

Supplementary Materials for

Continuous Flow Photochemical and Thermal Multi-Step Synthesis of Bioactive 3-Arylmethylene-2,3-Dihydro-1*H*-Isoindolin-1-Ones

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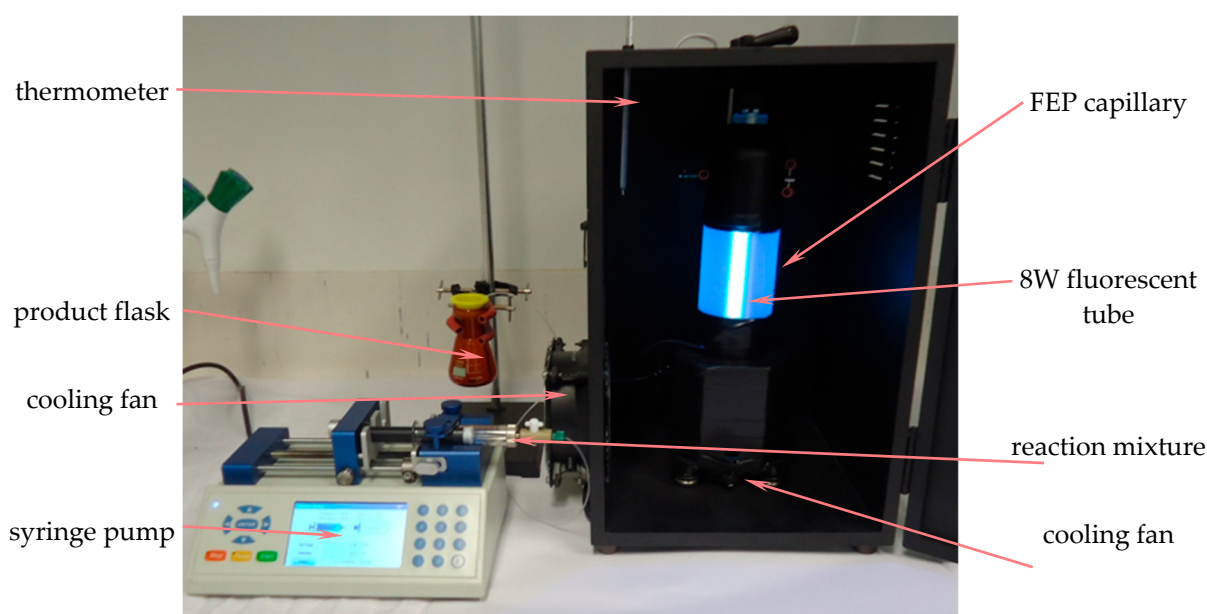
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1. Technical Details

1.1. In-House Photochemical Continuous-Flow Capillary Reactor

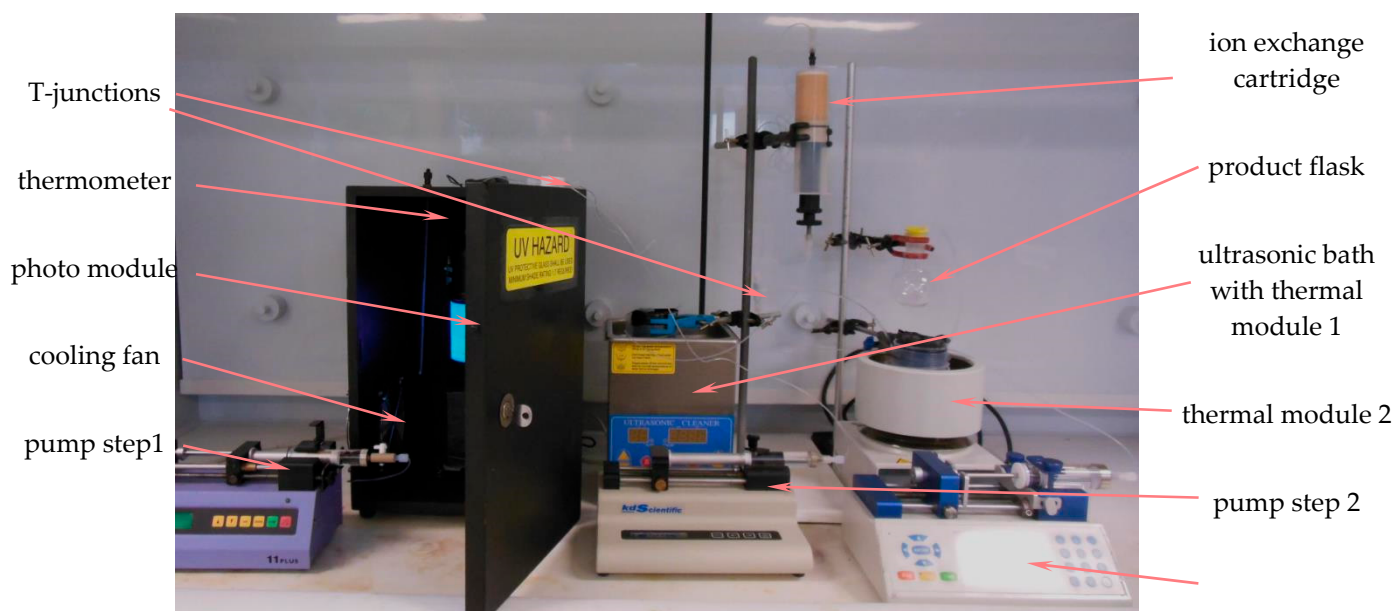
Tube material	Fluorinated ethylene propylene (FEP), Bohlender GmbH
External diameter	1.58 mm
Internal diameter	0.8 mm
Length of tube	10 m (plus additional ~70 cm on each end)
Volume of tube	5 mL (exposed)
Syringe	ILS Innovative Labor Systeme GmbH gas-tight syringe (25 mL)
Pump	Chemyx syringe pump (Model: Fusion 200)
Light source	Ushio G8T5E UVB (300 ± 25 nm; 8 W)



