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Green and Rapid Hydrothermal Crystallization and Synthesis of Fully Conjugated Aromatic Compounds

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Abstract: Highly fused, fully conjugated aromatic compounds are interesting candidates for organic electronics. With higher crystallinity their electronic properties improve. Here we show that the crystallization of three archetypes of such molecules – pentacenetetrone, indigo and perinone – can be achieved hydrothermally. Given their molecular structure, this is a truly startling finding. In addition, we demonstrate that perinone can also be synthesized in solely high-temperature water from the starting compounds naphthalene bisanhydride and o-phenylene diamine without the need for co-solvents or catalysts. The transformation can be drastically accelerated by the application of microwave irradiation. This is the first report on the hydrothermal generation of two fused heterocycles.

Organic colorants are molecules that show strong color when interacting with light. Aside from their oldest use, *i.e.* coloring other substances, in recent years they have become of interest for optoelectronic applications in *e.g.* organic solar cells,^[1] or as organic transistors.^[2] One important class of organic colorants are so-called carbonyl dyes, which are typically highly resistant to heat, solvents and weathering.^[3] Perinone, *i.e.* naphthalene tetracarboxylic acid bisbenzimidazole, is such a carbonyl dye. The name perinone is generally used for mixtures of *cis*- and *trans*-isomers (Fig. 1).



Figure 1. HT synthesis of perinone: o-PDA and NBA undergo cylcocondensation to a mixture of *cis*- and *trans*-perinone. The initially white-yellow suspension is transformed into a red solid and an orange, translucent supernatant.

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These mixtures are of intense red color. The pure, separated isomers show cleaner, individual colors: cis-perinone is of blueish-red hue, while the industrially more important transperinone has a brilliant orange-reddish shade.^[4] To the best of our knowledge, there is not a single direct synthetic approach that allows for obtaining exclusively either of the two isomers. This is due to the fact that they are able to co-crystallize: Indeed, both isomers form a solid solution, which is structurally highly tolerant as reflected by the fact that the two isomers can be combined in a broad range of ratios by local, translational and positional disorder.^[5] As research on perinone was in the last decades dominated by the development of isomer separation techniques rather than syntheses, there is only a handful of synthetic procedures towards perinone. These include (1) refluxing the starting compounds in conc. acetic acid for several of hours;^[6] (ii) condensing the starting compounds in imidazole using Zn(OAc)2 as catalyst,^[7] which is analogous to LANGHALS' method for generating perylene bisimides;^[8] (*iii*) rapid condensation (15 min) in H₃PO₄ at 190 °C;^[9] and (*iv*) precondensation to α -aminoimidazoles or α-carboxylic acid imides in H₂O at reflux, followed by solid-state condensation to perinone.^[10] Clearly, all of the these syntheses except the latter two-step route reported by MAMADA et al. are far from being green approaches.^[10]

With this contribution, we have set out to hydrothermally prepare perinone using nothing but high-temperature water (HTW) and the starting compounds in a stoichiometric ratio prompted by our recent reports on the fully green hydrothermal (HT) synthesis of perylene and naphthalene bisimides,^[11] and polyimides.^[12–14] While others have used near-critical water (250 350 °C) for the preparation of benzimidazoles,^[15] and supercritical water (≈ 400 °C) for various benzazoles,[16] our HT method only requires HTW (typically 180 - 250 °C). Consequently, energy consumption is lower and required safety measures are reduced. However, to date HT condensation has only been reported for the formation of single heterocycles and non-cyclic amides. [12-14,17] In the latter cases, the action of HTW has been shown to generate superior crystallinity. Therefore, we were intrigued to expand the scope of HT synthesis and crystallization for the very first time towards fused heterocycles.

