

Photochemical Catalyst-Free Synthesis of Pyrrolidines via a Hofmann-Löffler-Freytag Reaction

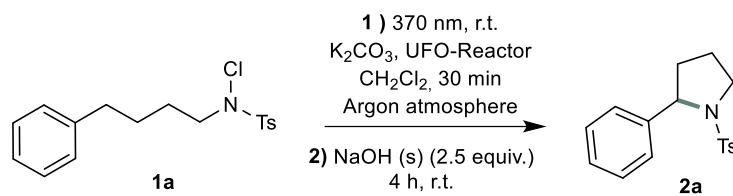
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SUPPORTING INFORMATION

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Control experiments

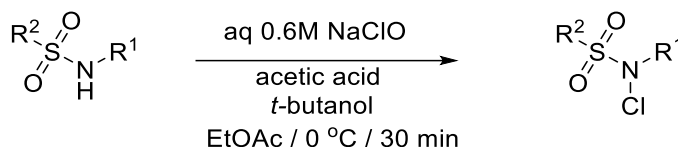


Entry	Deviation from standard conditions	Conversion (%) ^[a]
1	No irradiation	0
2	No irradiation and heating of reaction mixture at 60 °C	0

The reaction was performed with *N*-chloro-4-methyl-*N*-(4-phenylbutyl)benzenesulfonamide (**1a**) (67 mg, 0.20 mmol, 1.0 equiv.), K₂CO₃ (33 mg, 0.24 mmol, 1.2 equiv.) in CH₂Cl₂ (4 mL) without irradiation for 30 min, under an argon atmosphere. Afterwards, solid NaOH (20 mg, 0.50 mmol, 2.5 equiv.) was added to the reaction mixture and it was left stirring for 4 hours. ^[a] Conversion was determined by ¹H-NMR.

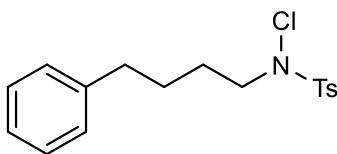
Synthesis of Starting Materials

General Procedure for the Synthesis of *N*-Chloro Sulfonamides

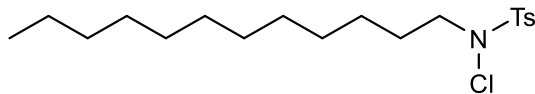


In a round-bottom flask with a magnetic stirrer, *t*-butanol (0.22 g, 0.3 mL, 3.00 mmol, 10.0 equiv.), acetic acid (0.36 g, 0.4 mL, 6.00 mmol, 20.0 equiv.) and sulfonamide (0.30 mmol, 1.0 equiv.) were dissolved in ethyl acetate (10 mL). The reaction mixture was cooled at 0 °C. An aqueous solution of NaClO (0.6 M, 7.6 mL, 4.50 mmol, 15.0 equiv.) was added dropwise and the reaction mixture was left stirring for 30 min. The reaction mixture was diluted with EtOAc (20 mL) and washed with a saturated aqueous solution of NaHCO₃ (10 mL) and brine (10 mL), dried over Na₂SO₄, filtered, and evaporated to dryness. The product was used without further purification.

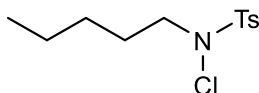
N-Chloro-4-methyl-*N*-(4-phenylbutyl)benzenesulfonamide (**1a**)¹



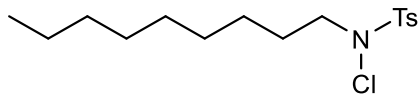
White solid; m.p.: 64-66 °C; **Yield:** 91%; ¹H NMR (400 MHz, CDCl₃): δ = 7.80 (2H, d, *J* = 7.7 Hz, ArH), 7.38 (2H, d, *J* = 7.7 Hz, ArH), 7.30-7.26 (2H, m, ArH), 7.20-7.16 (3H, m, ArH), 3.25-3.21 (2H, m, NCH₂), 2.66-2.63 (2H, m, CH₂), 2.46 (3H, s, CH₃), 1.72-1.70 (4H, m, 2 x CH₂); ¹³C NMR (100 MHz, CDCl₃): δ = 145.4, 141.8, 129.8, 129.7, 129.6, 128.4, 128.4, 125.9, 56.4, 35.2, 27.7, 26.5, 21.7; **MS (ESI)** *m/z* 337 [M+H]⁺.