1.2. In-House Triple Photochemical–Thermal–Thermal Continuous-Flow Capillary Reactor

Tube material	Fluorinated ethylene propylene (FEP) , Bohlender GmbH
External diameter	1.58 ^{a,b} /3.2 ^c mm
Internal diameter	0.8 ^{a,b} /1.6 ^b mm
Length of tube	10 m each
Volume of tube	5 ^{a,b} /19.6 ^c mL
T-junctions	Fluorinated ethylene propylene (FEP), Bohlender GmbH
Syringes	ILS Innovative Labor Systeme GmbH gas-tight syringes (25 mL)
Pumps	Harvard apparatus (Model: 11Plus) ^a , kdScientific (Model: KDS-100-CE) ^b , Chemyx syringe pump (Model: Fusion 200) ^c
Light source	Ushio G8T5E UVB (300 ± 25 nm; 8 W) ^a

^a Photo loop. ^b Ultrasonic loop. ^c Thermal heating loop.



2. Experimental Details

2.1. General Methods

Solvents and Reagents

All solvents and reagents were commercially available (Sigma-Aldrich or Alfa Aesar) and were used without purification.

2.2. Analytical Methods

2.2.1. Melting Point

Melting points were measured using a Tathastu melting point apparatus and are uncorrected.

2.2.2. IR

Infrared spectra were recorded on a Perkin Elmer Spectrum One FT-IR Spectrometer as solids or thin films, and were recorded in the range 600–4000 cm^{-1} . IR peaks are listed in wavenumbers ($\tilde{\nu}$; in cm^{-1}).

2.2.3. NMR

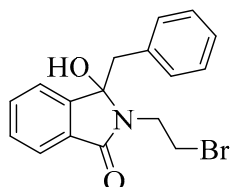
NMR spectra were recorded on an Oxford 300 (^1H : 300 MHz and ^{13}C : 75 MHz) with a UNITYINOVA system console using the Varian Software VnmrJ program or a Bruker AV300 (^1H : 300 MHz and ^{13}C : 75 MHz) Nuclear Magnetic Resonance spectrometer with dual probe operating TopSpin 2.1 software. Residual solvent peaks served as an internal standard and samples were prepared in CDCl_3 ($\delta = 7.26/77.3$ ppm) or acetone- d_6 ($\delta = 2.09/30.6$ ppm).

2.2.4. FTMS

High resolution mass spectroscopic data were determined on a Bruker BioApex 47 FT mass spectrometer with an electrospray (ESI) Analytica of Branford source. Ions were detected in positive mode and/or negative mode within a mass range of m/z 50–2000. Direct infusion of sample (0.2 mg mL^{-1}) was carried out using a Cole Palmer 74900 syringe pump at a flow rate of $100 \mu\text{L h}^{-1}$. N_2 (sourced from a Domnick Hunter UHPLCMS18 Nitrogen Generator, flow of 3 L/min and maintained at 200°C) was used as the drying gas to assist in desolvation of the droplets produced by ESI from an on axis grounded needle directed to a metal capped nickel coated glass capillary, approximately 1 cm away. All experimental event sequences were controlled and data reduction performed using Bruker Daltonics XMASS ver. 7.0.3.0 software. Detection was in the direct mode from time domain data sets of 512 k (16 scans per experiment). Each spectrum was subjected to zerofill, Gaussian multiplication, and fast Fourier transform and displayed in magnitude mode. The instrument was calibrated using a methanolic solution of sodium trifluoroacetate (0.1 mg/mL MeOH), 200–2000 m/z .

