Supporting information

Synthesis of novel D-π-A-based photosensitive alkoxyamine : Application of two-photon polymerization via nitroxide-mediated photopolymerization

Nam Hoai Nguyen[a]†, Xingyu Wu[b]†, Yohann Guillaneuf[a], Arnaud Spangenberg[b], Didier Gigmes*[a], Jean-Louis Clément*[a]

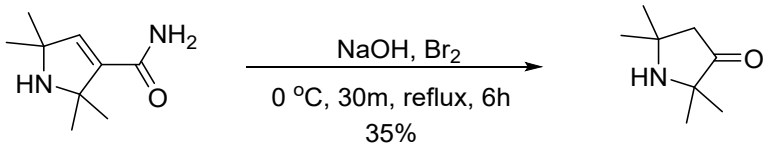
[a] Aix Marseille Univ, CNRS, Institut de Chimie Radicalaire UMR 7273, Marseille, France.

Email : didier.gigmes@univ-amu.fr, jean-louis.clement@univ-amu.fr

[b] Institut de Science des Matériaux de Mulhouse (IS2M), CNRS – UMR 7361, Université de Haute-Alsace, 15 rue Jean Starcky, 68057 Mulhouse, France Université de Strasbourg, France

1. Synthesis

1.1. Synthesis of 2,2,5,5-Tetramethylpyrrolidin-3-one (1)



Scheme S1: The synthesis of 2,2,5,5-Tetramethylpyrrolidin-3-one.

In a 250 ml one-neck flask equipped with a water-cooling condenser, NaOH (3 g, 106.99 mmol, 6.0 eq.) was dissolved in H_2O (30 ml) and cooled down to 0 ºC in an ice bath. Bromine (3.56g, 22.29 mmol, 1.25eq.) was added dropwise via syringe to the solution of NaOH at 0 ºC for 20 minutes. Then, a solution of 2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrole-3-carboxamide (3 g, 17.83 mmol, 1.0 eq.) in H_2O (30 ml) was added in one portion and the mixture was heated at reflux temperature for 6 hours. After cooling to room temperature, the mixture was extracted with EtOAc (2 x 50 ml). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purification by chromatography (diethyl ether – THF, 60 – 40) to afford **1** as the yellow oil (900 mg, 35%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.31 (s, 2H), 1.67 (s, 1H), 1.22 (s, 6H), 1.17 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) 62.48, 53.66, 50.70, 30.94, 27.87 (**Figure S1**).

1.2. Synthesis of 4.4.1.1.7-bromo-1,1,3,3-tetramethyl-2,3-dihydro-1H-pyrrolo[3,4-b]quinolin-9-amine (2)

1 (500 mg, 3.54 mmol, 1.0 eq.), 2-amino-5-bromo benzonitrile (838 mg, 4.25 mmol, 1.20 eq.) and toluene were sequentially added into a round-flask equipped with a water-cooling condenser. The resulting mixture was stirred at room temperature for 15 minutes. Anhydrous aluminum chloride was then added in one portion and the mixture reaction was heated at reflux for 18 hours. After completion, the mixture was cooled down to room temperature and 10% aq. NaOH solution (100 ml) was added into the flask and stirred for 30 minutes. The organic phase was separated by a separatory funnel and the aqueous phase was extracted with CH_2Cl_2 (2 x 30 ml). The combined organic layers were washed with saturated NaCl solution (60 ml), dried over MgSO4, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (DCM/MeOH, v/v = 10/0 to 9/1) to afford **2** as a yellow solid (675 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.87 – 7.77 (m, 2H), 7.63 – 7.56 (m, 1H), 4.56 (s, 1H), 1.54 (s, 6H), 1.47 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.77, 148.08, 142.65, 131.87, 131.31, 125.51, 122.46, 119.76, 117.79, 62.42, 59.88, 30.17, 29.26; HRMS-ESI: m/z calculated for $[M+H]^+$ $C_{15}H_{19}BrN_3^+$ 320.0757, found 320.0756, (**Figure S2**).

1.3. 9-amino-7-bromo-1,1,3,3-tetramethyl-1,3-dihydro-2H-pyrrolo[3,4-b]quinolin-2-oxyl (3)

2 was dissolved in dichloromethane and cooled to 0 ºC in the ice bath. m-chloroperoxybenzoic (70% purity) (m-CPBA, 500 mg, 2.03 mmol, 1.30 eq.) was added by few portions over 30 minutes at 0 ºC. The reaction mixture was then stirred at room temperature overnight. After completion of reaction, a saturated aq. $NaHCO_3$ solution (60 ml) was added and the resulting mixture was stirred for 30 minutes. The organic phase was separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 30 ml). The combined organic layers were washed with saturated NaCl solution (60 ml), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel chromatography (pentane/THF, v/v = 3/2) to afford the bromo nitroxide **3** as a yellow solid (390 mg, 75%). FT-IR (cm^{-1}): 3500 - 3300 (ν (N-H) amino), and 1672 (ν (C=N)); HRMS-ESI: m/z calculated for $[M+H]^+$ $C_{15}H_{18}BrN_3O^{\bullet+}$ 335.0628, found 335.0625; EPR : a_N = 14.0 G (**Figure S3**).

