

Comparison of the Thermal Stabilities of Diazonium Salts and Their Corresponding Triazenes

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ABSTRACT: A range of diazonium salts and their corresponding triazenes have been prepared in order to directly compare their relative thermal stabilities (via initial decomposition temperature) from differential scanning calorimetry (DSC) data. A structure–stability relationship has been explored to investigate trends in stability, depending on the aromatic substituent and the structure of the secondary amine component of the diazonium salts and triazenes. All of the triazenes investigated show significantly greater stability (many are stable above 200 °C) compared with the corresponding diazonium salts, which show varying stabilities.

KEYWORDS: triazene, diazonium salt, thermal stability, DSC, continuous processing

INTRODUCTION

Diazonium salts are important intermediates in synthetic chemistry, as they permit functionalization or transformation at the attached aromatic carbon. Consequently, many transformations utilizing diazonium salts have been developed.^{1–3} However, variability in the stability of diazonium salts renders their use at large scale problematic.^{4,5} The stabilities of diazonium salts range from excellent to explosive, though very few are in the latter category. Nonetheless, the existence of some explosive compounds raises caution and concern, which provides motivation for the development of alternative synthetic route design to avoid diazonium salt chemistry. The isolation of some diazonium salts can be especially hazardous, as they are shock-sensitive and decompose readily, while aryl diazonium tetrafluoroborate, tosylate, disulfonimide or carboxylate salts are often deemed stable for isolation, depending on the substituents on the aromatic ring.^{6–10} The thermal instability of diazonium salts and the evolution of large volumes of nitrogen gas upon decomposition are particular issues for industrial-scale syntheses, and it is important to understand and control these reactive intermediates.¹¹ These issues have led to the development of a number of continuous flow procedures in which diazonium salts are made and consumed in situ.^{12,13} The increased temperature control and presence of only small amounts of reactive diazonium salt at any one time make this way of processing inherently safer.

Another tactic for manipulating diazonium salts is to protect them in the form of triazenes (Figure 1).^{14–20} Triazenes can be prepared by protecting diazonium salts with secondary amines, leading to products that exhibit very similar reactivity to diazonium salts.²¹ Typically, under acidic conditions, triazenes re-establish the reactivity exhibited by the parent diazonium salt through an on–off equilibrium. While the diazonium compound is still present in this situation, it is never isolated in dry form, and thus, no shock sensitivity is encountered. Hence, triazenes participate in much of the reactivity already established for

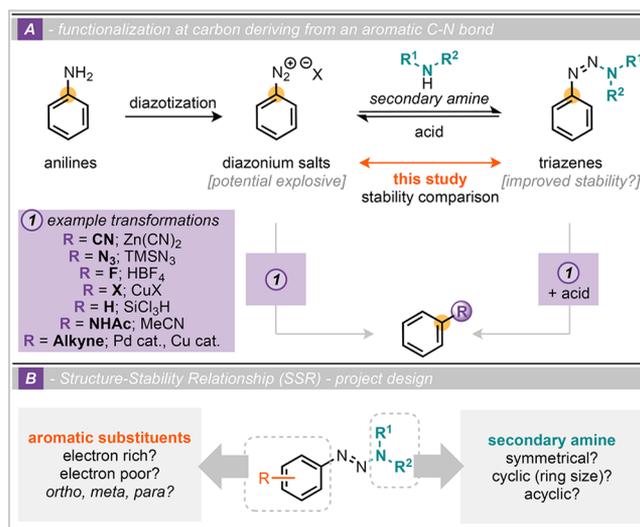


Figure 1. Overview of the reactivities of diazonium salts and triazenes and the structure–stability relationship project design.

diazonium salts as long as a Lewis or Brønsted acid is present, but with reduced risk and hence greater safety. Triazenes have also been used as directing groups for metalation reactions and as linkers in solid-phase synthesis, as they are usually stable toward alkylating agents, strong bases, oxidation, and reduction. Furthermore, most importantly, they are bench-stable.^{8,15,17,18,22–29}

