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Revisiting the synthesis of the benzothioxanthene imide five decades later

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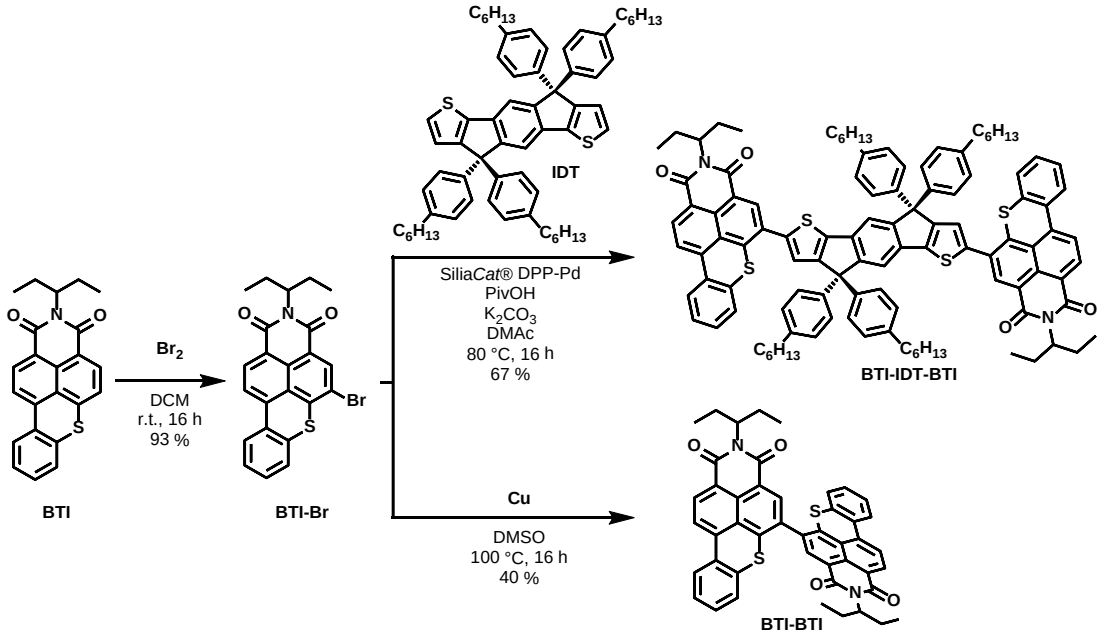
Abstract: With amazing optical and electrochemical properties, the benzothioxanthene imide, a sulfur containing rylene, has only recently been demonstrated as promising building block for organic electronics. As a result, the seminal synthetic procedure, published almost 50 years ago, has never been amended nor revisited so far. Given the great potential of this dye and numerous application perspectives, we thus report herein a significant update and modernization of its synthesis.

Introduction:

Since its first publication in the early 70's,[1, 2] the benzothioxanthene imide (**BTI**) has gone completely unnoticed by the organic electronic community though characterized by remarkable optical and electrochemical properties. In this context, we have initiated, almost five years ago, an exploratory work aiming at functionalizing its core to prepare original π-conjugated active materials for optoelectronic devices (Scheme 1). Selectively monobrominated,[3] **BTI-Br** was successfully engaged in various palladium and copper-catalyzed coupling reactions, affording, for instance, **BTI-IDT-BTI** and **BTI-BTI**[4] *via* direct (hetero)arylation and Ullmann reaction respectively. While the indacenodithiophene (**IDT**) based derivative was found to be an interesting donor material in binary and ternary organic solar cells, particularly to reach high open circuit voltages,[5] the dimer was, in turn, effectively used as emitting material for the preparation of solution-processed OLEDs.



*Scheme 1. Structure of the **BTI**, **BTI-Br** and **BTI** based structures used as active materials in organic solar cells and light emitting devices.*