***N*-Chloro-*N*-dodecyl-4-methylbenzenesulfonamide (1b)**

Colorless oil; **Yield:** 95%; **¹H NMR** (400 MHz, CDCl₃): δ = 7.81 (2H, d, J = 7.9 Hz, ArH), 7.37 (2H, d, J = 7.9 Hz, ArH), 3.21 (2H, t, J = 6.8 Hz, NCH₂), 2.46 (3H, s, CH₃), 1.69-1.62 (2H, m, CH₂), 1.37-1.20 (18H, m, 9 x CH₂), 0.87 (3H, t, J = 6.5 Hz, CH₃); **¹³C NMR** (100 MHz, CDCl₃): δ = 145.3, 130.0, 129.7, 129.6, 56.7, 31.9, 29.6, 29.6, 29.5, 29.5, 29.3, 29.0, 27.0, 26.1, 22.7, 21.7, 14.1; **MS (ESI)** m/z 373 [M+H]⁺.

***N*-Chloro-4-methyl-*N*-pentylbenzenesulfonamide (1c)¹**

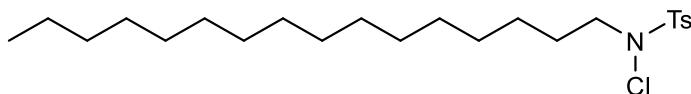
Colorless oil; **Yield:** 93%; **¹H NMR** (400 MHz, CDCl₃): δ = 7.80 (2H, d, J = 7.8 Hz, ArH), 7.37 (2H, d, J = 7.8 Hz, ArH), 3.20 (2H, m, NCH₂), 2.46 (3H, s, CH₃), 1.69-1.62 (2H, m, CH₂), 1.35-1.29 (4H, m, 2 x CH₂), 0.89 (3H, t, J = 6.1 Hz, CH₃); **¹³C NMR** (100 MHz, CDCl₃): δ = 145.3, 129.6, 129.5, 127.0, 56.6, 28.1, 26.6, 22.1, 21.6, 13.8; **MS (ESI)** m/z 275 [M+H]⁺.

***N*-Chloro-4-methyl-*N*-nonylbenzenesulfonamide (1d)**

Colorless oil; **Yield:** 60%; **¹H NMR** (400 MHz, CDCl₃): δ = 7.81 (2H, d, J = 7.5 Hz, ArH), 7.38 (2H, d, J = 7.5 Hz, ArH), 3.20 (2H, t, J = 6.3 Hz, NCH₂), 2.46 (3H, s, CH₃), 1.69-1.62 (2H, m, CH₂), 1.35-1.21 (12H, m, 6 x CH₂), 0.86 (3H, t, J = 6.5 Hz, CH₃); **¹³C NMR** (100 MHz, CDCl₃):

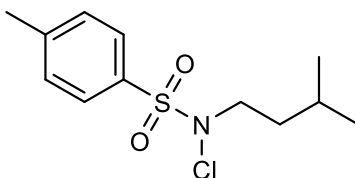
δ = 145.2, 129.9, 129.7, 129.6, 56.7, 31.8, 29.4, 29.2, 29.1, 27.0, 26.0, 22.7, 21.7, 14.1; **MS (ESI)** m/z 331 $[M+H]^+$.

N-Chloro-N-hexadecyl-4-methylbenzenesulfonamide (1e)

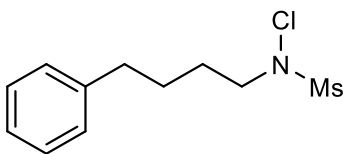


Colorless oil; **Yield:** 96%; **^1H NMR** (400 MHz, CDCl_3): δ = 7.81 (2H, d, J = 8.2 Hz, ArH), 7.37 (2H, d, J = 8.2 Hz, ArH), 3.21 (2H, t, J = 6.9 Hz, NCH_2), 2.46 (3H, s, CH_3), 1.69-1.62 (2H, m, CH_2), 1.37-1.20 (26H, m, 13 x CH_2), 0.87 (3H, t, J = 6.7 Hz, CH_3); **^{13}C NMR** (100 MHz, CDCl_3): δ = 145.3, 130.0, 129.7, 129.6, 56.7, 31.9, 29.7, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4, 29.1, 27.1, 26.1, 22.7, 21.7, 14.1; **MS (ESI)** m/z 429 $[M+H]^+$.