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While it is widely accepted that triazenes offer improved thermal and shock sensitivity compared with the corresponding diazonium salts, we have been unable to find any systematic studies of structure–stability relationship (SSR) trends between these two species. Herein we report a preliminary study toward establishing such structure–stability relationships. Our project design features the preparation of a set of tetrafluoroborate diazonium salts bearing electron-rich, electron-poor and ortho, meta, and para substituents, together with the corresponding triazenes. In the triazene series, the secondary amine component could also impact the stability of these materials, so a range of secondary amines was designed, encompassing examples that are cyclic (with different ring sizes), acyclic, and of different symmetries. A few reports have measured decomposition energies and decomposition temperatures of triazenes but have not compared them directly to those of the corresponding diazonium salts in a systematic manner. Lippert et al. showed that the decomposition temperature of triazenes decreases with the electron-withdrawing capacity of the substituents on the aromatic ring, whereas the steric properties of the amine do not have a strong influence.³⁰ Döbele et al. used triazenes for the formation of aryl fluorides via the Wallach reaction and measured DSC data for one of their triazene precursors to demonstrate the high stability of triazenes.³¹ Although the stability of triazenes compared with their diazonium salts is mentioned in most publications, no direct comparison of their relative stabilities has been established.

RESULTS AND DISCUSSION

The designed compounds were synthesized using known methods. The diazonium salts (2a to 8a) were prepared on a small scale in batch by first treating the corresponding anilines with boron trifluoride diethyl etherate followed by addition of isoamyl nitrite. Diazonium salt 1a, derived from anthranilic acid, was not prepared because it is known to be a contact explosive.^{32–38} The triazene compound series was prepared using a telescoped continuous flow process optimized to generate and consume the diazonium salt in situ while avoiding precipitation of the intermediate diazonium salt (see Figure 3).^{39–41}

The degradation temperature of each compound was assessed using differential scanning calorimetry (DSC). DSC is a thermoanalytical technique in which a sample and a reference (typically an empty sample holder) are heated or cooled at a constant rate. The mode of operation differs for different types of DSC instrument (e.g., power-compensated DSC or heat-flux DSC), but the basic principle is that the instrument attempts to maintain the sample and reference at the same temperature throughout the heating/cooling process by varying the amounts of heat that the instrument exchanges with the sample and with the reference or by allowing heat exchange to occur between the sample and the reference. As the present work is focused on studying sample degradation at high temperature, the DSC experiments involved heating the sample (and reference) from 20 °C to a temperature in the range of 160–250 °C at a rate of 20 °C min⁻¹. If an endothermic or exothermic process occurs in the sample, the amount of energy required to heat the sample differs from the amount of energy required to heat the reference. For example, during an endothermic process in the sample (e.g., melting), the energy supplied to the sample must increase in order to maintain the sample and reference at the same temperature; conversely, during an exothermic process in the sample (e.g., decomposition), the energy supplied to the sample

must decrease in order to maintain the sample and the reference at the same temperature. In the DSC data shown here and in the Supporting Information, endothermic processes appear as negative peaks (increased heat flow to the sample) while exothermic processes appear as positive peaks (decreased heat flow to the sample). In the present work, significant exothermic events are assigned as compound degradation.^{30,42} For some of the samples studied, the DSC data exhibit overlapping peaks because of the occurrence of different thermal events, which complicates the extraction of peak onset temperatures. For this reason, our analysis of exothermic peaks assigned as decomposition is focused on the initial decomposition temperature rather than the onset temperature (see Figure 2). It is

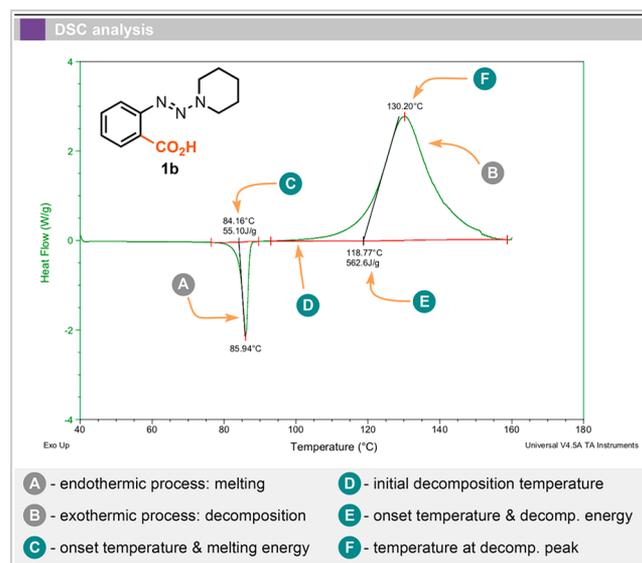


Figure 2. DSC data for the anthranilic acid derived triazene 1b, annotated to show the analysis and interpretation of different thermal events.

important to note that, for a given sample, the initial decomposition temperature will vary depending on the heating rate used in the DSC measurement. However, as the DSC data for all of the samples studied here were recorded at the same heating rate (20 °C min⁻¹), differences in the initial decomposition temperatures of different samples provide a reliable qualitative indication of their relative thermal stabilities.