In an initial experiment, we investigated the general feasibility of hydrothermally generating perinone from the starting compounds *o*-phenylene diamine (*o*-PDA) and naphthalene bisanhydride (NBA), as shown in Fig. 1. Therefore, *o*-PDA and NBA (2:1 molar ratio; at an equivalent concentration $c_{eq} = 0.01$ mol/L) were suspended in deionized H₂O and subjected to 200 °C in a non-stirred batch autoclave (see SI for experimental details). After a reaction time t_R of 16 h, the autoclave contained two distinct phases: a red, flocculent solid, sedimented at the bottom, and an orange, translucent aqueous supernatant phase (see Fig. 1). The bottom phase, whose red color was already indicative for the formation of perinone, was collected, dried and characterized without further purification. Attenuated total reflectance Fourier

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transform infrared (ATR-FTIR) analysis (Fig. 2; SI for details) of the crude product revealed the absence of modes characteristic for the starting compounds. Instead, we found several intense modes indicative for perinone.



Figure 2. ATR-FTIR spectra of crude perinone (red) and starting compounds (black).

The amount of obtained crude perinone corresponded to approximately 90 % of the theoretical yield. In order to further ascertain the formation of perinone, we performed ¹H solution nuclear magnetic resonance (NMR) analysis. ¹H-NMR measurements (Fig. 3; SI) revealed, that the crude perinone is composed of a mixture of *cis*- and *trans*- isomers.^[10,18] However, the two multiplets labeled as A and B in Fig. 3 indicated the presence of a small amount of byproduct. Attempts to remove this byproduct *via* extraction were not successful. Therefore, we turned our attention to selective precipitation - a technique commonly used to purify or fractionate polydisperse polymers.^[19] Selective precipitation from trifluoroacetic acid (TFA) with H₂O finally allowed for purifying the target compound and isolating the byproduct. The combined results of ATR-FTIR, ¹H-NMR and laser



Figure 3. ¹H-NMR spectrum of crude perinone and peak assignment for H_a , H_b , H_c and H_d . The signals A and B can be attributed to the presence of the minor byproduct NMM.

desorption/ionization high resolution mass spectrometry (LDI HRMS) measurements (see SI) allowed to identify the byproduct as naphthalene tetracarboxylic acid monoanhydride monobenzimidazole (NMM). Consequently, it was also possible to calculate NMM's amount in crude perinone. According to ¹H-NMR analysis NMM accounts for approximately 7 mol% of the unpurified product mixture (see SI for calculation). From these measurements the *cis:trans* ratio in crude as well as in reprecipitated perinone was determined to be approximately 2:3 (see SI for details).

A further set of experiments revealed, that (*i*) a minimum of $t_{\rm R} = 12$ h was necessary to yield maximum conversion of the starting compounds, and (*ii*) that NMM's formation could not be avoided at any tested $t_{\rm R}$ (up to 48 h). Moreover, it became evident, that NMM is formed as an intermediate during the reaction and its amount steadily decreases with $t_{\rm R}$ until a certain threshold is reached (after $t_{\rm R} \ge 12$ h).

The HT method for the condensation of o-PDA and NBA described so far clearly qualifies as green synthesis, since (i) no co-solvents or catalysts are required, and (ii) H₂O is not only the sole reaction medium but also forms as sole condensation byproduct. Nonetheless, we were interested in making the transformation even greener and more energy-efficient. We therefore turned our attention towards microwave (MW) assisted HT condensation.^[20,21] We conducted a series of experiments in a stirred MW oven, where it was possible to exactly control reaction temperature $T_{\rm R}$, heating time $t_{\rm H}$ (time until $T_{\rm R}$ is reached), and $t_{\rm R}$ (reaction time at $T_{\rm R}$). When we performed those experiments at $T_{\rm R} = 200$ °C and $t_{\rm H} = 10$ min, we found, that already after $t_{\rm R} = 2$ min the starting compounds had completely reacted to form perinone. Evidently, not only efficient heating via MW irradiation, but also the application of stirring is highly beneficial for the reaction in order to proceed rapidly. Hence, by using this MW-assisted set-up it was possible to decrease the total reaction time at $T_{\rm R}$ = 200 °C from 12 h to 12 min. Lowering $T_{\rm R}$ to 180 °C drastically increases $t_{\rm R}$, whereas at the highest tested $T_{\rm R}$ of 250 °C it is not even necessary to keep this $T_{\rm R}$ for a certain time. This tremendous reduction of t_R upon increasing T_R can be attributed - among other factors - to temperature-dependent, significant changes in H₂O's physicochemical properties.^[22] With increasing $T_{\rm R}$ the static dielectric constant decreases steadily, which allows for better dissolving organic compounds that are completely insoluble in H₂O at rt. Furthermore, an elevation of T_R leads to an increasing ionic product of H₂O until a maximum at 250 °C is reached. This phenomenon makes H₂O itself a powerful acid/base catalyst in the HT regime, which is indeed beneficial for organic condensation reactions.