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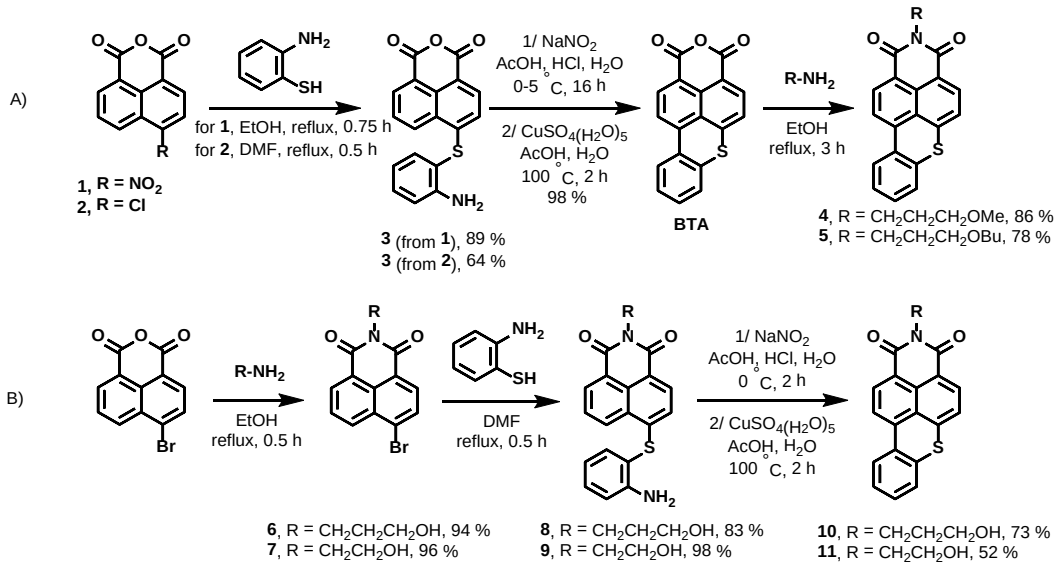
Beyond demonstrating the potential of **BTI**-based materials for organic electronics, these seminal results opened doors to myriad of new design principles and potential chemical modifications.[6-8] Consequently, to provide sufficient starting materials required for such an exploratory process, with minimum time and synthetic effort, we undertook to update the preparation of this sulfur containing rylene, namely the **BTI**. Published by Grayshan, Khadim and Petters, the latter was initially prepared in three steps through two possible approaches (A and B, Scheme 2).[1]



*Scheme 2. Seminal synthesis of the **BTI** reported by Grayshan, Khadim and Petters in 1974 through two approaches (A and B)*

Both relying on three common reactions, namely a nucleophilic aromatic substitution (S_NAr), a Pschorr cyclization and an imidization condensation, the latter simply differ according to the applied sequence order, *ie*, whether alkyl chains are introduced at the beginning or the end. Hence, the objective is to simplify, shorten and adapt this preparation to modern technologies to save time, increase safety and minimize synthetic costs.

Results and discussion

As depicted in Scheme 2, three naphthalene derivatives functionalized with different leaving groups (Cl, Br or NO_2) were seminally used for the S_NAr reaction with the 2-aminobenzenethiol. Considering that all of them led to the target compound in good yield, the cheapest and most easily accessible, since available from most usual chemical suppliers, was selected for this study, namely the 4-bromo-1,8-naphthalic anhydride. Hence, the seminal synthetic route, illustrated in scheme 3, was first reproduced to afford the alkylated and soluble **BTI**. Albeit the anhydride (**BTA**) was successfully isolated with similar yields, attempts of condensation with pentan-3-amine in the early reported and used solvent, namely ethanol systematically failed.

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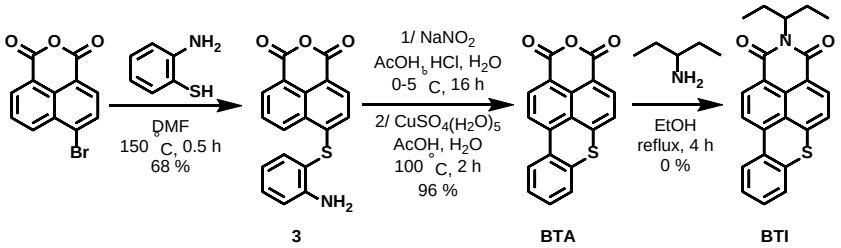

*Scheme 3. Synthetic route considered for the preparation of **BTI** from the commercially available 4-bromo-1,8-naphthalic anhydride*

Seemingly, the presence of one or several heteratoms or heterogroups within the alkane chain turns out to be a key parameter to succeed in preparing the imide under these conditions. Stemming from the perylene diimide-related literature, ethanol was thereafter replaced by imidazole.[9] Solid at room temperature, the latter can indeed be used as solvent once heated above 91 °C. However, to reach decent yields, the reaction mixture requires to be heated to 140 °C for at least five hours (table 1, entry 1).