Our ¹³C NMR data for the triazene series suggest that these molecules undergo restricted rotation, as previously reported for such materials (i.e., variable-temperature ¹³C NMR experiments demonstrate temperature-dependent coalescence behavior).^{30,43–50} There is inconsistency in the manner in which this issue is reported in the literature—in some cases, the observation of fewer ¹³C environments than expected is not even addressed, while other cases simply note that the NMR data are inconsistent with the proposed structure (with reference to the restricted rotation phenomenon). To address this issue more rigorously, the present paper reports ¹³C NMR data at three different temperatures for each triazene studied (see the Supporting Information), and we also demonstrate how these temperature-dependent ¹³C NMR data can be used to calculate the rotational energy barrier in the case of triazene 8b.

The initial decomposition temperatures derived from the DSC measurements are presented in Figure 3 (with further analysis discussed in the Supporting Information), revealing

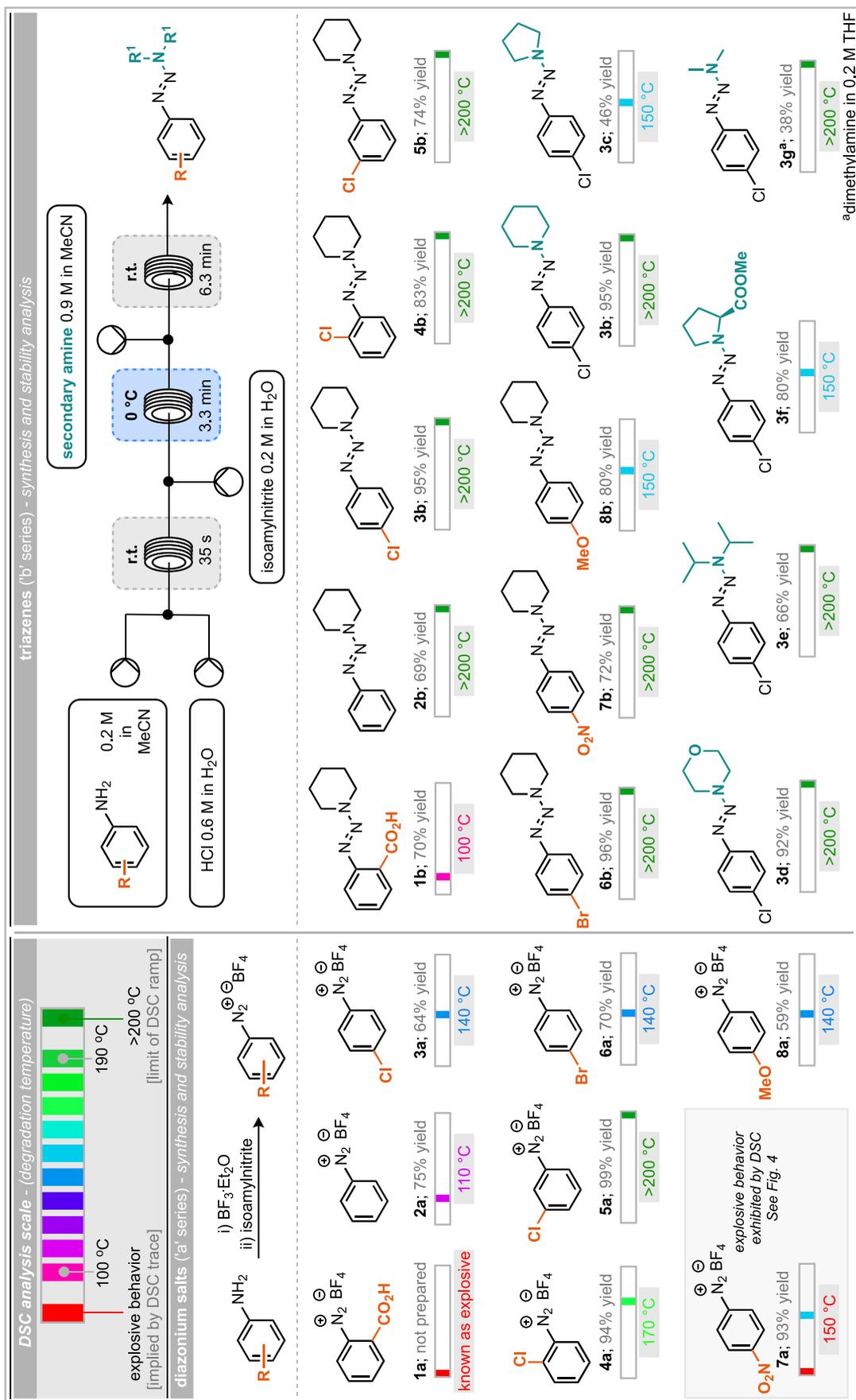


Figure 3. Syntheses and initial decomposition temperatures (assigned from DSC data) for the diazonium salt ("a") series and the triazine ("b") series. The estimated error in determining decomposition temperatures is ± 5 °C.