1.4. Synthesis of 4.4.1.3.7-bromo-1,1,3,3-tetramethyl-2-(1-phenylethoxy)-2,3-dihydro-1H-pyrrolo[3,4-b]quinolin-9-amine (4)

A deoxygenated (Argon bubbling) solution of toluene (2 ml), (1-bromoethyl) benzene (290 mg, 1.57 mmol, 1.50 eq.) and N,N,N',N',N"-pentamethyl diethylenetriamine (PMDETA) (543 mg, 3.13 mmol, 3.0 eq.) was added via a syringe to a deoxygenated (Argon bubbling) solution of toluene (5 ml), **3** (350 mg, 1.04 mmol, 1.0 eq.), copper (100 mg, 1.57 mmol, 1.50 eq.) and copper (I) bromide (225 mg, 1.57 mmol, 1.50 eq.) contained in a 20 ml crimp headspace vial. The resulting mixture was stirred at room temperature for overnight under an argon atmosphere. The mixture was then filtered over a silica pad and eluted with CH_2Cl_2 and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (pentane/ ethyl acetate, v/v = 9/1) to afford **4** as a white solid (276 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.82 (m, 2H), 7.58 (d, J = 8.9 Hz, 1H), 7.39 – 7.20 (m, 5H), 4.84 (q, J = 6.7 Hz, 1H), 4.69 (brs, 1H), 4.57 (brs, 1H), 1.72 (d, J = 5.3 Hz, 3H), 1.54 (d, J = 6.7 Hz, 3H), 1.46 – 1.31 (m, 3H), 1.30 – 1.16 (m, 3H), 1.13 – 0.92 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.77, 146.35, 143.68, 141.39, 130.76, 130.16, 127.17, 126.45, 126.03, 125.82, 121.35, 119.17, 116.68, 116.18, 115.96, 82.95, 66.97, 66.35, 64.95, 64.32, 29.29, 28.66, 28.04, 27.76, 27.50, 27.00, 22.49, 22.28, 21.53, 20.60, 20.38; HRMS-ESI: m/z calculated for $[M+H]^+$ $C_{23}H_{27}BrN_3O^+$ 442.1315, found 442.1313.

1.5. Synthesis of 4.4.1.6.1,1,3,3-tetramethyl-2-(1-phenylethoxy)-7-(phenylethynyl)-2,3-dihydro-1H-pyrrolo[3,4-b]quinolin-9-amine (5)

In a 20 ml crimp headspace vial, a solution of **4** (220 mg, 0.5 mmol, 1.0 eq.), copper (I) iodide (2.40 mg, 0.125 mmol, 0.025 eq) and $PdCl_2(PPh_3)_2$ (17.50 mg, 0.25 mmol, 0.05 eq.) in anhydrous triethylamine (4 ml) was deoxygenated by argon bubbling at 0 ºC for 30 minutes. A previously deoxygenated solution of phenylacetylene (66.30 mg, 0.65 mmol, 1.30 eq.) in anhydrous triethylamine (1ml) was added dropwise via a syringe to the solution of **4**. The reaction mixture was stirred at room temperature for 1 hour before heating at 60 ºC for 18 hours under an argon atmosphere. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residue was purified by silica chromatography (pentane/ethyl acetate, v/v = 4/1) to afford **5** as an off-white solid 136 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.85 (d, J = 13.9 Hz, 2H), 7.62 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 5.2 Hz, 2H), 7.38 – 7.20 (m, 8H), 4.86 (q, J = 6.7 Hz, 1H), 4.70 (brs, 1H), 4.59 (brs, 1H), 1.72 (d, J = 5.9 Hz, 3H), 1.55 – 1.42 (m, 6H), 1.55 – 1.26

– 1.00 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.97, 165.66, 147.37, 143.76, 141.92, 134.80, 130.60, 130.21, 128.68, 127.39, 127.35, 127.19, 126.46, 126.07, 125.86, 124.50, 122.41, 122.18, 117.83, 117.67, 116.01, 115.79, 88.66, 88.60, 82.95, 67.05, 66.43, 64.97, 64.35, 28.68, 28.12, 27.83, 27.58, 27.07, 22.56, 22.35, 21.57, 20.66, 20.45, 20.16; HRMS-ESI: m/z calculated for $[M+H]^+$ $C_{31}H_{32}N_3O^+$ 462.2540, found 462.2539.