Table 1. 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

On the other hand, although these conditions led to the preparation of the target **BTI**, difficulties to get rid of the imidazole without recurring to thorough purifications, thus limiting the scale up, prompted us to consider other experimental conditions. Hence, while no conversion of the starting anhydride into the imide was monitored in both glacial acetic acid and under a solvent-free procedure (table 1, entries 2 and 3), modest yields were laboriously achieved with “green” solvents, namely the 2-methyl THF and a mixture of xylenes (entries 4 and 5). Furthermore, the use of the polar and high

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boiling temperature 2-ethoxyethanol (135 °C) led, *a contrario*, to synthetic yields as good as those achieved with the imidazole with, nonetheless, a major difference since it can be easily removed by simple successive washing cycles during the work-up (entry 6). In addition, it is noteworthy that reaction time can be significantly reduced by replacing the conventional heating bath by micro wave irradiations (table 1, entries 7 and 8). Finally, it is noteworthy that only a simple filtration through a plug of silica is required to reach a sufficient level of purity as shown by NMR analysis (Figure 1).

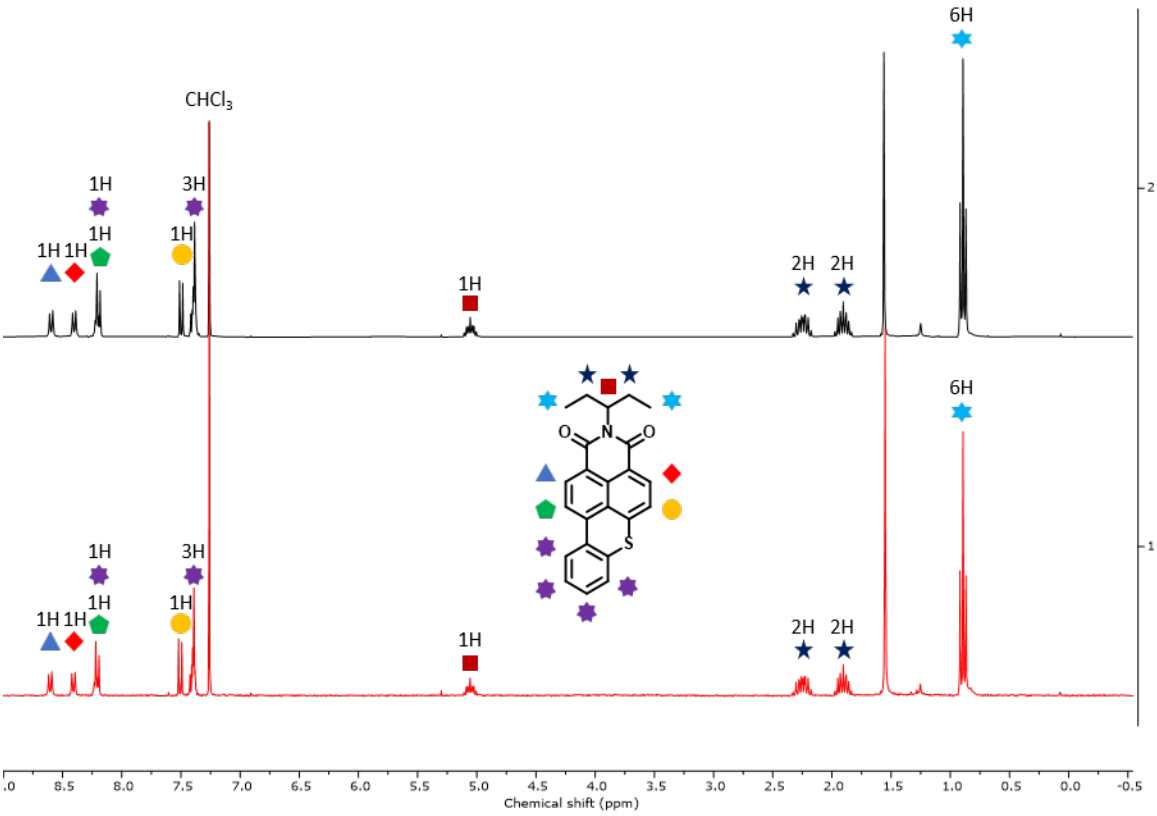
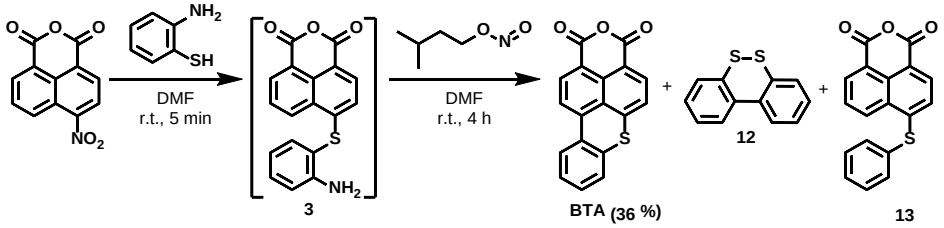