some key observations both within and between the different compound series. To aid interpretation, the results in Figure 3 are color-coded on a scale from red (low decomposition temperature or explosive behavior) via blue (intermediate decomposition temperature) to green (high decomposition temperature). We note that instead of degradation, the diazonium salts may undergo a Balz–Schiemann reaction with the release of nitrogen gas and boron trifluoride and formation of the corresponding aryl fluoride.⁵¹ In the present study, the occurrence of the Balz–Schiemann transformation is regarded as a decomposition pathway. Among the seven diazonium salts studied by DSC analysis, the results in two cases (2a and 8a) are considered as potentially indicative of Balz–Schiemann processes; when these materials are heated, a melting endotherm is followed by an exothermic or endothermic Balz–Schiemann reaction, which is followed by an endothermic phase change (boiling) of the product aryl fluoride at higher temperature (we note that the boiling points of the corresponding aryl fluorides are below the temperatures at which the Balz–Schiemann process occurs, congruent with this interpretation). Three of the other five diazonium salts (3a, 4a, and 6a) undergo a melting endotherm, which is quickly followed by an exothermic decomposition; this sequence of thermal events is consistent with the melting behavior of those previously studied, which are reported to exhibit “decomposition on melting”.⁵² Of the remaining two diazonium salts, one (5a) does not decompose below 200 °C, and the other (7a) decomposes in a manner congruent with a “thermal runaway”.

Some general observations can also be made with regard to the triazene series. The triazenes that are solid at room temperature all exhibit a melting endotherm below 100 °C, and in most cases below 60 °C; in contrast, the triazenes that are liquids at room temperature do not show this endothermic transition in the DSC data. Typically, the triazenes do not decompose below 200 °C. However, some of the triazenes exhibit broad exotherms below 200 °C that are assigned as degradation, including compound 1b (initial decomposition temperature ca. 100 °C) and compounds 3c and 3f (initial decomposition temperatures ca. 150 °C). The actual decomposition pathways for these triazenes are not yet assigned; however, the Balz–Schiemann reaction can be ruled out, as no fluoride source is present in the preparation of these materials. For five of the triazenes (2b, 4b, 5b, 6b, and 3e) a very broad endothermic feature is observed, which is consistent with evaporation of a liquid phase. In three of these cases (2b, 4b, and 6b), the material is a solid at room temperature; when the solid is heated, a sharp endotherm due to melting is observed, followed by the broad endotherm. In the other two cases (5b and 3e), the material is already a liquid/oil at room temperature, and the broad endotherm is the only feature observed below 200 °C in the DSC data.

Comparison between the whole diazonium salt series and the whole triazene series highlights that the triazenes are more stable than the corresponding diazonium salts with respect to thermally induced degradation (i.e., more compounds in the triazene series are color-coded green). This difference is particularly notable between 1a and 1b, for which the anthranilic acid-derived triazene (1b) is isolable and not shock-sensitive and degrades in a controlled exothermic process with initial decomposition temperature of ca. 100 °C; in contrast, the corresponding diazonium salt (1a) is explosive, as noted above. Direct comparison between the set of “a” compounds (diazonium salts) and the corresponding “b” compounds

(triazenes) highlights the greater stability of the triazene molecules.

With regard to aromatic substituents, the sample set is too small to draw firm conclusions, but comparison of the results for the three monochloro anilines (para, ortho, and meta; 3a, 4a, and 5a, respectively) points toward increased stability within the diazonium series for meta substitution, with thermal stability above 200 °C for 5a. The corresponding triazenes (3b, 4b, and 5b, respectively, with piperidine as the secondary amine) show increased stabilities (decomposition above 200 °C). The same trend in relative stability is observed for the *p*-bromo-substituted diazonium salt 6a (initial decomposition temperature of 140 °C) versus the corresponding piperidine triazene 6b (decomposition temperature above 200 °C). The electron-rich *p*-methoxy-substituted diazonium salt 8a degrades at a lower temperature (140 °C) than its triazene congener, although in this case it appears that the para electron-donating group present in 8b leads to increased instability, resulting in a broad exothermic decomposition with an initial temperature of 150 °C. The electron-poor *p*-nitro-substituted diazonium salt 7a is rendered significantly more thermally stable in its piperidine triazene form 7b. In the case of 7a, the initial decomposition temperature is 150 °C (Figure 4); however, the exothermic peak in the DSC data in this case is sharp and leans toward higher temperatures, indicative of an uncontrollable exothermic event corresponding to thermal runaway during decomposition. Although the use of a different DSC heating ramp might give rise to a more well-defined exothermic behavior, for ease of

