, 134.4, 168.7.

Anal. Calcd. for $C_{11}H_{10}ClNO_3$: C, 55.13; H, 4.21; N, 5.84. Found: C, 55.42; H, 4.38; N, 5.99.

2-(3-bromo-2-hydroxypropyl)-1*H*-isoindole-1,3(2*H*)-dione (3b).

By following the General Procedure A, starting from **2** (4.00 mmol, 820 mg) and HBr 48% (6 mL), compound **3b** was obtained in 98% yield (1113 mg), mp 114-115°C.

IR (NaCl) 3309, 1769, 902, 730, 651 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) 2.84 (bs, 1H), 3.50 (dd, *J* = 5.2 Hz, *J* = 11.3 Hz, 2H), 3.90 (dd, *J* = 14.1 Hz, *J* = 23.3 Hz, 2H), 4.10-4.27 (m, 1H), 7.78 (dd, *J* = 3.0 Hz, *J* = 5.1 Hz), 7.88 (dd, *J* = 3.0 Hz, *J* = 5.2 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 36.6, 42.3, 69.7, 124.1, 132.2, 134.1, 168.9.

Anal. Calcd. for $C_{11}H_{10}BrNO_3$: C, 46.50; H, 3.55; N, 4.93. Found: C, 46.71; H, 3.73; N, 5.08.

2-(2-hydroxy-3-iodopropyl)-1*H*-isoindole-1,3(2*H*)-dione (3c).

By following the General Procedure A, starting from **2** (4.00 mmol, 820 mg) and HI 57% (5 mL), compound **3c** was obtained in quantitative yield (1324 mg) as a brown syrup.

IR (NaCl) 3334, 1773, 904, 725, 649 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) 2.85 (bs, 1H), 3.34 (dd, *J* = 4.6 Hz, *J* = 10.8 Hz, 2H), 3.86-3.97 (m, 3H), 7.74 (dd, *J* = 3.1 Hz, *J* = 5.1 Hz), 7.85 (dd, *J* = 3.1 Hz, *J* = 5.2 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 10.7, 42.2, 43.6, 69.4, 123.6, 131.9, 134.2, 168.6.

Anal. Calcd. for $C_{11}H_{10}INO_3$: C, 39.90; H, 3.04; N, 4.23. Found: C, 40.09; H, 3.33; N, 4.39.

4-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-3-hydroxybutanenitrile (3d).

To a cooled (0°C) solution of **2** (2.00 mmol, 410 mg) in ethanol (15 mL) and acetic acid (3 mL), was added an aqueous solution (10 mL) of sodium cyanide (3.00 mmol, 147 mg) and the resulting mixture was stirred for 5 hours after removing of the cooling bath. After completion of the reaction, the crude reaction mixture was extracted with ethyl acetate (2 x 20 mL), and the organic phases were dried on anhydrous sodium sulfate and filtered. After removal of the organic solvent and subsequent purification by flash chromatography (petroleum ether – ethyl acetate, 1:1) compound **3d** was obtained as a white solid (419 mg, 91% yield), mp 104°C (lit.,[2] 104°C).

IR (NaCl) 3469, 2931, 2246, 2201, 1718, 1690, 716 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) 2.58 (m, 2H), 3.21 (bs, 1H), 3.89 (dd, $_J$ = 5.3 Hz, $_J$ = 10.1 Hz, 2H), 4.21 (m, 1H), 7.73-7.91 (m, 4H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 23.7, 43.1, 66.6, 116.8, 123.8, 131.2, 134.5, 168.8.

Anal. Calcd. for $C_{12}H_{10}N_2O_3$: C, 62.60; H, 4.38; N, 12.17. Found: C, 62.31; H, 4.49; N, 12.33.

2-(3-azido-2-hydroxypropyl)-1*H*-isoindole-1,3(2*H*)-dione (3e).

To an aqueous solution of sodium azide (845 mg, 13.00 mmol, 13 mL) cooled at 0°C, were added **2** (508 mg, 2.30 mmol) and acetic acid (2.3 mL). The mixture was stirred at 30°C for 6 hours and then was washed with saturated (aq) NaHCO3 and extracted with dichloromethane (2 x 30 mL). Organic phases were dried on anhydrous sodium sulfate, filtered and after removal of

the organic solvents in vacuo, compound **3e** was obtained as a white solid (549 mg, 97% yield), mp 65°C (lit.,[3] 64-66°C)

IR (NaCl) 3330, 2190, 2100, 1770, 900, 721 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 2.99 (bs, 1H), 3.43 (m, 2H), 3.85 (m, 2H), 4.10 (m, 1H), 7.70-7.93 (m, 4H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 41.5, 54.6, 69.0, 123.2, 131.9, 134.3, 168.8.