*Figure 1. Comparison of ^{1}H NMR spectra ($CDCl_3$) of **BTI** prepared in imidazole (top, black, purification by column chromatography) or 2-ethoxyethanol (bottom, red, simple filtration through a small plug of silica).*

In parallel, Khadim and Petters demonstrated the same year that the successive two steps Pschorr cyclization can be simplified through the use of alkyl nitrite.[2] While conventional Pschorr cyclization is performed under strong acidic conditions and requires the manipulation of boiling reaction mixtures, this mild alternative only consists in adding isoamyl nitrite to a solution of **3** and stirring this reaction mixture for half an hour at room temperature. Interestingly, attempts of "one-pot" synthesis of the anhydride **BTA** *via* this nitrite assisted heterocyclization led to moderate yields (36 %), mainly due to the formation of 2.2'-diaminodiphenyldisulphide **12**, the product resulting from the hydrolysis of the diazonium intermediate (**13**) and uncharacterized high molecular weight derivatives (Scheme 4).



*Scheme 4. One pot synthesis of the **BTA** attempt reported by Khadim and Petters from 4-nitro-1,8-naphthalic anhydride*

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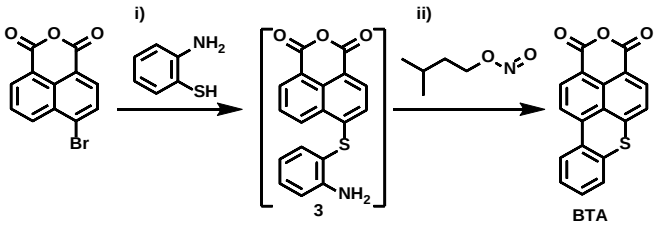
Appealing, this strategy was thus investigated and adapted to the 4-bromo-1,8-naphthalic anhydride since higher synthetic yields were achieved for the S_NAr reaction than with its nitro counterpart. (Table 2).

*Table 2. Optimization of the one-pot synthesis of the anhydride **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

To that end, 2-aminobenzenthiol was first added to a solution of 4-bromo-1,8-naphthalic anhydride in DMF (table 2, entry 1). After 30 min of stirring at room temperature and the full conversion of the starting materials, isoamyl nitrite was added and the reaction mixture was heated overnight at 150 °C to afford the target anhydride **BTA** with a slightly better yield than that obtained with the initial two steps procedure (65 %, scheme 2). Furthermore, by replacing the conventional heating system with microwave irradiations, higher synthetic yields were achieved while significantly reducing the reaction time (table 2, entry 2). However, to ease the product work up, attempts to replace the DMF by an "easier to remove" solvent were thus carried out. Hence, based on optimized imidization condensation results, reaction in 2-ethoxyethanol were subsequently investigated. While similar and high synthetic yields were achieved with both heating modes (table 2, entries 3 and 4), the use of microwave offers the unique advantage of cutting down the reaction time. Considering that a simple work up followed by a filtration through a pad of silica were found to be sufficient to purify the crude, the **BTA** can now be prepared and isolated in less than two hours.

Moreover, since all three key reactions were successfully demonstrated in the same solvent, namely the 2-ethoxyethanol, the subsequent addition of pentan-3-amine into the above-mentioned **BTA** containing reaction mixture to afford the **BTI** through a one-pot like synthesis was naturally undertaken (Figure 2).

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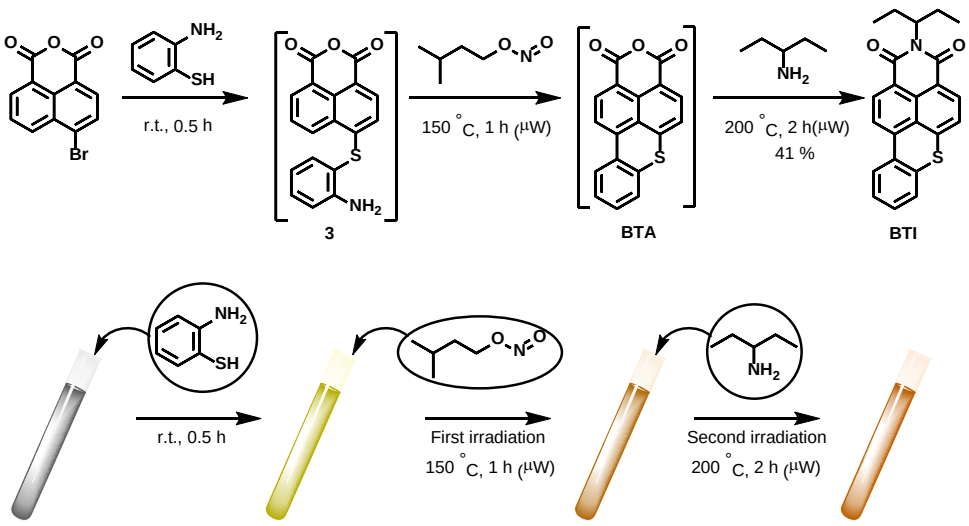
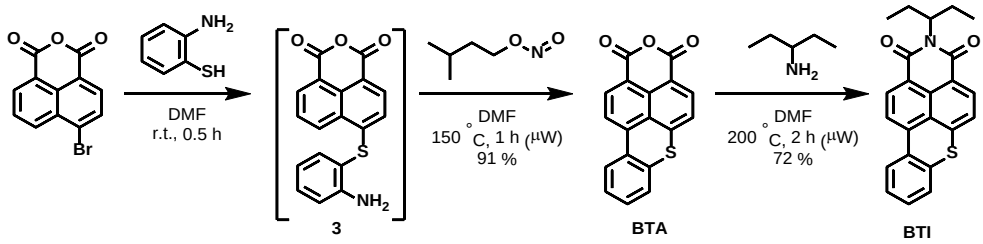