2.3. Spectroscopic Data

2.3.1. 3-Benzyl-2-(2-Bromoethyl)-3-Hydroxy-2,3-Dihydro-1H-Isoindol-1-One (3a)



Appearance: colorless crystalline solid.

Melting point: 148°C .

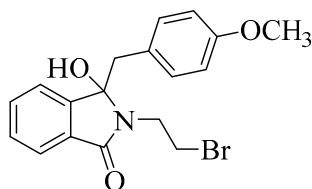
IR (film): $\tilde{\nu}$ (cm^{-1}) = 3310 br, 3123, 1700, 1611, 1320, and 632.

^1H -NMR (300 MHz, CDCl_3): δ (ppm): 2.70 (br s, 1 H, OH), 3.14 (d, $J = 15 \text{ Hz}$, 1H, CH_2Ph), 3.52 (d, $J = 15 \text{ Hz}$, 1H, CH_2Ph), 3.61–3.82 (m, 3H, CH_2Br , NCH_2), 4.11–4.17 (m, 1H, NCH_2), 6.89 (d, $J = 9 \text{ Hz}$, 2H, CH), 7.11–7.17 (m, 3H, CH), 7.20–7.23 (d, $J = 9 \text{ Hz}$, 1H, CH), 7.43–7.58 (m, 2H, CH), 7.62 (d, $J = 9 \text{ Hz}$, 1H, CH).

^{13}C -NMR (75 MHz, CDCl_3): δ (ppm): 29.5 (t, 1C, CH_2Br), 41.4 (t, 1C, CH_2Ph), 43.3 (t, 1C, NCH_2), 91.0 (s, 1C, COH), 122.9 (d, 1C, CH), 123.4 (d, 1C, CH), 127.3 (d, 1C, CH), 128.2 (d, 2C, CH), 129.9 (d, 1C, CH), 130.2 (d, 2C, CH), 130.9 (d, 1C, Cq), 132.3 (d, 1C, CH), 134.3 (s, 1C, Cq), 146.1 (s, 1C, Cq), 167.0 (s, 1C, C=O).

HRMS (ESI/MeOH): m/z : calcd for $\text{C}_{17}\text{H}_{16}\text{O}_2\text{NBr}$ ($\text{M} + \text{H}$) $^+$: 346.0437 ($\text{M} + \text{Na}$) $^+$ 368.0257, found: 368.0261 ± 1 ppm.

2.3.2. 2-(2-Bromoethyl)-3-Hydroxy-3-(4-Methoxybenzyl)-2,3-Dihydro-1H-Isoindol-1-One (3b)



Appearance: pale yellow crystalline solid.

Melting point: 167–168 °C.

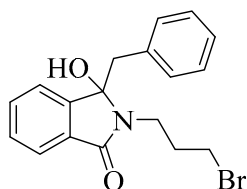
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3379 br, 3106, 1685, 1583, 1366, 1268, and 630.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 2.78 (br s, 1H, OH), 3.13 (d, *J* = 15 Hz, 1H, CH₂Ar), 3.49 (d, *J* = 15 Hz, 1H, CH₂Ar), 3.77 (s, 3H, OCH₃), 3.72–3.82 (m, 3 H, CH₂Br, NCH₂), 4.15–4.24 (m, 1H, NCH₂), 6.71 (d, *J* = 9 Hz, 2H, CH), 6.84 (d, *J* = 9 Hz, 2H, CH), 7.30 (m, 1H, CH), 7.53 (m, 2H, CH), 7.70 (d, *J* = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, acetone-d₆): δ (ppm): 29.7 (q, 1C, OCH₃), 41.7 (t, 1C, NCH₂), 42.5 (t, 1C, CH₂Ar), 55.2 (t, 1C, CH₂Ph), 91.9 (s, 1C, COH), 113.8 (d, 2C, CH), 123.1 (d, 1C, CH), 123.7 (d, 1C, CH), 127.8 (s, 1C, Cq), 129.8 (d, 1C, CH), 131.8 (d, 2C, CH), 132.5 (d, 1C, Cq), 135.1 (d, 1C, CH), 147.8 (s, 1C, Cq), 159.4 (s, 1C, Cq), 167.0 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₁₈H₁₈NO₃Br (M + Na)⁺: 398.0362, found: 398.0369 ± 2 ppm.

2.3.3. 3-Benzyl-2-(3-Bromopropyl)-3-Hydroxy-2,3-Dihydro-1H-Isoindol-1-One (3c)



Appearance: colorless crystalline solid.

Melting point: 160 °C.