Anal. Calcd. for $C_{11}H_{10}N_4O_3$: C, 53.66; H, 4.09; N, 22.75. Found: C, 53.88; H, 4.21; N, 22.91.

2-(3-fluoro-2-hydroxypropyl)-1*H*-isoindole-1,3(2*H*)-dione (3f).

To a solution of 2,3-epoxypropylphthalimide (**2**) (4.00 mmol, 820 mg) in toluene (15 mL) were added ammonium hydrogen sulfate (0.80 mmol, 92 mg), 18-crown-6 (500 mg), potassium hydrogen difluoride (8.00 mmol, 825 mg) and the resulting mixture was heated at 120°C during 18 h. After cooling, the crude was diluted with ethyl acetate (20 mL), washed with brine (15 mL) and extracted with ethyl acetate (4 x 15 mL). The organic phase was dried on anhydrous sodium sulfate, filtered and after removal of the organic solvent in vacuo and subsequent purification by flash chromatography (silica gel, ethyl acetate : petroleum ether, 7/3) pure compound **3f** (696 mg, 78% yield) was obtained as a white solid (mp, 91°C, lit.,[4] 91-93°C).

IR (NaCl) 3330, 1770, 901, 720, 651 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) 2.93 (bs, 1H), 3.88-3.95 (m, 2H), 4.09-4.18 (m, 1H), 4.43 (m, 1H), 4.55 (m, 1H), 7.75 (dd, J = 3.0 Hz, J = 5.3 Hz), 7.88 (dd, J = 3.0 Hz, J = 5.3 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 40.6 (d, ^{3}J = 7.1 Hz), 68.9 (d, ^{2}J = 20.5 Hz), 84.2 (d, ^{1}J = 70.4 Hz), 123.7, 131.8, 134.3, 168.7.

^{19}F NMR (235 MHz, $CDCl_3$) δ -170.8.

Anal. Calcd. for $C_{11}H_{10}FNO_3$: C, 59.19; H, 4.52; N, 6.28. Found: C, 59.42; H, 4.71; N, 6.40.

2-[2-hydroxy-3-(phenylthio)propyl]-1*H*-isoindole-1,3(2*H*)-dione (3g).

To a chloroform (20 mL) solution of **2** (4.00 mmol, 820 mg) were added zinc (II) perchlorate hexahydrate (20 mol %, 0.80 mmol, 298 mg) and thiophenol (4.00 mmol, 441 mg, 0.41 mL). The mixture was stirred at rt for 6 hours and then washed with water and extracted with dichloromethane (2 x 20 mL). After drying over anhydrous sodium sulfate, filtration and removal of the solvent in vacuo, the crude reaction product was purified by flash

chromatography (petroleum ether – ethyl acetate, 8:2), affording **3g** (1139 mg, 91% yield) as a light yellow solid (mp 37°C, lit.,[2] 38-40°C).

IR (NaCl) 3454, 1771, 1709, 1468, 1374, 1313, 1167, 904, 725, 684 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$) 2.90 (dd, *J* = 8.3 Hz, *J* = 16.3 Hz, 2H), 3.90-4.12 (m, 3H), 7.07-7.91 (m, 9H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 39.5, 42.9, 68.9, 123.2, 123.7, 124.0, 126.9, 129.2, 130.5, 132.1, 132.5, 134.2, 134.3, 134.5, 135.0, 168.2.

Anal. Calcd. for $C_{17}H_{15}NO_3S$: C, 65.16; H, 4.82; N, 4.47; S, 10.23. Found: C, 65.39; H, 4.99; N, 4.62; S, 10.09.

2-{2-hydroxy-3-[methyl(phenyl)amino]propyl}-1*H* isoindole-1,3(2*H*)-dione (3h).

To a chloroform (20 mL) solution of 1 (4.00 mmol, 820 mg) were added zinc (II) perchlorate hexahydrate (20 mol %, 0.80 mmol, 298 mg) and N-methylaniline (4.00 mmol, 429 mg, 0.43 mL). The mixture was stirred at rt for 4 hours and then washed with water and extracted with dichloromethane (2 x 20 mL). After drying over anhydrous sodium sulfate, filtration and removal of the solvent in vacuo, the crude reaction product was purified by flash chromatography (petroleum ether – ethyl acetate, 8:2), affording 3h (1092 mg, 88% yield) as a yellow solid (mp 75-76°C).