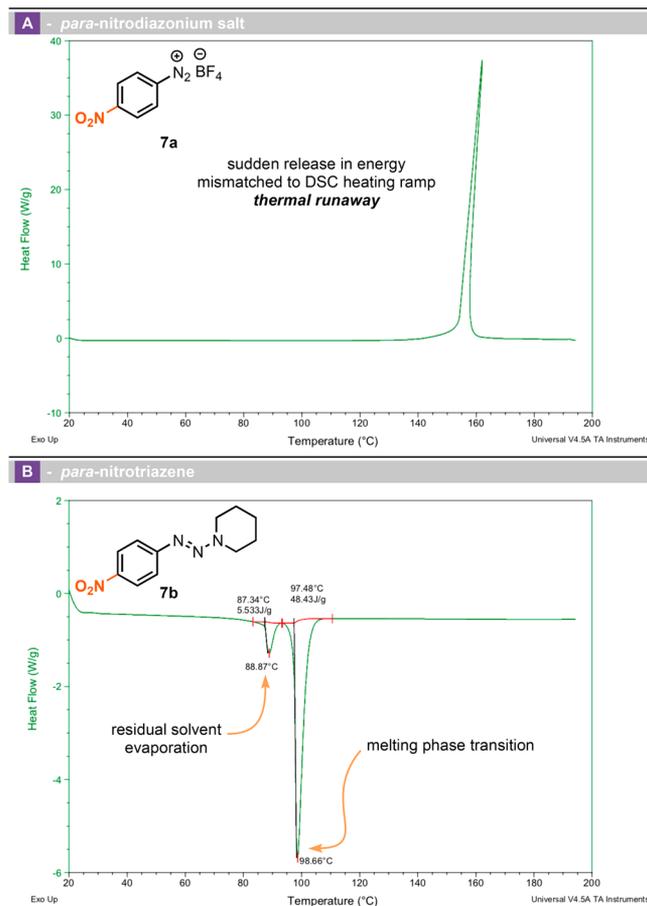


Figure 4. DSC data for the *p*-nitrodiazonium salt (7a) and the *p*-nitrotriazene (7b).

comparison all of the compounds in this study were assessed using an identical DSC ramp protocol (with heating at 20 °C/min), and 7a was the only compound to show such behavior. Notably, the corresponding triazene 7b exhibits two endothermic events (Figure 4), probably arising from residual solvent evaporation followed by a phase transition (melting), with no decomposition exotherm observed up to the highest temperature studied (200 °C). For the triazene series bearing different secondary amines (3b–g; Figure 3), pyrrolidines (3c and 3f) appear to have reduced stability compared with other secondary amines, including both acyclic and cyclic examples. Nonetheless, compared with the parent diazonium salts, the triazenes have greater stability. Clearly, a larger data set would allow the dependence of the stability on the specific nature of the substituents to be explored in greater depth.

CONCLUSION

The structure–stability relationship study reported here has compared the decomposition of a series of diazonium salts with the decomposition of the corresponding triazenes. We have demonstrated that triazenes derived from treatment of their diazonium salt congeners with piperidine exhibit enhanced stability, although preliminary studies suggest that this may not be true for electron-rich systems. Moreover, the improved stability appears to be applicable to a range of secondary amines, with those based on a pyrrolidine motif exhibiting reduced stability in comparison with other triazene systems. However, the number of materials studied here is insufficient to allow more precise conclusions on structure–stability relationships to be derived. The continuous flow method used to prepare the triazenes in this work obviates the requirement for large-scale preparation of diazonium salts and thus delivers triazenes as worthy candidates when planning synthetic routes requiring functionalization at the carbon of an aromatic C–N bond. Future work will investigate a larger matrix of compounds with regard to both the aromatic substituents and the secondary amine components.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.oprd.0c00162>.

Compound characterization and copies of NMR spectra (PDF)

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Author Contributions

The manuscript was written through contributions of all authors. All of the authors approved the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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