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SUPPORTING INFORMATION

Revisiting the synthesis of the benzothioxanthene imide five decades later

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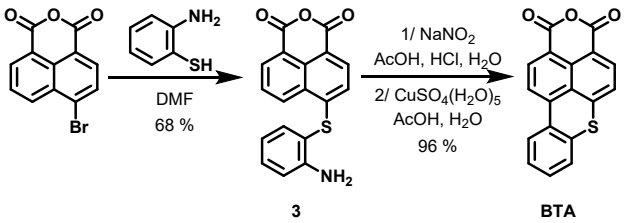
General methods

All reagents and chemicals from commercial sources were used without further purification unless specified. Solvents were dried and purified using standard techniques. Flash chromatography was performed with analytical-grade solvents using ALDRICH silica gel (technical grade, pore size 60 Å, 230–400 mesh particle size). Flexible plates ALUGRAM Xtra SIL G UV254 from MACHEREY-NAGEL were used for TLC. Compounds were detected by UV irradiation (BIOBLOCK SCIENTIFIC). NMR spectra were recorded with a BRUKER AVANCE III 300 (^{1}H, 300 MHz and ^{13}C, 75 MHz) or a BRUKER AVANCE DRX500 (^{1}H, 500 MHz; ^{13}C, 125 MHz). Chemical shifts are given in ppm relative to TMS and coupling constants *J* in Hz. High resolution mass spectrometry (HRMS) was performed with a JEOL JMS-700 B/E.

Synthetic procedures

Original synthesis of BTA[1]



*Scheme S1. Original synthesis of **BTA***

6-((2-aminophenyl)thio)-1H,3H-benzo[de]isochromene-1,3-dione (3): 4-Bromo-1,8-naphthalic anhydride (2 g, 1 eq), potassium carbonate (498 mg, 0.5 eq) and 2-aminothiophenol (1.16 mL, 1.5 eq) were refluxed in 20 mL DMF for 30 minutes. The reaction mixture was cooled and poured into water (100 mL). The solids were filtered and washed thoroughly with water. After drying under vacuum the resulting yellow-greenish solid (1.57 g, 68 % yield) was found to be of sufficient purity to be engaged in next reactions. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.75 (dd, *J* = 8.5, 1.0 Hz, 1H), 8.68 (dd, *J* = 7.3, 1.1 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 7.87 (dd, *J* = 8.5, 7.3 Hz, 1H), 7.54 – 7.45 (m, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.96 – 6.83 (m, 2H), 4.30 (s, 2H).

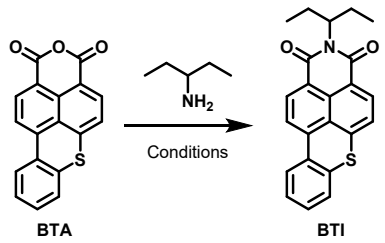
1H,3H-thioxantheno[2,1,9-def]isochromene-1,3-dione (BTA): To a stirred suspension of **3** (1 g, 1 eq) in glacial acetic acid (7.5 mL), water (1.25 mL) and concentrated hydrochloric acid (37 % w/v, 0.78 mL) at 0 °C was added dropwise a solution of sodium nitrite (2.15 g, 10 eq) in water (2.2 mL). After addition, the reaction mixture was allowed to warm to room temperature and was stirred overnight. This diazonium liquor was then added over 30 minutes to a boiling solution of hydrated copper sulphate (2.33 g, 3 eq) in water (30 mL) and glacial acetic acid (1.9 mL). After addition, the reaction mixture was refluxed for 30 minutes before being cooled and filtered. The orange solid collected was washed thoroughly with water and dried under vacuum. The obtained **BTA** (909 mg, 96 %) was then used without further purifications. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.3 Hz, 1H), 8.40 (d, *J* = 8.1 Hz, 1H), 8.26 – 8.20 (m, 2H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.47 – 7.42 (m, 3H).