2. ^{1}H and ^{13}C NMR spectra, HMRS-ESI

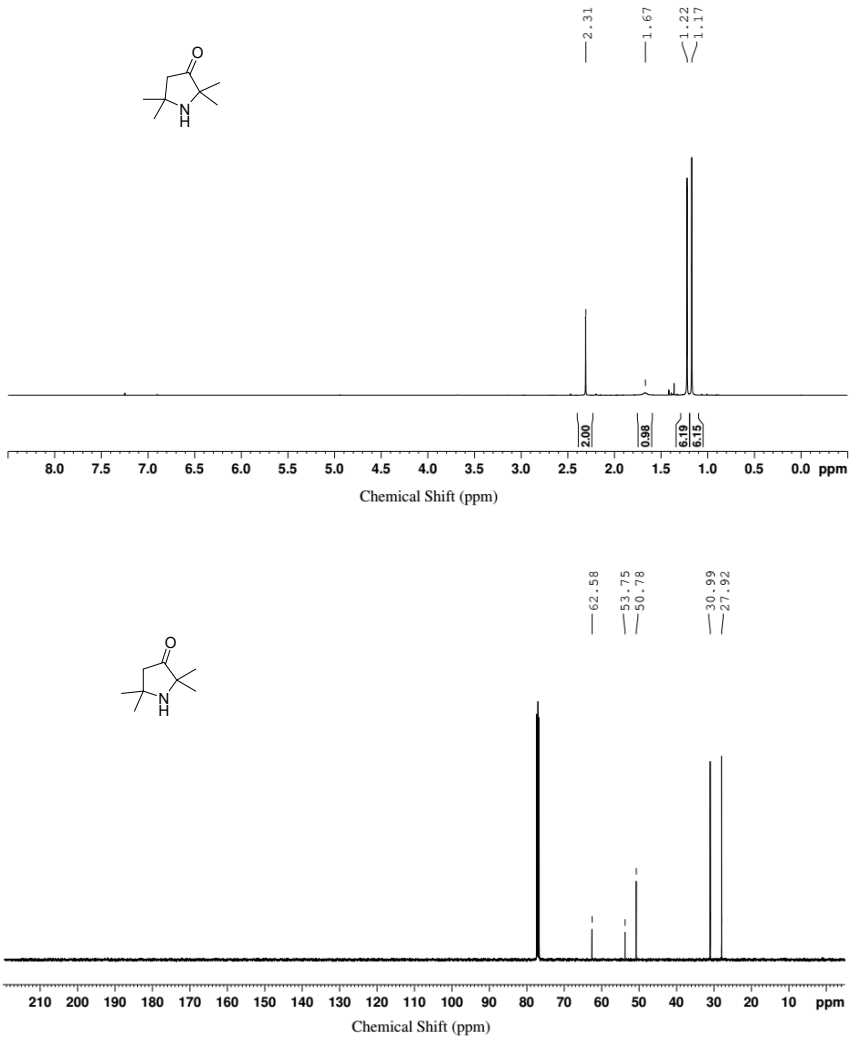


Figure S1: ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **1**.