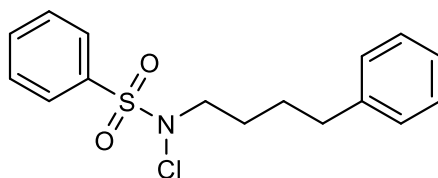
N-Chloro-N-isopentyl-4-methylbenzenesulfonamide (1f)



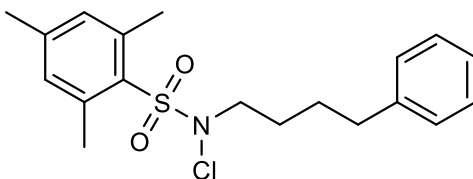
Pale yellow oil; **Yield:** 88%; **^1H NMR** (400 MHz, CDCl_3): δ = 7.83 (2H, d, J = 8.1 Hz, ArH), 7.40 (2H, d, J = 8.1 Hz, ArH), 3.26 (2H, t, J = 6.9 Hz, NCH_2), 2.48 (3H, s, CH_3), 1.77-1.67 (1H, m, CH), 1.59-1.54 (2H, m, CH_2), 0.93 (6H, d, J = 6.7 Hz, 2 x CH_3); **^{13}C NMR** (100 MHz, CDCl_3): δ = 145.4, 129.8, 129.7, 129.6, 55.1, 35.7, 25.1, 22.3, 21.7; **MS (ESI)** m/z 275 $[M+H]^+$.

***N*-Chloro-*N*-(4-phenylbutyl)methanesulfonamide (1g)¹**

Pale yellow oil; **Yield:** 89%; **¹H NMR** (400 MHz, CDCl₃): δ = 7.34-7.31 (2H, m, ArH), 7.25-7.21 (3H, m, ArH), 3.48 (2H, t, J = 5.9 Hz, NCH₂), 3.08 (3H, s, CH₃), 2.66-2.63 (2H, t, J = 6.9 Hz, CH₂), 1.84-1.74 (4H, m, 2 x CH₂); **¹³C NMR** (100 MHz, CDCl₃): δ = 141.6, 128.3, 128.3, 125.8, 55.6, 35.1, 33.6, 27.5, 26.5; **MS (ESI)** m/z 261 [M+H]⁺.

***N*-Chloro-*N*-(4-phenylbutyl)benzenesulfonamide (1h)**

Pale yellow oil; **Yield:** 88%; **¹H NMR** (400 MHz, CDCl₃): δ = 7.96 (2H, d, J = 7.6 Hz, ArH), 7.43 (1H, t, J = 7.6 Hz, ArH), 7.62 (2H, t, J = 7.6 Hz, ArH), 7.43-7.29 (3H, m, ArH), 7.23-7.19 (2H, m, ArH), 3.28 (2H, t, J = 5.7 Hz, NCH₂), 2.68 (2H, t, J = 6.7 Hz, CH₂), 1.80-1.70 (4H, m, 2 x CH₂); **¹³C NMR** (100 MHz, CDCl₃): δ = 141.8, 134.3, 132.9, 129.5, 129.1, 128.4, 128.4, 125.9, 56.5, 35.2, 27.7, 26.5; **MS (ESI)** m/z 325 [M+H]⁺.