*Figure 2. Preparation of the **BTI** via an optimized one-pot like reaction*

Although demonstrated, the **BTI** was isolated with modest synthetic yields, mainly due to the formation of several side products thus requiring a thorough purification by column chromatography. Considering that the gain of time is clearly minimal, it is thus highly recommended to isolate the **BTA** first, then proceed to the imidization cyclization in order to avoid time and material consuming purifications (Scheme 5).



*Scheme 5. Optimized conditions reported herein to afford the **BTI** in a minimum of time with high yield*

Beyond a good overall synthetic yield of 65 %, these mild optimized conditions provide a safer and faster access to a soluble **BTI** derivative than those seminally reported since grams of the latter can now be prepared in less than four hours from a two steps microwave assisted and column-free procedure.

Conclusion

Despite amazing optical and electrochemical properties, the benzothioxanthene imide clearly went unnoticed by the scientific community. Consequently, its almost 50 years old synthesis has not been revisited nor modernized. Given the great potential of this dye recently demonstrated by our group, we have seen fit to spend time on optimizing its preparation. Initially reported in three steps, performed over several days, the **BTI** can now be afforded in less than 4 hours owing to microwave irradiations from cheap commercially available reactants through a two steps and column-free procedure. The ease and accessibility of the latter, even compatible with undergraduate practical classes, guarantees access to large stocks helping us in pursuing our exploratory functionalization work and use of this promising building block.

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Acknowledgments

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Conflicts of interest

There are no conflicts to declare.

References

1. P. H. Grayshan, A. M. Kadhim and A. T. Perters, *J. Heterocycl. Chem.*, 1974, **11**, 33-38.
2. A. M. Kadhim and A. T. Peters, *Tetrahedron*, 1974, **30**, 2245-2249.
3. 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 and C. Cabanetos, *J. Mater. Chem. C*, 2018, **6**, 761-766.
4. J. M. Andrés Castán, C. Dalinot, S. Dayneko, L. Abad Galan, P. Simón Marqués, O. Alévêque, M. Allain, O. Maury, L. Favereau, P. Blanchard, G. C. Welch and C. Cabanetos, *Chem. Commun.*, 2020, **56**, 10131-10134.
5. S. V. Dayneko, A. D. Hendsbee, J. R. Cann, C. Cabanetos and G. C. Welch, *New J. Chem.*, 2019, **43**, 10442-10448.
6. J. M. Andrés Castán, L. Abad Galán, S. Li, C. Dalinot, P. Simón Marqués, M. Allain, C. Risko, C. Monnereau, O. Maury, P. Blanchard and C. Cabanetos, *New J. Chem.*, 2020, **44**, 900-905.
7. C. Dalinot, P. Simón Marqués, J. M. Andrés Castán, P. Josse, M. Allain, L. Abad Galán, C. Monnereau, O. Maury, P. Blanchard and C. Cabanetos, *Eur. J. Org. Chem.*, 2020, **2020**, 2140-2145.
8. P. Simón Marqués, J. M. Andrés Castán, L. A. Galan, M. Allain, O. Maury, T. Le Bahers, P. Blanchard and C. Cabanetos, *J. Org. Chem.*, 2021, **86**, 5901-5907.
9. A. D. Hendsbee, J.-P. Sun, W. K. Law, H. Yan, I. G. Hill, D. M. Spasyuk and G. C. Welch, *Chem. Mater.*, 2016, **28**, 7098-7109.

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