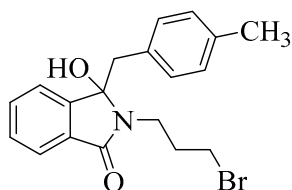
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3260 br, 3150, 1680, 1650, 1300, and 685.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 2.26–2.45 (m, 2 H, CH₂), 2.80 (br s, 1H, OH), 3.13 (d, *J* = 12 Hz, 1H, CH₂Ph), 3.48–3.58 (m, 4H, CH₂Ph, CH₂Br, NCH₂), 3.78–3.87 (m, 1H, NCH₂), 6.92 (d, *J* = 9 Hz, 2H, CH), 7.19–7.26 (m, 4H, CH), 7.41–7.47 (m, 2H, CH), 7.62 (d, *J* = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 32.6 (t, 1C, CH₂), 33.6 (t, 1C, CH₂Br), 39.0 (t, 1C, NCH₂), 43.5 (t, 1C, CH₂Ph), 90.1 (s, 1C, COH), 123.0 (d, 1C, CH), 123.8 (d, 1C, CH), 127.4 (d, 1C, CH), 128.5 (s, 2C, CH), 130.0 (s, 1C, Cq), 131.0 (d, 2C, CH), 132.3 (d, 1C, CH), 132.7 (d, 1C, CH), 136.2 (s, 1C, Cq), 147.8 (s, 1C, Cq), 167.2 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₁₈H₁₈NO₂Br (M + Na)⁺: 382.0413, found: 382.0435 ± 6 ppm.

2.3.4. 2-(3-Bromopropyl)-3-(4-Methylbenzyl)-3-Hydroxy-2,3-Dihydro-1H-Isoindol-1-One (3d)



Appearance: colorless crystalline solid.

Melting point: 156–157 °C.

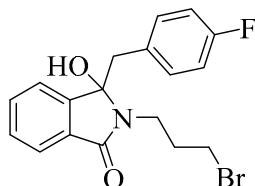
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3442 br, 3232, 1680, 1600, 1272, and 664.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 2.25 (s, 3H, CH₃), 2.28–2.43 (m, 3H, CH₂, CH₂Ar), 3.11 (d, *J* = 12 Hz, 1H, CH₂Ar), 3.48–3.57 (m, 4H, CH₂Br, NCH₂), 6.78 (d, 2H, *J* = 9 Hz, CH), 6.94 (d, 2H, *J* = 9 Hz, CH), 7.18–7.21 (m, 1H, CH), 7.39–7.50 (m, 2H, CH), 7.62 (d, *J* = 9 Hz, 1H, CH), not observed (1H, OH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 20.6 (q, 1C, CH₃), 30.2 (t, 1C, CH₂), 34.7 (t, 1C, CH₂Br), 40.1 (t, 1C, NCH₂), 45.0 (t, 1C, CH₂Ar), 90.3 (s, 1C, COH), 121.3 (d, 2C, CH), 122.7 (d, 1C, CH), 125.0 (d, 2C, CH), 129.0 (s, 1C, Cq), 130.8 (s, 1C, CH), 131.3 (s, 1C, CH), 132.0 (s, 1C, CH), 134.3 (s, 1C, Cq), 135.9 (s, 1C, Cq), 140.4 (s, 1C, Cq), 166.5 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₁₉H₂₀O₂NBr (M + Na)⁺: 396.0570, found: 396.0568 ± 1 ppm.

2.3.5. 2-(3-Bromopropyl)-3-(4-Fluorobenzyl)-3-Hydroxy-2,3-Dihydro-1*H*-Isoindol-1-One (**3e**)



Appearance: yellowish solid.

Melting point: 161 °C.

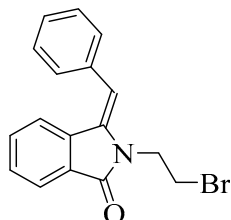
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3382 br, 3110, 1690, 1660, 1146, and 680.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 2.16–2.44 (m, 2H, CH₂), 3.09 (d, *J* = 12 Hz, 1H, CH₂Ar), 3.47–3.54 (m, 4H, CH₂Ar, CH₂Br, NCH₂), 3.76–3.83 (m, 1H, NCH₂), 6.80–6.89 (m, 4H, CH), 7.11 (d, *J* = 9 Hz, 1H, CH), 7.42–7.47 (m, 2H, CH), 7.61 (d, *J* = 9 Hz, 1H, CH), not observed (1H, OH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 30.0 (t, 1C, CH₂), 34.8 (t, 1C, CH₂Br), 40.2 (t, 1C, NCH₂), 45.5 (t, 1C, CH₂Ar), 93.1 (s, 1C, COH), 120.1 (d, 1C, CH), 122.7 (d, 1C, CH), 124.7 (d, 1C, CH), 128.2 (d, 2C, CH), 130.7 (s, 1C, Cq), 131.3 (d, 2C, CH), 132.9 (d, 1C, CH), 135.7 (s, 1C, Cq), 136.2 (s, 1C, Cq), 158.1 (s, 1C, Cq), 167.0 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₁₈H₁₇O₂NFBr (M + Na)⁺: 400.0319, found: 400.0340 ± 5 ppm.