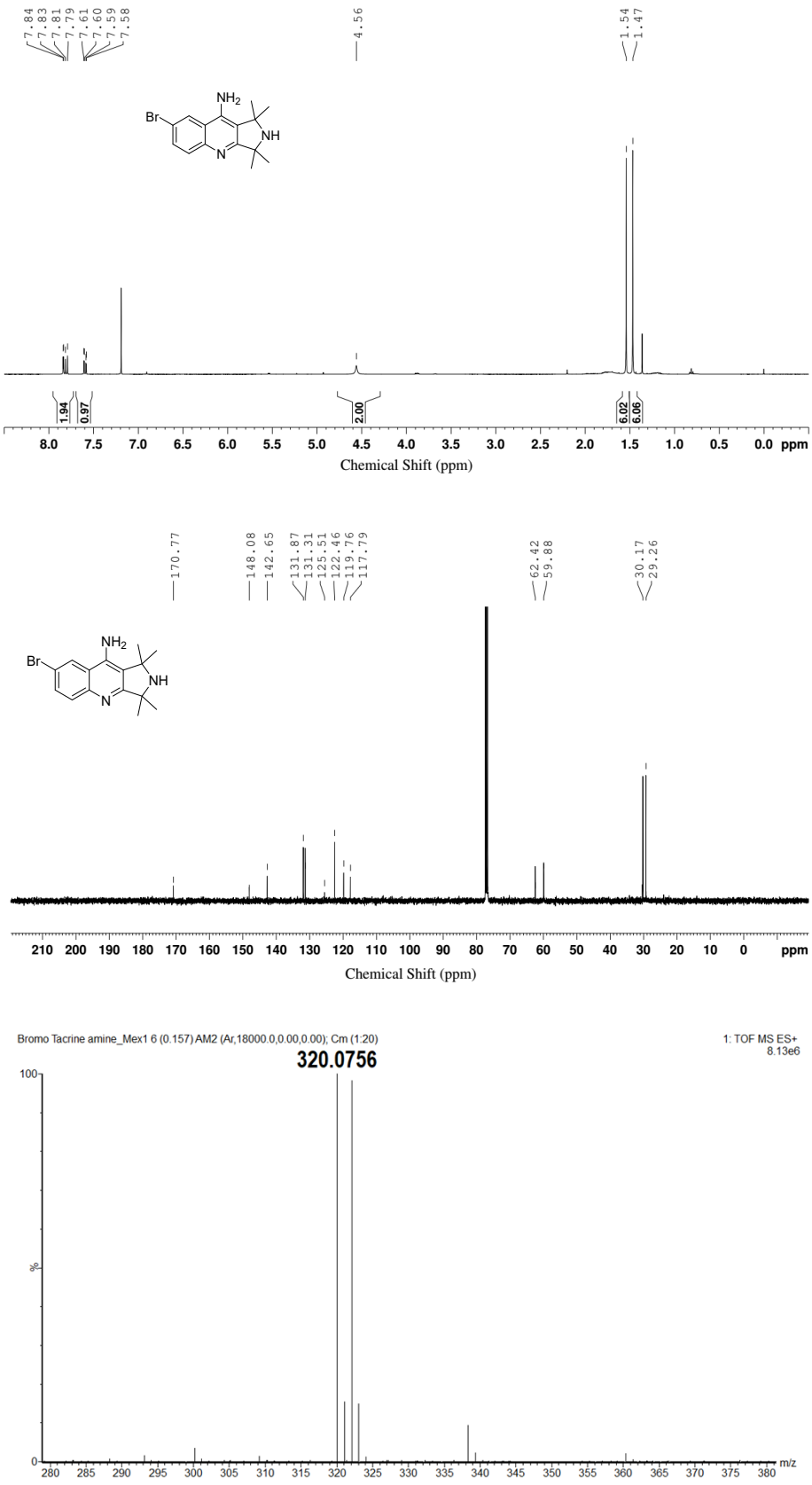


Figure S2: ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra, HR-MS spectra of **2**.