Optimization of imidization cyclization

BTA (200 mg, 1 eq) and pentan-3-amine (763 μL, 2 eq) were charged into a 5 mL microwave pressure vial. 5 mL of solvent were added and the reaction mixture was sealed with a Teflon® cap. The mixture was then heated to reflux of the solvent for the appropriate amount of time. All data are gathered in Table S1. When reaction was completed or no further evolution monitored by TLC, the mixture was cooled down before being diluted with CH_2Cl_2 (≈ 30 mL). The organic phase was washed twice with water and once with brine, then dried over $MgSO_4$ and finally filtered. After removal of the solvent by rotary evaporation, the crude was subjected to a silica plug flash chromatography (eluent CH_2Cl_2) to afford **BTI** as an orange powder. Spectroscopic data matched those previously reported by our group.[2] **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.1 Hz, 1H), 8.40 (d, *J* = 8.0 Hz, 1H), 8.25 – 8.15 (m, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.39 (m, 3H), 5.11 – 5.00 (m, 1H), 2.33 – 2.18 (m, 2H), 1.97 – 1.83 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 6H).

In the case of the ball-mill reaction, no solvent is involved and **BTA** (1 g, 1 eq) is directly reacted with pentan-3-amine (420 μL, 1.1 eq). The reagents were charged into a 50 mL stainless steel grinding jar. The latter was inserted in a Retsch® MM 400 mixer mill and subjected to a 30 Hz grinding process for 90 minutes. Unfortunately, the reaction did not occur as the starting **BTA** was entirely recovered.

Table S1. Conditions used for the imidization cyclization with pentan-3-amine



Entry	Solvent	Temperature (°C) / time (h)	Heating source	Yield (%)
1	Imidazole	140 / 5	Lab Armor™ Beads bath	65
2	AcOH	130 / 48	Lab Armor™ Beads bath	0
3	Ball-mill	N.A. / 1.5	N.A.	0
4	2-methylTHF	90 / 48	Lab Armor™ Beads bath	14
5	Xylenes	150 / 36	Lab Armor™ Beads bath	9
6	2-ethoxyethanol	150 / 18	Lab Armor™ Beads bath	67
7	2-ethoxyethanol	150 / 6	Microwave	70
8	2-ethoxyethanol	200 / 2	Microwave	72

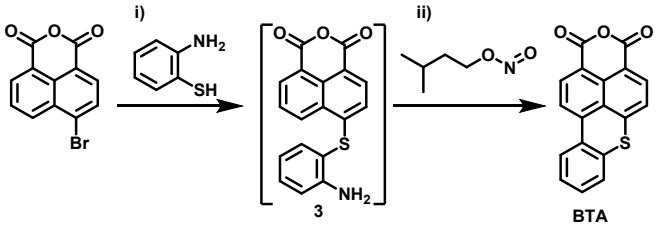
One-pot synthesis of BTA

Procedure for the synthesis of **BTA** *via* conventional heating (Table S2, entries 1 and 3): 4-Bromo-1,8-naphthalic anhydride (200 mg, 1 eq), potassium carbonate (50 mg, 0.5 eq) and 2-aminothiophenol (93 μL, 1.2 eq) were charged into a 5 mL microwave pressure vial. 5 mL of solvent were added and the mixture was sealed with a Teflon® cap. After 30 minutes of stirring at room temperature, isoamyl nitrite (290 μL, 3 eq) was added with a syringe and the vial was transferred into a Lab Armor™ Beads bath to be heated at 150 °C for 16 hours. After cooling down to room temperature, the reaction mixture was poured into water (100 mL) and filtered. The resulting orange solid was thoroughly washed with water, dried under vacuum and weighed.

Microwave-assisted one-pot synthesis of **BTA** (Table S2, entries 2 and 4): 4-Bromo-1,8-naphthalic anhydride (200 mg, 1 eq), potassium carbonate (50 mg, 0.5 eq) and 2-aminothiophenol (93 μL, 1.2 eq) were charged into a 5 mL microwave pressure vial. 5 mL of solvent were added and the mixture was sealed with a Teflon® cap. The vial was inserted into the cavity of a Biotage® Initiator+ where it was

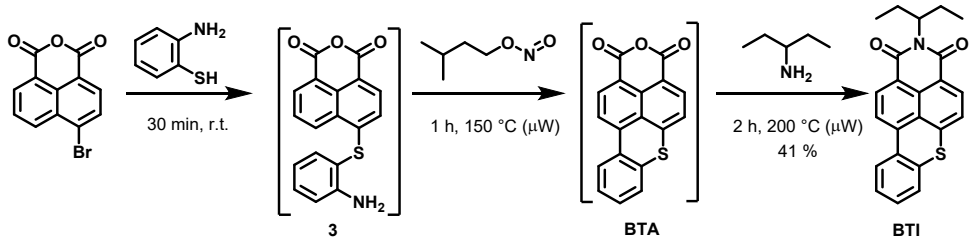
subjected to microwave irradiation. After 15 minutes of irradiation at 150 °C, isoamyl nitrite (290 μL, 3 eq) was added with a syringe (temperature was cooled to 50°C) and the vial was irradiated again at 150 °C for 1 hour. The reaction mixture was allowed to cool down to room temperature and poured into water (100 mL). After filtration, the resulting orange solid was thoroughly washed with water, dried under vacuum and weighed.