2.3.6. *E*-3-Benzylidene-2-(2-Bromoethyl)-2,3-Dihydro-1*H*-Isoindol-1-One (**4a**)



Appearance: yellowish powder.

TLC (SiO₂, ethyl acetate/*n*-hexane 1:1): *R_f* = 0.89.

Melting point: 102 °C.

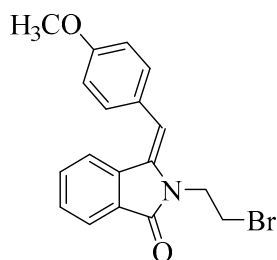
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3140, 1658, 1620, 1580, 1301, 832, and 689.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 3.67 (t, *J* = 6 Hz, 2H, CH₂Br), 4.34 (t, *J* = 6 Hz, 2H, NCH₂), 6.65 (s, 1H, CH), 7.30–7.50 (m, 8H, CH), 7.90 (d, *J* = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 27.7 (t, 1C, CH₂Br), 41.1 (t, 1C, NCH₂), 110.4 (d, 1C, CH), 123.3 (s, 1C, Cq), 123.4 (d, 2C, CH), 128.9 (d, 2C, CH), 129.3 (d, 1C, CH), 129.6 (d, 1C, CH), 129.6 (d, 1C, CH), 129.9 (d, 1C, CH), 132.0 (s, 1C, Cq), 134.8 (d, 1C, CH), 135.7 (d, 1C, Cq), 135.8 (s, 1C, Cq), 166.6 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₁₇H₁₄ONBr (M + Na)⁺: 350.0151, found: 350.0149 ± 1 ppm.

2.3.7. *E*-2-(2-Bromoethyl)-3-(4-Methoxybenzylidene)-2,3-Dihydro-1*H*-Isoindol-1-One (**4b**)



Appearance: yellow oil.

TLC (SiO₂, ethyl acetate/n-hexane 1:1): R_f = 0.74.

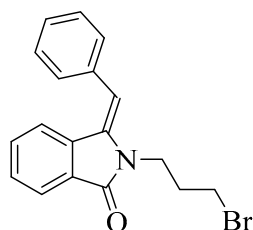
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3126, 1685, 1583, 1581, 1366, 1268, 826, and 630.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 3.66 (t, J = 9 Hz, 2H, CH₂Br), 3.93 (s, 3H, OCH₃), 4.33 (t, J = 9 Hz, 2H, NCH₂), 6.60 (s, 1H, CH), 7.02 (d, J = 9 Hz, 2H, CH), 7.40–7.43 (m, 5H, CH), 7.90 (d, J = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 27.8 (t, 1C, CH₂Br), 42.1 (t, 1C, NCH₂), 55.2 (q, 1C, OCH₃), 107.0 (d, 1C, CH), 114.3 (d, 2C, CH), 123.5 (d, 1C, CH), 123.7 (s, 1C, Cq), 127.0 (s, 1C, Cq), 128.2 (d, 1C, CH), 129.4 (d, 1C, CH), 130.9 (d, 2C, CH), 131.9 (s, 1C, Cq), 134.4 (d, 1C, CH), 134.3 (s, 1C, Cq), 159.6 (s, 1C, Cq), 166.6 (s, 1C, C=O).

HRMS (ESI/MeOH): m/z : calcd for C₁₈H₁₆O₂NBr (M + Na)⁺: 380.0257, found: 380.0252 $\pm$ 1 ppm.

2.3.8. *E*-3-Benzylidene-2-(3-Bromopropyl)-2,3-Dihydro-1*H*-Isoindol-1-One (4c)



Appearance: pale yellow solid.

TLC (SiO₂, ethyl acetate/n-hexane 1:1): R_f = 0.91.

Melting point: 127 °C.