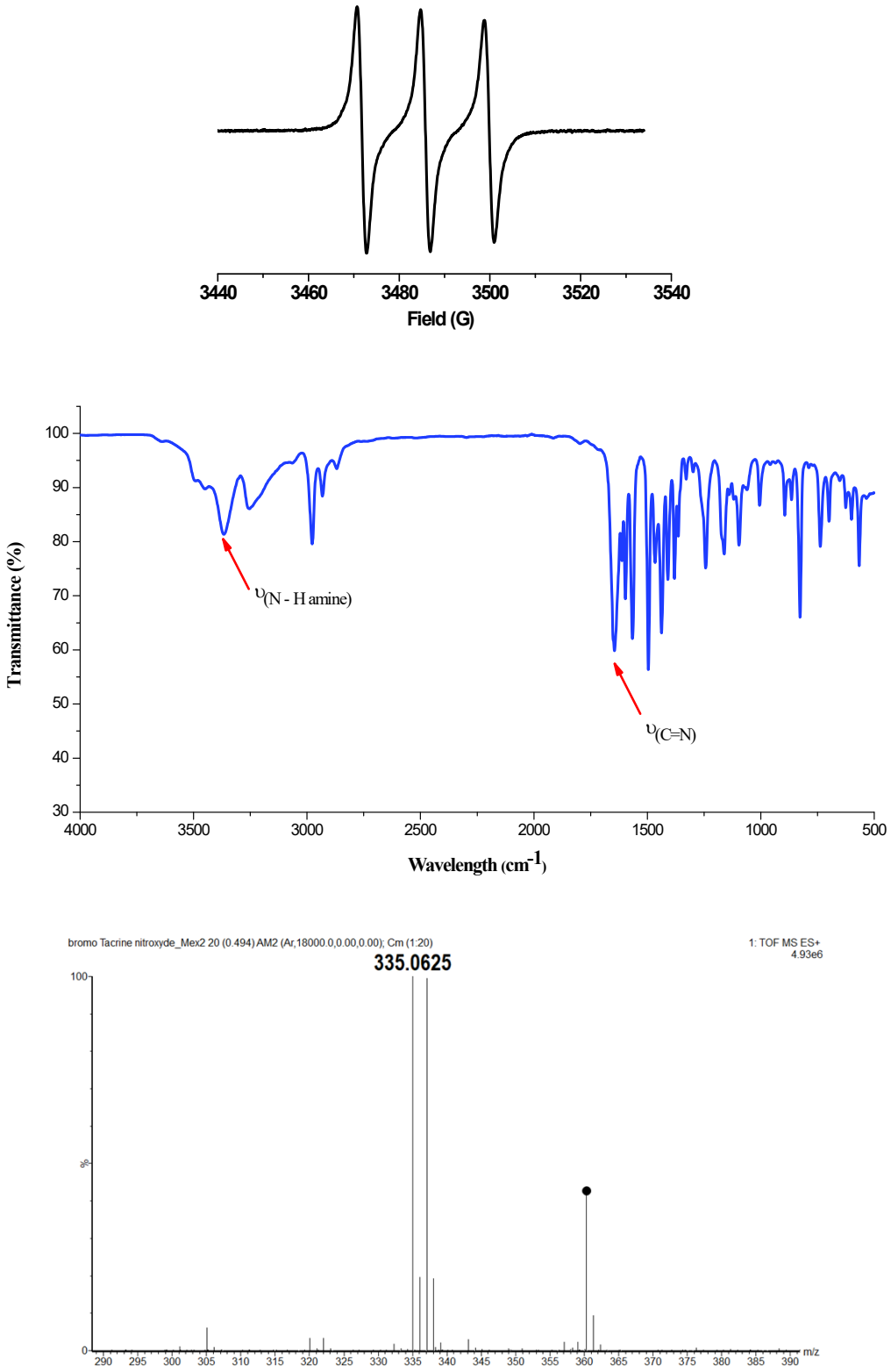


Figure S3: EPR, IR spectra and HR-MS spectra of **3**. The signal annotated with a black dot at m/z 360.3 is present in blank analysis

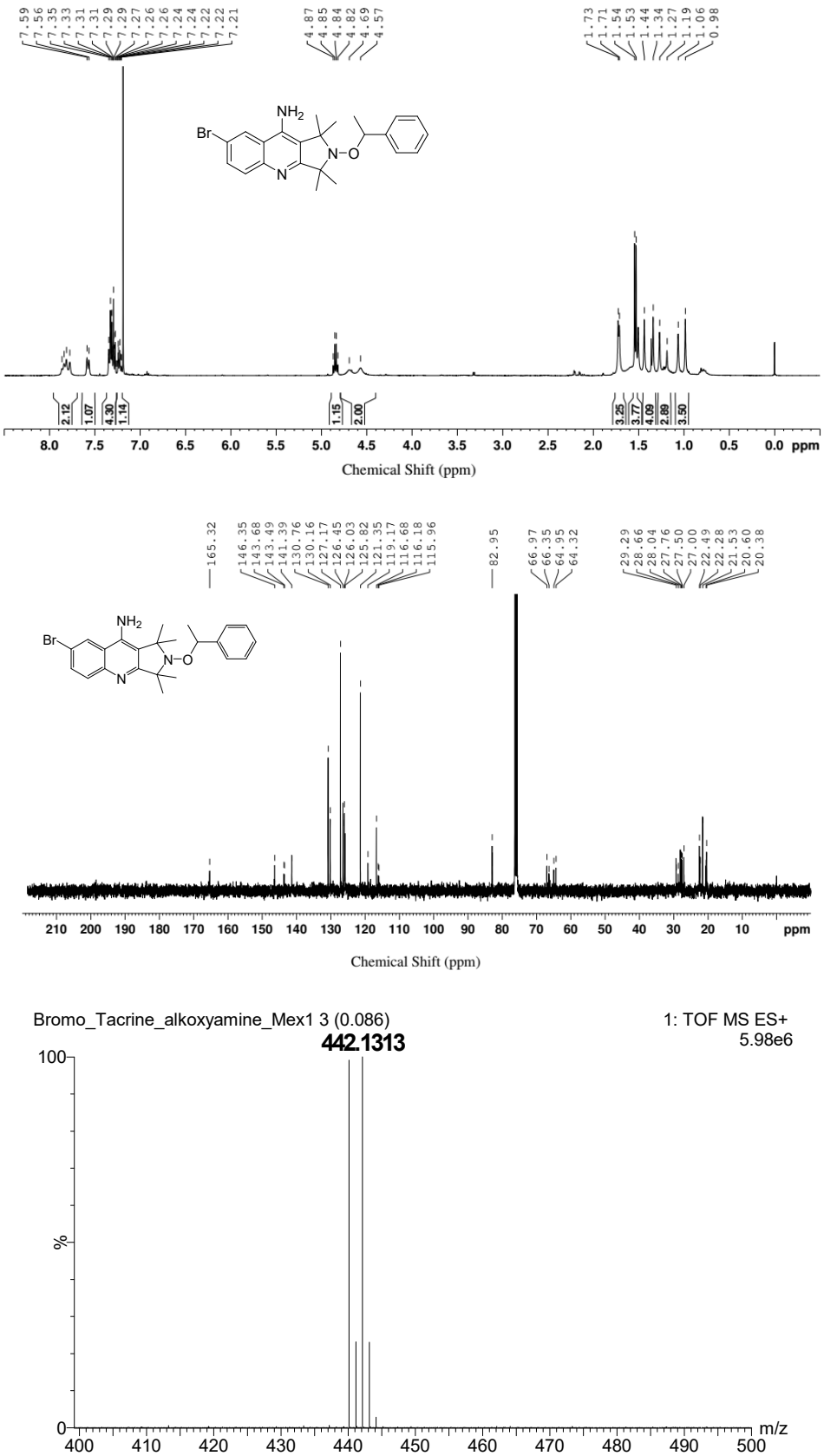


Figure S4: ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR, HR-MS spectra of **4**.