IR (NaCl) 3464, 3070, 1770, 1713, 1392, 1040, 912, 722 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$) 2.77 (bs, 1H), 3.00 (s, 3H), 3.53 (m, 2H), 3.95 (m, 2H), 4.25 (m, 1H), 6.74-6.84 (m, 3H), 7.23 (m, 2H), 7.71-7.89 (m, 4H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 36.4, 42.2, 68.3, 69.3, 113.5, 123.5, 123.6, 129.3, 131.9, 134.2, 134.3, 149.9, 168.7.

Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.91; H, 6.01; N, 8.88.

Dess-Martin oxidation of aminoalcohols 3a-h. (General Procedure B)

To a solution of alcohol (1.00 equiv.) in dichloromethane (10 mL) at room temperature, Dess-Martin Periodinane (1.20 equiv.) was added and the mixture was stirred at the same temperature for the appropriate time (Table 2). Then, diethyl ether (20 mL) and a saturated aqueous solution of sodium thiosulfate (15 mL) followed by addition of saturated solution of sodium bicarbonate were added and the resulting mixture was stirred for 5 min. The organic phase was separated, dried under sodium sulphate, filtered and concentrated.

2-(3-chloro-2-oxopropyl)-1*H*-isoindole-1,3(2*H*)-dione (4a).

By following the General Procedure B, starting from 479 mg of **3a** (2.00 mmol) and 1018 mg (2.40 mmol) of DMP, ketone **4a** was obtained in 97% yield (461 mg) as a white solid (mp 122°C, lit.,[1] 122°C).

IR (NaCl) 1772, 1732, 1718 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 4.20 (s, 2H), 4.75 (s, 2H), 7.80 (dd, *J* = 3.0 Hz, *J* = 5.1 Hz, 2H), 7.94 (dd, *J* = 3.0 Hz, *J* = 5.1 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 44.7, 46.2, 123.7, 132.6, 134.3, 167.4, 195.5.

Anal. Calcd. for $C_{11}H_8ClNO_3$: C, 55.60; H, 3.39; N, 5.89. Found: C, 55.79; H, 3.52; N, 6.09.

2-(3-bromo-2-oxopropyl)-1*H*-isoindole-1,3(2*H*)-dione (4b).

By following the General Procedure B, starting from 568 mg of **3b** (2.00 mmol) and 1018 mg (2.40 mmol) of DMP, ketone **4b** was obtained in 99% yield (558 mg) as a white solid (mp 147°C, lit.,[5] 147-148°C).

IR (NaCl) 1773, 1732, 1719 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 4.03 (s, 2H), 4.80 (s, 2H), 7.76 (dd, *J* = 3.0 Hz, *J* = 5.2 Hz, 2H), 7.94 (dd, *J* = 3.0 Hz, *J* = 5.2 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 35.1, 45.8, 123.1, 132.9, 134.5, 167.8, 196.8.

Anal. Calcd. for $C_{11}H_8BrNO_3$: C, 46.84; H, 2.86; N, 4.97. Found: C, 47.08; H, 2.97; N, 5.08.

2-(3-iodo-2-oxopropyl)-1*H*-isoindole-1,3(2*H*)-dione (4c).

By following the General Procedure B, starting from 662 mg of **3c** (2.00 mmol) and 1018 mg (2.40 mmol) of DMP, ketone **4c** was obtained in 94% yield (619 mg) as a yellow solid (mp 182°C, lit.,[1] 182-185°C).

IR (NaCl) 1774, 1730, 1721 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 3.96 (s, 2H), 4.82 (s, 2H), 7.76 (dd, *J* = 3.0 Hz, *J* = 5.4 Hz, 2H), 7.90 (dd, *J* = 3.0 Hz, *J* = 5.4 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 1.2, 43.4, 123.7, 132.0, 134.3, 167.5, 195.4.

Anal. Calcd. for $C_{11}H_8INO_3$: C, 40.15; H, 2.45; N, 4.26. Found: C, 40.34; H, 2.59; N, 4.41.

4-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-3-oxobutanenitrile (4d).