*Table S2. Optimization of the one-pot synthesis of **BTA***



Entry	Solvent	Heating source	Temperature (°C) / time (h) for i)	Temperature (°C) / time (h) for ii)	Yield (%)
1	DMF	Lab Armor™ Beads bath	r.t / 0.5	150 / 16	70
2	DMF	Microwave	150 / 0.25	150 / 1	91
3	2-ethoxyethanol	Lab Armor™ Beads bath	r.t / 0.5	150 / 16	92
4	2-ethoxyethanol	Microwave	150 / 0.25	150 / 1	91

One-pot synthesis of BTI



*Scheme S2. One-pot synthesis of **BTI***

Microwave-assisted one-pot synthesis of **BTI**: 4-Bromo-1,8-naphthalic anhydride (200 mg, 1 eq), potassium carbonate (50 mg, 0.5 eq) and 2-aminothiophenol (93 μL, 1.2 eq) were charged into a 5 mL microwave pressure vial. 5 mL of solvent were added and the mixture was sealed with a Teflon® cap. After 30 minutes of stirring at room temperature, isoamyl nitrite (290 μL, 3 eq) was added with a

syringe and the vial was transferred into the cavity of a Biotage® Initiator+ where it was subjected to microwave irradiation. After 1 hour at 150 °C, pentan-3-amine (168 μL, 2 eq) was added to the mixture before a second round of irradiation (at 200 °C for 2 hours). After cooling down to room temperature, the reaction mixture was diluted with CH_2Cl_2 (≈ 30 mL). The organic phase was washed 2 times with water, one time with brine and was then dried over $MgSO_4$. The solvent was removed by rotary evaporation and the crude was subjected to silica gel column chromatography (eluent CH_2Cl_2) to afford **BTI** (110 mg, 41 % yield).