N-Chloro-N-(4-phenylbutyl)mesitylsulfonamide (1i)

Yellow oil; **Yield:** 88%; **¹H NMR** (400 MHz, CDCl₃): δ = 7.32-7.26 (2H, m, ArH), 7.22-7.16 (3H, m, ArH), 7.00 (2H, s, ArH), 3.55 (2H, t, J = 6.6 Hz, NCH₂), 2.69 (6H, s, 2 x CH₃), 2.64 (2H, t, J = 7.5 Hz, ArCH₂), 2.33 (3H, s, CH₃), 1.86-1.79 (2H, m, CH₂), 1.74-1.67 (2H, m, CH₂); **¹³C NMR** (100 MHz, CDCl₃): δ = 144.2, 141.9, 141.8, 132.0, 129.0, 128.4, 128.4, 125.9, 52.6, 35.2, 27.9, 26.4, 23.0, 21.2; **MS (ESI)** m/z 365 [M+H]⁺.

Reaction setup for the HLF Reaction

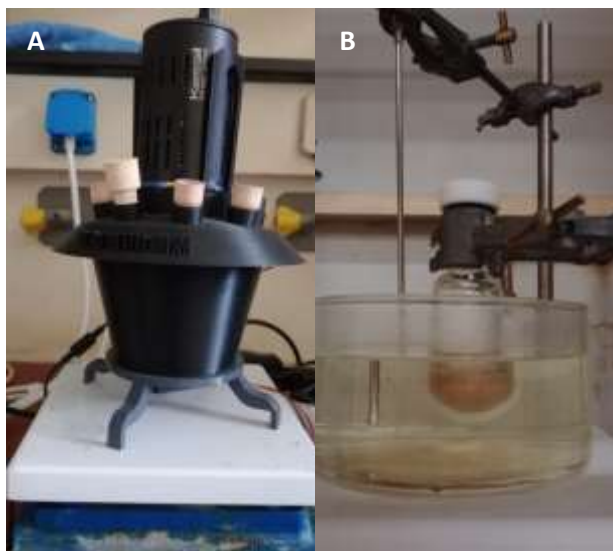


Figure S1. A) Reaction setup for the photochemical step, B) Reaction setup for the cyclization process.

UV-Vis Studies

UV-Vis studies were conducted with 4 mL of CH_2Cl_2 and 0.20 mmol (67 mg) of *N*-chloro-4-methyl-*N*-(4-phenylbutyl)benzenesulfonamide (**1a**).

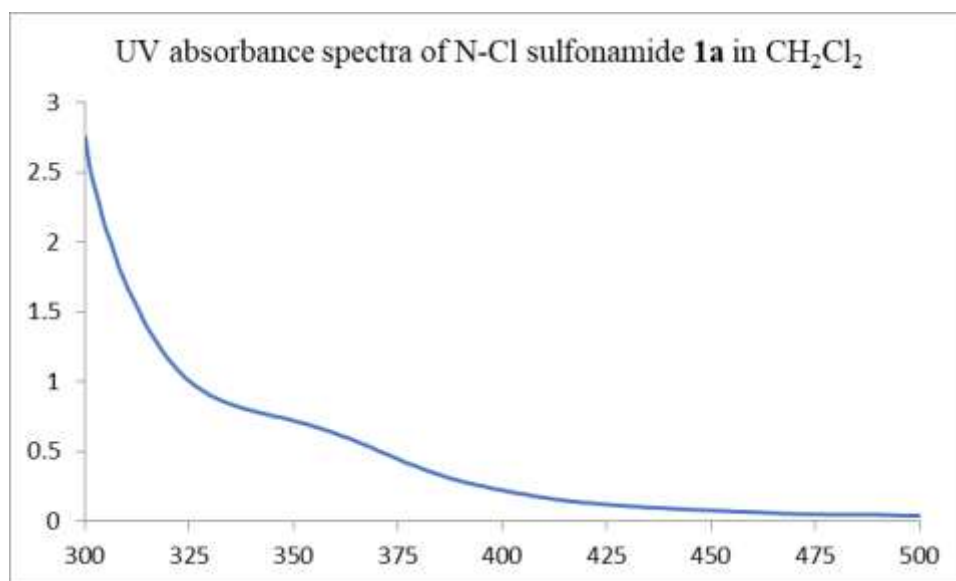


Figure S2. UV-Vis absorbance spectra of **1a** in CH_2Cl_2 (50 mM).

References

1. D. Chang, R. Zhao, C. Wei, Y. Yao, Y. Liu, L. Shi, *J. Org. Chem.* **2018**, 83, 3305-3315.

NMR Spectra