By following the General Procedure B, starting from 460 mg of **3d** (2.00 mmol) and 1018 mg (2.40 mmol) of DMP, ketone **4d** was obtained in 95% yield (433 mg) as a light yellow syrup.

IR (NaCl) 2201, 2130, 1770, 1733, 1722 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 3.59 (s, 2H), 4.74 (s, 2H), 7.80 (dd, *J* = 3.0 Hz, *J* = 5.1 Hz, 2H), 7.87 (dd, *J* = 3.0 Hz, *J* = 5.1 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 39.2, 42.6, 113.6, 123.5, 131.8, 134.1, 167.2, 195.8.

Anal. Calcd. for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28. Found: C, 63.34; H, 3.68; N, 12.45.

2-(3-azido-2-oxopropyl)-1*H*-isoindole-1,3(2*H*)-dione (4e).

By following the General Procedure B, starting from 492 mg of **3e** (2.00 mmol) and 1018 mg (2.40 mmol) of DMP, ketone **4e** was obtained in 98% yield (479 mg) as a white solid (mp 125°C, lit.,[6] 124-126°C).

IR (NaCl) 3328, 2190, 2101, 1774, 1736, 1715 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 4.16 (s, 2H), 4.60 (s, 2H), 7.76 (dd, *J* = 3.1 Hz, *J* = 5.2 Hz, 2H), 7.88 (dd, *J* = 3.1 Hz, *J* = 5.2 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 44.1, 45.5, 123.7, 131.6, 134.1, 168.9, 196.9.

Anal. Calcd. for $C_{11}H_8N_4O_3$: C, 54.10; H, 3.30; N, 22.94. Found: C, 53.88; H, 3.48; N, 22.51.

2-(3-fluoro-2-oxopropyl)-1*H*-isoindole-1,3(2*H*)-dione (4f)

By following the General Procedure B, starting from 446 mg of **3f** (2.00 mmol) and 1018 mg (2.40 mmol) of DMP, ketone **4f** was obtained in 91% yield (402 mg) as a white solid after purification by flash chromatography on silica gel (petroleum ether/ ethyl acetate, 7:3).

IR (NaCl) 1770, 1729, 1713 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$) δ 4.68 (s, 2H), 4.99 (d, ^2J = 47.5 Hz, 2H), 7.71 (dd, J = 3.0 Hz, J = 5.3 Hz, 2H), 7.81 (dd, J = 3.0 Hz, J = 5.3 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 44.5, 85.1 (d, ^1J = 182.6 Hz), 123.7, 131.9, 134.5, 167.6, 199.0.

^{19}F NMR (235 MHz, $CDCl_3$) δ -169.6.

Anal. Calcd. for $C_{11}H_8FNO_3$: C, 59.73; H, 3.65; N, 6.33. Found: C, 59.52; H, 3.86; N, 6.49.

2-[2-oxo-3-(phenylthio)propyl]-1*H*-isoindole-1,3(2*H*)-dione (4g)

By following the General Procedure B, starting from 627 mg of **3g** (2.00 mmol) and 1018 mg (2.40 mmol) of DMP, ketone **4g** was obtained in 92% yield (573 mg) as a thick oil after purification by flash chromatography on silica gel (petroleum ether/ ethyl acetate, 8:2).

IR (NaCl) 1772, 1736, 1719 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$) δ 3.71 (s, 2H), 4.67 (s, 2H), 7.19-7.41 (m, 5H), 7.66 (dd, J = 2.8 Hz, J = 4.9 Hz, 2H), 7.79 (dd, J = 2.8 Hz, J = 4.9 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 42.1, 44.7, 123.5, 127.5, 129.1, 130.4, 131.9, 133.6, 134.5, 167.5, 197.5.

Anal. Calcd. for $C_{17}H_{13}NO_3S$: C, 65.58; H, 4.21; N, 4.50; S, 10.30. Found: C, 65.80; H, 4.39; N, 4.31; S, 10.12.

2-{3-[methyl(phenyl)amino]-2-oxopropyl}-1*H*-isoindole-1,3(2*H*)-dione (4h)

By following the General Procedure B, starting from 621 mg of **3f** (2.00 mmol) and 1018 mg (2.40 mmol) of DMP, ketone **4h** was obtained in 86% yield (530 mg) as a yellow thick oil after purification by flash chromatography on silica gel (petroleum ether/ ethyl acetate, 9:1).