Spectral data

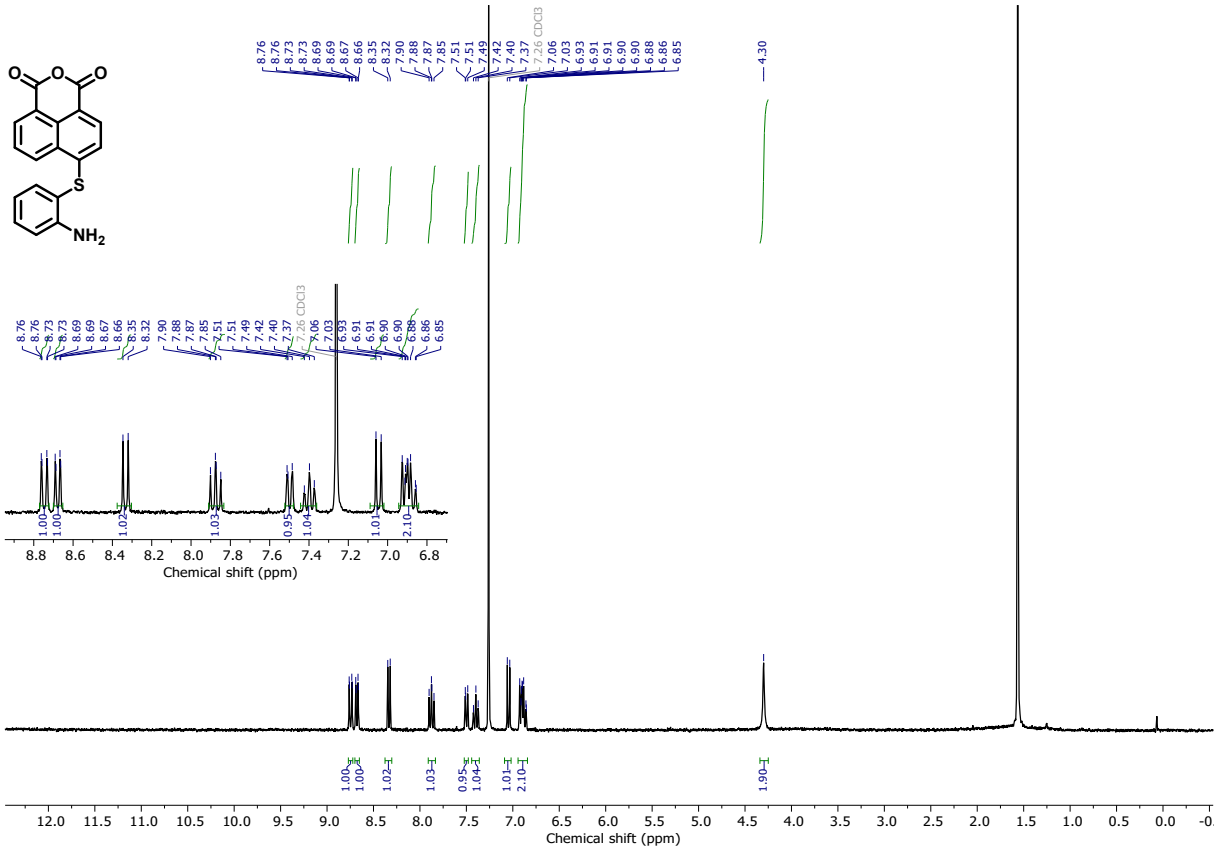


*Figure S1. ^{1}H NMR spectrum of **3** ($CDCl_3$)*

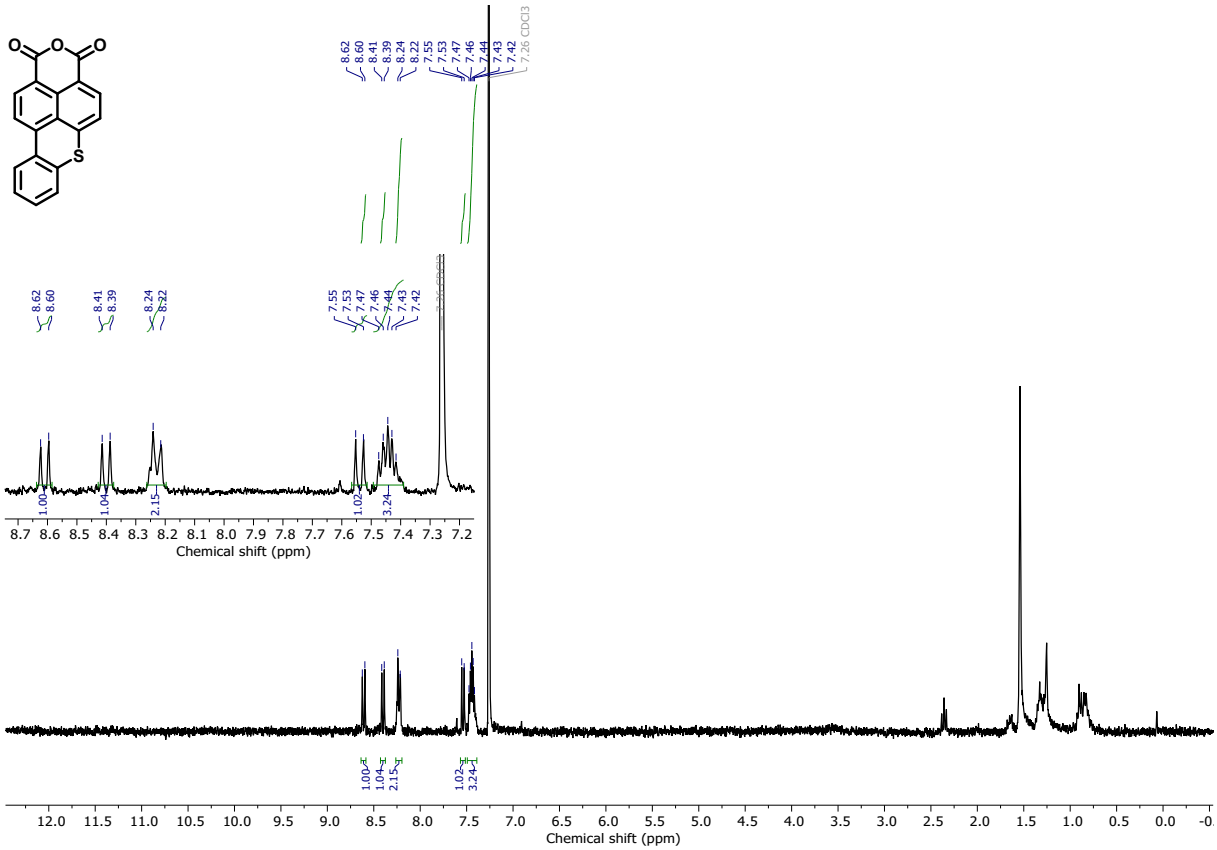


*Figure S2. ^{1}H NMR spectrum of **BTA** ($CDCl_3$)*

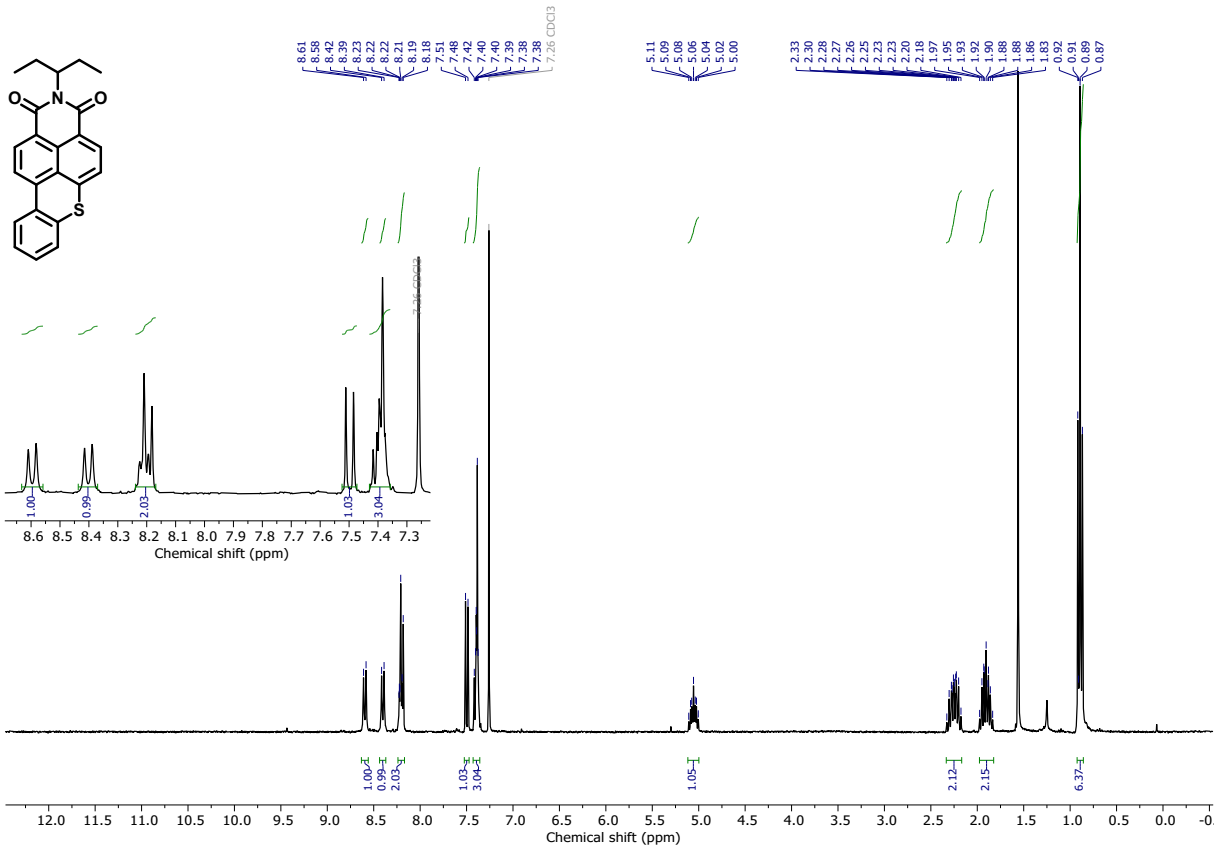


*Figure S3. ^{1}H NMR spectrum of **BTI** ($CDCl_3$)*

References

[1] P. H. Grayshan, A. M. Kadhim, A. T. Perters, *J. Heterocycl. Chem.* **1974**, *11*, 33-38.

[2] P. Josse, S. Li, S. Dayneko, D. Joly, A. Labrunie, S. Dabos-Seignon, M. Allain, B. Siegler, R. Demadrille, G. C. Welch, C. Risko, P. Blanchard, C. Cabanetos, *J. Mater. Chem. C* **2018**, *6*, 761-766.