Interestingly, as long as full conversion of *o*-PDA and NBA is achieved, the NMM-content as well as the *cis:trans* ratio (\approx 2:3) stayed constant independent of the reaction conditions. The typical amount of \approx 7 mol% of NMM was always formed. Even extending t_R , increasing t_H , varying the pH or lowering c_{eq} had no impact on the ratio of isomers as well as the byproduct content. For the HT condensation of perylene and naphthalene bisanhydride with monoamines to yield bisimides it had been shown that the presence of a non-nucleophilic base such as HÜNIG's base had a positive effect (reduction of t_R , increasing yields) on the formation of some derivatives.^[11] Unfortunately, for the reaction of NBA with o-PDA the addition of HÜNIG's base did not suppress or reduce the formation of NMM. One could furthermore speculate that NMM always forms due to a lack of o-

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PDA, which could be consumed by the well-known oxidative polymerization of aromatic amines.^[12] When we evaporated the liquid, orange supernatant phase – that was always found after the HT reaction – to dryness, a small amount of dark purple solid was obtained. FTIR-ATR, ¹H-NMR and ¹³C-NMR analysis yielded spectra with a multitude of signals (SI), which are likely to correspond to various products of the oxidative autopolymerization of *o*-PDA. In order to check if *o*-PDA's oxidative polymerization is responsible for NMM's formation, we employed a slight molar excess of *o*-PDA. However, this did not result in the suppression of NMM formation. Clearly, in the absence of O₂, oxidative polymerization of *o*-PDA cannot occur. However, performing a perinone synthesis after thoroughly degassing the reaction mixture still led to the usual amount of NMM.

The fact that the formation of NMM is not suppressed under any of the tested conditions, including the addition of a condensation promoter or the use of an excess *o*-PDA, points at an incorporation of NMM into the crystal lattice of perinone as alternative explanation. We suspect that the similar size and the planarity of NMM as well as the electronic similarity to *cis*- and *trans*-perinone facilitate NMM's incorporation into perinone's crystal lattice through local, positional and translational disorder. Once NMM is implemented, it can be considered as "entrapped" and consequently it is not available for further condensation. As for the curious fact that we always find \approx 7 mol% of NMM in crude perinone, we speculate that perinone crystals incorporate the amount of NMM that the crystal lattice can maximally tolerate.

Therefore, although the HT condensation of o-PDA and NBA was found to be highly robust and proceeds rapidly at $T_{RS} \ge 200$ °C, selective precipitation from TFA was inevitable to remove traces of NMM. Interestingly, powder X-ray diffraction (PXRD) measurements revealed that this purification technique significantly decreased crystallinity (Fig. 4). In fact, reprecipitation with a non-solvent rapidly quenches the perinone solution, thereby generating a strongly disordered liquid-crystalline (LC) phase. When attempting to index the reflections to a rectangular lattice all peaks fitted relatively well (see SI for detailed information) to a columnar rectangular LC phase.