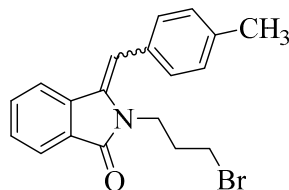
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3148, 1633, 1663, 1574, 1327, 841, and 680.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 2.34 (m, 2H, CH₂), 3.52 (t, J = 9 Hz, 2H, CH₂Br), 4.05 (t, J = 9 Hz, 2H, NCH₂), 6.60 (s, 1H, CH), 7.29–7.32 (m, 2H, CH), 7.42–7.46 (m, 6H, CH), 7.83 (d, J = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 30.7 (t, 1C, CH₂), 31.5 (t, 1C, CH₂Br), 38.1 (t, 1C, NCH₂), 110.5 (d, 1C, CH), 123.2 (d, 1C, CH), 123.3 (s, 1C, Cq), 128.0 (d, 1C, CH), 128.3 (s, 1C, Cq), 128.4 (d, 2C, CH), 128.8 (d, 1C, CH), 129.6 (d, 2C, Cq), 130.1 (s, 1C, Cq), 131.7 (d, 1C, CH), 135.0 (s, 1C, Cq), 136.1 (s, 1C, Cq), 166.8 (s, 1C, C=O).

HRMS (ESI/MeOH): m/z : calcd for C₁₈H₁₆NOBr (M + Na)⁺: 364.0307, found: 364.0316 $\pm$ 3 ppm.

2.3.9. *E*-2-(3-Bromopropyl)-3-(4-Methylbenzylidene)-2,3-Dihydro-1*H*-Isoindol-1-One (4d)



Appearance: yellow oil.

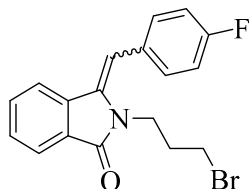
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3101, 1679, 1602, 1581, 1372, 846, and 669.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 2.31–2.36 (m, 2H, CH₂), 2.43 (s, 3H, CH₃), 3.51 (t, J = 6 Hz, 2H, CH₂Br), 4.04 (t, J = 6 Hz, 2H, NCH₂), 6.58 (s, 1H, CH), 7.23–7.29 (m, 1H, CH), 7.32–7.45 (m, 6H, CH), 7.83 (d, J = 6 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 21.3 (q, 1C, CH₃), 28.3 (t, 1C, CH₂), 30.6 (t, 1C, CH₂Br), 41.3 (t, 1C, NCH₂), 107.1 (d, 1C, CH), 114.2 (d, 1C, CH), 119.1 (d, 1C, CH), 123.0 (d, 1C, CH), 123.5 (d, 1C, Cq), 127.9 (d, 1C, CH), 129.2 (d, 1C, CH), 130.9 (d, 1C, CH), 131.3 (d, 1C, CH), 131.6 (d, 1C, Cq), 134.5 (d, 1C, CH), 135.7 (s, 1C, Cq), 138.0 (s, 1C, Cq), 141.4 (s, 1C, Cq), 166.5 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₁₉H₁₈NOBr (M + Na)⁺: 378.0464, found: 378.0471 ± 2 ppm.

2.3.10. *E*-2-(3-Bromopropyl)-3-(4-Fluorobenzylidene)-2,3-Dihydro-1*H*-Isoindol-1-One (**4e**)



Appearance: yellow oil.

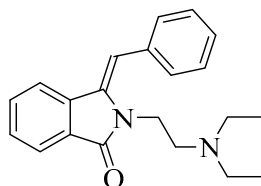
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3129, 1654, 1663, 1582, 1151, 825, and 683.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 2.33 (m, 2 H, CH₂), 3.51 (t, *J* = 6 Hz, 2 H, CH₂Br), 4.04 (t, *J* = 6 Hz, 2 H, NCH₂), 6.54 (s, 1 H, CH), 7.14 (dd, *J* = 6, 3 Hz, 2 H, CH), 7.31–7.47 (m, 5 H, CH), 7.84 (d, *J* = 6 Hz, 1 H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 27.8 (t, 1 C, CH₂), 30.6 (t, 1 C, CH₂Br), 39.3 (t, 1 C, NCH₂), 110.9 (d, 1 C, CH), 114.6 (d, 1 C, CH), 119.4 (d, 1 C, CH), 123.1 (d, 1 C, CH), 126.9 (d, 1 C, Cq), 129.1 (d, 1 C, CH), 129.4 (d, 1 C, CH), 129.8 (d, 1 C, CH), 130.9 (d, 1 C, CH), 131.7 (d, 1 C, Cq), 132.3 (d, 1 C, CH), 135.1 (s, 1 C, Cq), 138.4 (s, 1 C, Cq), 159.5 (s, 1 C, Cq), 167.8 (s, 1 C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₁₈H₁₅NOBrF (M + Na)⁺: 382.0213, found: 382.0215 ± 1 ppm.

2.3.11. *Z*-3-Benzylidene-2-[2-(Diethylamino)Ethyl]-2,3-Dihydro-1*H*-Isoindol-1-One (**6a**)



Appearance: beige solid.

Melting point: 43 °C.