IR (NaCl) 2987, 1775, 1732, 1714 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$) δ 3.08 (s, 3H), 3.96 (s, 2H), 4.72 (s, 2H), 6.61-6.76 (m, 3H), 7.18 (m, 2H), 7.69 (dd, J = 3.0 Hz, J = 4.9 Hz, 2H), 7.79 (dd, J = 3.0 Hz, J = 4.9 Hz, 2H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 32.1, 44.9, 60.4, 112.5, 122.4, 123.7, 129.6, 132.0, 133.8, 148.6, 167.6, 194.7.

Anal. Calcd. for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 69.91; H, 5.46; N, 9.19.

***N*-[3-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-2-hydroxypropyl]acetamide (5)**

To a solution of azidoalcohol **3e** (320 mg, 1.30 mmol) in chloroform (10 mL) were added 2,6-lutidine (181 mg, 0.20 mL, 1.69 mmol) and thioacetic acid (129 mg, 0.12 mL, 1.69 mmol) and the resulting solution was stirred at 60°C during 6 hours. After cooling at rt, a solution of saturated sodium bicarbonate was added (15 mL) and then the mixture was extracted with dichloromethane (3 x 15 mL). After drying the organic phase over anhydrous sodium sulfate, filtration and removal of the solvent in vacuo, the crude reaction product was purified by flash chromatography (petroleum ether – ethyl acetate, 8:2), affording **5** (286 mg, 84% yield) as a yellow thick oil.

IR (NaCl) 3450, 2980, 1775, 1698 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 1.83 (s, 3H), 2.96 (s, 1H), 3.20-3.45 (m, 2H), 3.66-3.83 (m, 2H), 4.30 (m, 1H), 7.61 (dd, *J* = 3.0 Hz, *J* = 5.0 Hz, 2H), 7.68 (dd, *J* = 3.0 Hz, *J* = 5.0 Hz, 2H), 7.96 (s, 1H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 21.7, 44.8, 53.8, 68.7, 123.1, 131.8, 134.2, 168.7, 175.0.

Anal. Calcd. for $C_{13}H_{14}N_2O_4$: C, 59.54; H, 5.38; N, 10.68. Found: C, 59.81; H, 5.53; N, 10.87.

***N*-[3-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-2-oxopropyl]acetamide (6)**

By following the General Procedure B, starting from 200 mg of **5** (0.76 mmol) and 388 mg (0.91 mmol) of DMP, ketone **6** was obtained in 87% yield (172 mg) as a light yellow oil after purification by flash chromatography on silica gel (petroleum ether/ ethl acetate, 8:2).

IR (NaCl) 1771, 1733, 1714, 1696 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ 1.83 (s, 3H), 4.41 (s, 2H), 4.73 (s, 2H), 7.72 (dd, *J* = 3.0 Hz, *J* = 5.1 Hz, 2H), 7.86 (dd, *J* = 3.0 Hz, *J* = 5.1 Hz, 2H), 8.02 (s, 1H).

^{13}C NMR (62.5 MHz, $CDCl_3$) δ 22.1, 46.8, 55.1, 123.6, 131.9, 134.1, 168.5, 169.9, 197.4.

Anal. Calcd. for $C_{13}H_{12}N_2O_4$: C, 60.00; H, 4.65; N, 10.76. Found: C, 60.23; H, 4.91; N, 10.90.

References

1. Pace, V.; Martínez, F.; Fernández, M.; Nova, C. I.; Sinisterra, J. V.; Alcántara, A. R. *Tetrahedron Lett.* **2009,** *50*, 3050-3053.
2. Itoh, T.; Takagi, Y.; Nishiyama, S. *J. Org. Chem.* **1991,** *56*, 1521-1524.
3. Madhusudhan, G.; Om Reddy, G.; Ramanatham, J.; Dubey, P. K. *Ind. J. Chem., Sect. B* **2006,** *45B*, 1264-1268.
4. Dobrotă, C.; Fasci, D.; Hădade, N. D.; Roiban, G.-D.; Pop, C.; Meier, V. M.; Dumitru, I.; Matache, M.; Salvesen, G. S.; Funeriu, D. P. *ChemBioChem* **2012,** *13*, 80-84.
5. Perumal, S. K.; Pratt, R. F. *J. Org. Chem.* **2006,** *71*, 4778-4785.
6. Gall, M.; Kamdar, B. V. *J. Org. Chem.* **1981,** *46*, 1575-1585.