Figure 4. PXRD patterns of crude, reprecipitated and crystallized perinone: crude perinone (bottom) is highly crystalline, whereas the purified, reprecipitated one (middle) shows a LC type of ordering. Subsequent HT treatment leads to a highly crystalline product (top) again.

The for us unexpectedly high disorder in reprecipitated perinone provided an excellent opportunity for attempting the very challenging task of its HT crystallization. This task is ambitious, because perinone is much more hydrophobic than its precursors NBA and o-PDA. Hence, higher difficulties regarding perinone's dissolution must be expected. At 250 °C H₂O's polarity compares to that of ethanol at rt,^[23] which is certainly not apolar enough for expecting it to be a good solvent for perinone.

For testing the feasibility of HT crystallization, perinone was simply dispersed in H₂O and heated to the HT regime. Fortunately, PXRD patterns showed that the HT treatment tremendously increased crystallinity (Fig. 4). Furthermore, scanning electron microscopy (SEM) measurements clearly revealed, that the HT treatment also improved the morphology (see SI): The reprecipitated roundish particles (0.1 - 0.5 μ m) with a rough, random surface texture were transformed into agglomerates of fine needles (1 - 2 μ m in length). When commercially available *trans*-perinone was subjected to HT conditions, the morphological improvement was even more significant: beautiful needles of approximately 5 - 10 μ m in length with a rather narrow size distribution featuring smooth crystal facets were obtained (Fig. 5).



Figure 5. SEM micrographs of *trans*-perinone: before (A) and after (B) HT treatment.

Hence, HT crystallization of perinone is indeed possible. These drastic morphological changes can only arise from HT dissolution of reprecipitated/commercially purchased perinone and its subsequent crystallization. Considering H_2O 's polarity at 250 °C, it is very surprising that perinone dissolves. We suspect that the increased ionic product of HTW allows for protonating perinone, which is indeed the mechanism for its dissolution in some strong acids such as TFA. Additionally, the gain in lattice energy upon passing from the LC to the fully crystalline state could be a major driving force.

Thrilled by these findings, we decided to attempt the HT crystallization of other, fully conjugated aromatic compounds, also of interest for organic electronics and for which crystallinity matters. Specifically, we chose indigo (2,2'-bis(2,3-dihydro-3-oxoindolyliden)) and pentacenetetrone (pentacene-5,7,12,14-tetrone).^[24,25] In accordance with perinone, both of these compounds are insoluble in H₂O at rt due to their ability to strongly π -stack.^[26,27] For testing the feasibility of their HT crystallization, we applied the optimized reaction conditions found for crystallizing reprecipitated perinone. ATR-FTIR, ¹H-NMR measurements revealed that both substances are stable under HT conditions (see SI). Furthermore, PXRD results indicated that dissolution and crystallization of these compounds is indeed possible under HT conditions, since reflections became sharper

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and more pronounced (see SI). SEM analysis (Fig. 6; SI) additionally showed a striking improvement of the morphology for both compounds.



Figure 6. SEM micrographs of indigo before (A) and after (B) HT treatment and pentacenetetrone before (C) and after (D) HT treatment.

In summary, we show with this contribution that perinone can be synthesized hydrothermally solely from its starting compounds in stoichiometric ratio. The synthesis is highly robust and remains unaffected by various reaction parameters (T_R , t_R , t_H , c_{eq} , pH, O₂ presence) and does not require condensation promotors or catalysts. The obtained product only contains minor amounts of NMM-byproduct. Moreover, we demonstrate that one can do both, crystallize intentionally amorphisized perinone, and recrystallize commercially obtained perinone. Furthermore, we could show that HT crystallization can also be successfully applied to other fully conjugated aromatic compounds. These crystallization experiments set the basis for our strong conviction that HTW is a promising, cheap and environmentally benign medium for crystallizing *T*-stable low-molecular weight compounds.

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