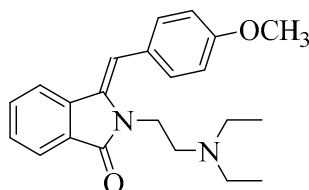
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3132, 1645, 1612, 1574, 1300, 824, and 691.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 1.13 (t, *J* = 9 Hz, 6H, 2 × CH₃), 2.67–2.74 (m, 4H, N(CH₂)₂), 2.83 (t, *J* = 9 Hz, 2H, NCH₂), 4.04 (t, *J* = 9 Hz, 2H, NCH₂), 6.68 (s, 1H, CH), 7.33–7.49 (m, 8H, CH), 7.87 (d, *J* = 9 Hz, 1H, CH).

¹³C-NMR (mixture of stereoisomers, 75 MHz, CDCl₃): δ (ppm): 12.1 (q, 2C, CH₃), 39.2 (t, 1C, CH₂N), 47.1 (t, 2C, N(CH₂)₂), 50.3 (t, 1C, NCH₂), 106.4 (d, 1C, CH), 119.3 (d, 1C, CH), 123.3 (s, 1C, Cq), 127.7 (d, 1C, CH), 128.4 (d, 2C, CH), 128.5 (d, 1C, CH), 129.0 (d, 2C, CH), 129.8 (d, 1C, CH), 131.9 (d, 1C, CH), 134.9 (s, 1C, Cq), 135.0 (s, 1C, Cq), 138.6 (s, 1C, Cq), 169.0 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₂₁H₂₄ON₂ (M + Na)⁺: 343.1781, found: 343.1792 ± 3 ppm.

2.3.12. *Z*-2-[2-(Diethylamino)Ethyl]-3-(4-Methoxybenzylidene)-2,3-Dihydro-1*H*-Isoindol-1-One (**6b**)



Appearance: beige oil.

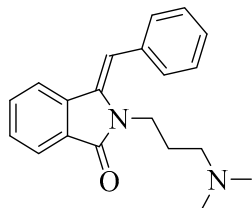
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3130, 1679, 1589, 1371, 1268, 830, and 680.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 1.12 (t, *J* = 9 Hz, 6H, 2 × CH₃), 2.65–2.72 (m, 4H, N(CH₂)₂), 2.81 (t, *J* = 9 Hz, 2H, NCH₂), 3.92 (s, 3H, OCH₃), 4.02 (t, *J* = 9 Hz, 2H, NCH₂), 6.61 (s, 1H, CH), 7.01 (d, *J* = 9 Hz, 2H, CH), 7.40–7.45 (m, 5H, CH), 7.87 (d, *J* = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 12.0 (q, 2C, CH₃), 38.0 (t, 1C, CH₂N), 47.2 (t, 2C, N(CH₂)₂), 50.3 (t, 1C, NCH₂), 55.4 (q, 1C, OCH₃), 106.4 (d, 1C, CH), 119.1 (d, 1C, CH), 123.1 (s, 1C, Cq), 127.0 (d, 1C, CH), 128.8 (d, 2C, CH), 129.1 (d, 1C, CH), 130.4 (d, 2C, CH), 131.9 (s, 1C, Cq), 134.4 (d, 1C, CH), 135.8 (s, 1C, Cq), 138.7 (s, 1C, Cq), 159.3 (s, 1C, Cq), 166.5 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₂₂H₂₆O₂N₂ (M + H)⁺: 351.2067, found: 351.2061 ± 2 ppm. calcd for C₂₂H₂₆O₂N₂ (M + Na)⁺: 373.1886, found: 373.1886 ± 0 ppm.

2.3.13. Z-3-Benzylidene-2-[3-(Dimethylamino)Propyl]-2,3-Dihydro-1*H*-Isoindol-1-One (6c)



Appearance: beige oil.

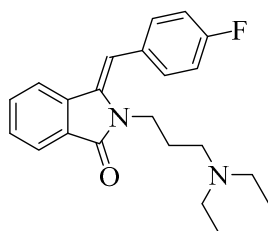
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3138, 1640, 1649, 1581, 1329, 852, and 678.

¹H-NMR (300 MHz, acetone-d₆): δ (ppm): 1.91–2.01 (m, 2H, CH₂), 2.28 (s, 6H, N(CH₃)₂), 2.43 (t, *J* = 9 Hz, 2H, NCH₂), 3.98 (t, *J* = 9 Hz, 2H, NCH₂), 6.67 (s, 1H, CH), 7.30–7.48 (m, 8H, CH), 7.87 (d, *J* = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 26.7 (t, 1C, CH₂), 37.6 (t, 1C, NCH₂), 45.5 (t, 2C, N(CH₃)₂), 56.9 (t, 1C, CH₂N), 110.4 (d, 1C, CH), 123.1 (d, 1C, CH), 123.2 (s, 1C, Cq), 127.8 (d, 1C, CH), 128.7 (d, 1C, CH), 129.2 (d, 2C, CH), 129.6 (d, 1C, CH), 129.9 (s, 1C, Cq), 130.4 (d, 1C, CH), 131.4 (d, 1C, CH), 135.1 (d, 1C, CH), 135.4 (s, 1C, Cq), 136.4 (s, 1C, Cq), 166.7 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₂₀H₂₂ON₂ (M + Na)⁺: 329.1624, found: 329.1624 ± 1 ppm.