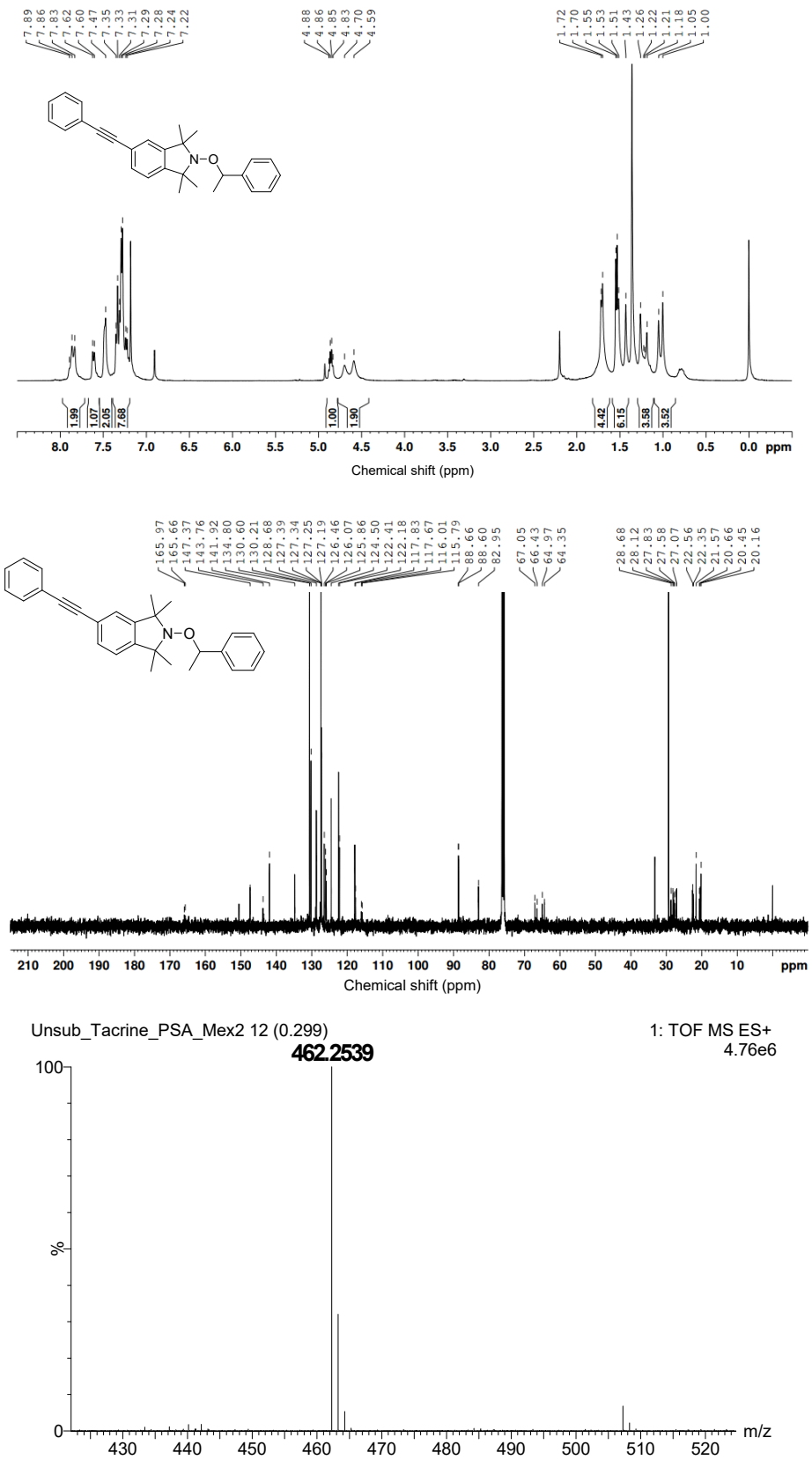


Figure S5: ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR, HR-MS of **5**.

3. Molar extinction coefficient measurements

The molar extinction coefficients were obtained by dilution of a stock solution (10^{-4} M) in *t*-butylbenzene using the Beer-Lambert formula (A = εlc).

3.1. 7-bromo-1,1,3,3-tetramethyl-2-(1-phenylethoxy)-2,3-dihydro-1H-pyrrolo[3,4-b]quinolin-9-amine (4) in t-butylbenzene

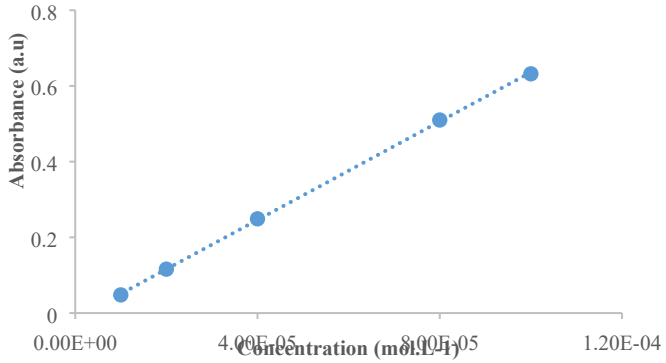


Figure S6: Molar extinction coefficient calculation of **4** measured at 308 nm.

3.2. 1,1,3,3-tetramethyl-2-(1-phenylethoxy)-7-(phenylethynyl)-2,3-dihydro-1H-pyrrolo[3,4-b]quinolin-9-amine (5) in t-butylbenzene

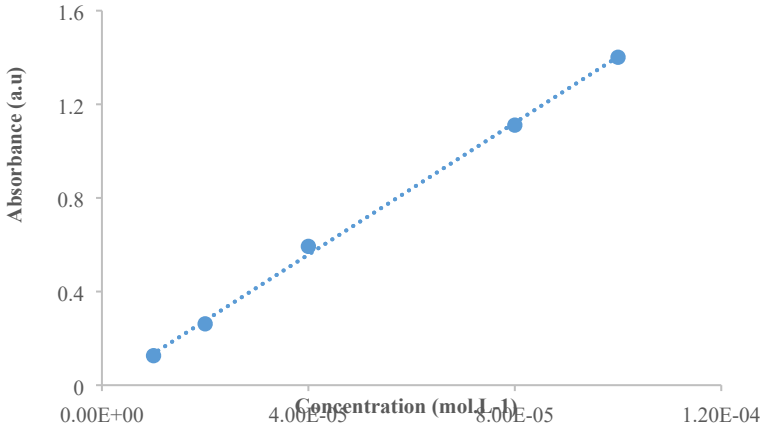


Figure S7: Molar extinction coefficient calculation of **5** measured at 327 nm

4. Light source

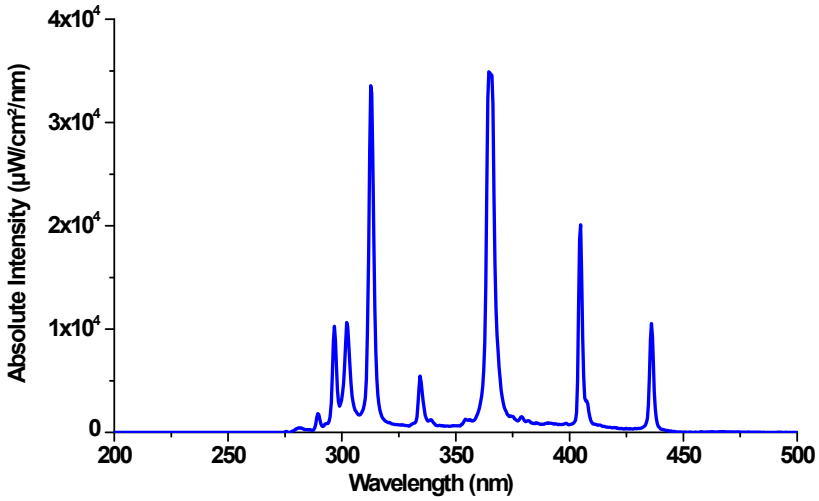


Figure S8: Emission spectrum of Hamamatsu Lighteningcure LC8 with a glass filter at 10% of intensity