2.3.14. Z-2-[2-(Diethylamino)Propyl]-3-(4-Fluorobenzylidene)-2,3-Dihydro-1*H*-Isoindol-1-One (6d)



Appearance: beige solid.

Melting point: 40 °C.

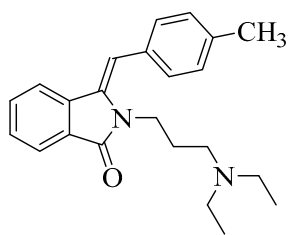
IR (film): $\tilde{\nu}$ (cm⁻¹) = 3230, 1671, 1648, 1576, 1148, 836, and 671.

¹H-NMR (300 MHz, acetone-d₆): δ (ppm): 1.02 (t, *J* = 6 Hz, 6H, 2 × CH₃), 1.90 (t, *J* = 6 Hz, 2H, CH₂), 2.54 (t, *J* = 6 Hz, 6H, N(CH₂)₂, NCH₂), 3.92 (t, *J* = 9 Hz, 2H, NCH₂), 6.54 (s, 1H, CH), 7.12 (t, *J* = 9 Hz, 2H, CH), 7.21 (d, *J* = 9 Hz, 1H, CH), 7.30–7.44 (m, 4H, CH), 7.83 (d, *J* = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 11.6 (q, 2C, CH₃), 25.7 (t, 1C, CH₂), 38.0 (t, 1C, CH₂N), 46.3 (t, 2C, N(CH₂)₂), 50.5 (t, 1C, NCH₂), 106.9 (d, 1C, CH), 110.7 (d, 1C, CH), 114.5 (s, 1C, Cq), 119.7 (d, 1C, CH), 127.5 (d, 1C, CH), 128.3 (d, 2C, CH), 130.4 (d, 1C, CH), 131.2 (s, 1C, Cq), 131.7 (s, 1C, Cq), 134.0 (d, 1C, CH), 135.8 (d, 1C, CH), 138.9 (s, 1C, Cq), 158.5 (s, 1C, Cq), 167.1 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₂₂H₂₅N₂OF (M + H)⁺: 353.2024, found: 353.2031 ± 2 ppm.

2.3.15. Z-2-[2-(Diethylamino)Propyl]-3-(4-Methylbenzylidene)-2,3-Dihydro-1*H*-Isoindol-1-One (6e)



Appearance: beige oil.

IR (film): $\tilde{\nu}$ (cm⁻¹) = 3101, 1682, 1612, 1565, 1361, 850, and 673.

¹H-NMR (300 MHz, CDCl₃): δ (ppm): 1.02 (t, *J* = 6 Hz, 6H, 2 × CH₃), 1.91 (m, 2H, CH₂), 2.42 (s, 3H, CH₃), 2.52–2.59 (m, 6H, N(CH₂)₂, NCH₂), 3.93 (t, *J* = 9 Hz, 2H, NCH₂), 6.58 (s, 1H, CH), 7.23 (d, *J* = 9 Hz, 2H, CH), 7.29–7.36 (m, 4H, CH), 7.40–7.43 (m, 1H, CH), 7.82 (d, *J* = 9 Hz, 1H, CH).

¹³C-NMR (75 MHz, CDCl₃): δ (ppm): 11.9 (q, 2C, CH₃), 19.5 (q, 1C, CH₃), 25.7 (t, 1C, CH₂), 38.8 (t, 1C, CH₂N), 43.7 (t, 2C, N(CH₂)₂), 51.3 (t, 1C, NCH₂), 106.1 (d, 1C, CH), 111.2 (d, 1C, CH), 114.0 (s, 1C, Cq), 120.3 (d, 1C, CH), 127.0 (d, 1C, CH), 128.4 (d, 2C, CH), 130.9 (d, 1C, CH), 131.1 (s, 1C, Cq), 131.7 (s, 1C, Cq), 134.4 (d, 1C, CH), 135.0 (d, 1C, CH), 138.7 (s, 1C, Cq), 140.1 (s, 1C, Cq), 166.7 (s, 1C, C=O).

HRMS (ESI/MeOH): *m/z*: calcd for C₂₃H₂₈N₂O (M + Na)⁺: 371.2094, found: 371.2103 ± 3 ppm.