5. Two-photon stereolithography

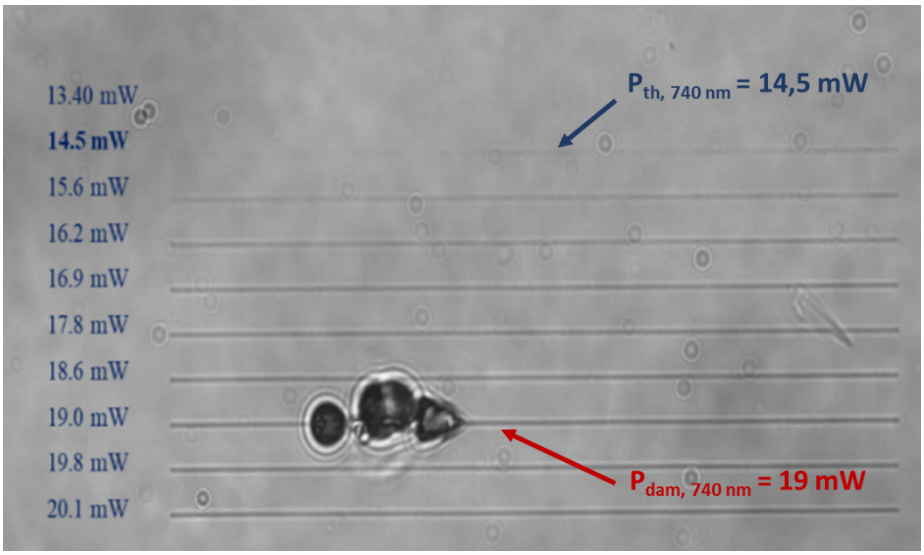


Figure S9: Determination of the two-photon polymerization threshold power P_{th} and of the damage power P_{dam} at λ_{exc}: 740 nm (exposure time: 10 ms, under air) by optical microscopy.

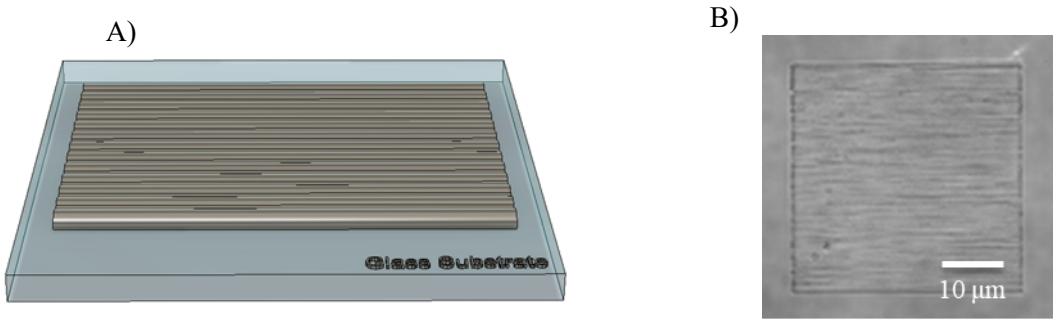


Figure S10: A) Schematic presentation of written square on the glass substrate and B) optical microscopy image of 50 x 50 µm^2 of the square 2D microstructure fabrication at λ_{exc} = 740 nm, 15.6 mW and exposure time = 10 ms, under air after one week of the development in ethanol.

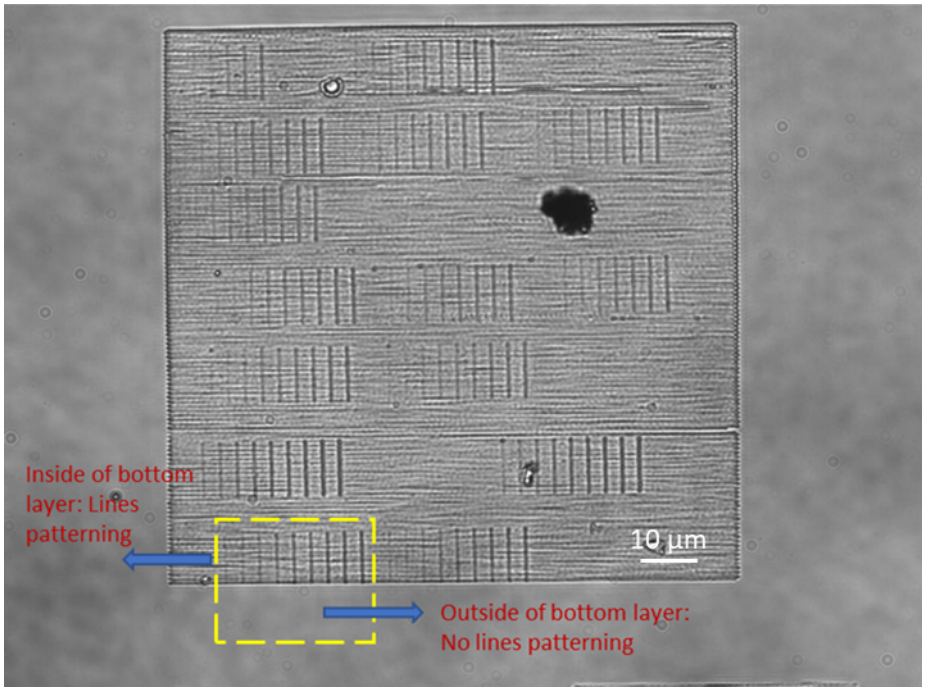


Figure S11: Re-polymerization of pure TMPTA on a first written square made of PETA + **5** 2%, Absence of lines patterns outside the square.