

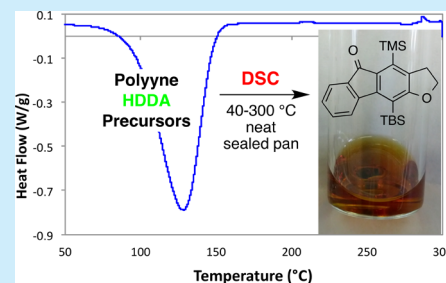
Differential Scanning Calorimetry (DSC) as a Tool for Probing the Reactivity of Polyynes Relevant to Hexadehydro-Diels–Alder (HDDA) Cascades

Brian P. Woods and Thomas R. Hoye*

Department of Chemistry, University of Minnesota, 207 Pleasant Street SE, Minneapolis, Minnesota 55455, United States

S Supporting Information

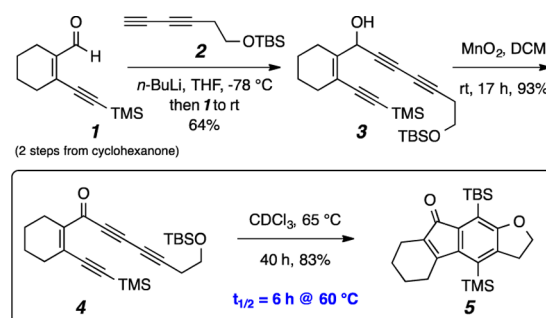
ABSTRACT: The differential scanning calorimetry (DSC) behavior of a number of alkyne-rich compounds is described. The DSC trace for each compound exhibits an exothermic event at a characteristic onset temperature. For the tri- and tetraynes whose [4 + 2] HDDA reactivity in solution has been determined, these onset temperatures show a strong correlation with the cyclization activation energy. The studies reported here exemplify how the data available through this operationally simple analytical technique can give valuable insights into the thermal behavior of small molecules.



Differential scanning calorimetry (DSC) is a commonly available and often-used tool for characterizing the thermal properties (melting and/or glass transition behaviors) of macromolecular assemblies, including both synthetic and biological polymers as well as bulk materials, crystalline solids, nanoparticles, etc. DSC has also been used, although much less frequently, to probe the behavior of small organic molecules. In that regard, one particular application has been as a preliminary screen for safety evaluation of potentially unstable, energetic, small molecules¹ (although more sophisticated thermal assessments are advisable in the course of bona fide process development^{1a,2}). The study of other aspects of small molecule reactivity using DSC is less common.^{3,4} Although more quantitative calorimetric measurements can give an impressively refined and in-depth understanding of mechanistic aspects of small molecule reactions through, e.g., kinetic profiling,⁵ we were surprised, nonetheless, by the variety and nature of the insights that we have been able to extrapolate from a collection of qualitative DSC data.

In the course of establishing the scope and generality of the hexadehydro-Diels–Alder (HDDA) reaction,⁶ we have explored the stability and reactivity of various polyynes. Tri- and tetrayne HDDA substrates are synthesized by reaction sequences that involve other polyyne intermediates (e.g., see the synthesis of benzenoid **5** via **1–4** shown in Scheme 1⁷). Although there are scattered reports of polyynes showing explosive behavior, these tend to be associated with low molecular weight, unsubstituted members of this functional group class.⁸ We have experienced no sign of such extreme reactivity with any of the compounds with which we have worked, as exemplified by those shown in this paper. Much more common are anecdotal comments implying slow decomposition of polyynes, e.g., the inability to obtain a

Scheme 1. Synthesis of HDDA Precursor **4** (via **1–3**) and Its Cyclization to Benzenoid **5**



well-defined melting point or change during routine handling in the laboratory.⁹

Given the large number of polyynes being prepared in our lab, we have often used DSC as a screening tool for evaluation of the potential hazard associated with each new class of intermediates encountered in our work. After accumulating a body of these DSC data, we came to realize that, beyond the comfort level provided from the standpoint of safe handling of these compounds,¹⁰ there was additional instructive information about thermal reactivity embedded in the data, some of which we describe here.¹¹ We present the DSC behavior of (i) several simple conjugated di- and triynes, (ii) various tri- and tetrayne HDDA substrates, many of whose kinetic behavior in solution we have previously benchmarked, and (iii) a final substrate that undergoes a clean thermal Alder ene reaction. We comment on a number of inferences that can be drawn relating to reactivity

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throughout this set of polyynes. All of the DSC data reported here were collected under identical conditions (single scan from 40–300 °C, 2 deg·min⁻¹ ramp rate, sample size of ca. 3–6 mg in a hermetically sealed aluminum pan).

Terminal diyne **2** is a substrate we have used frequently in the synthesis of HDDA-precursor triynes. We have observed that this terminal diyne is susceptible to slow decomposition when stored neat at room temperature. Its DSC behavior (Figure 1) shows an exothermic (downward) curve with an

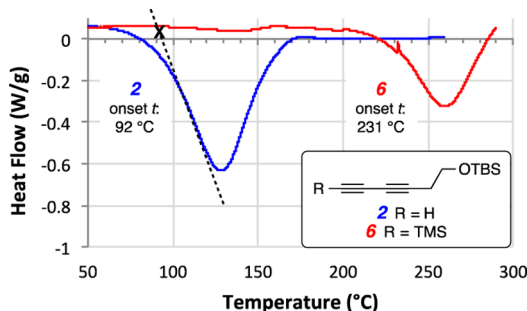


Figure 1. DSC traces for 1,3-diyne **2** and **6**.

onset temperature of only 92 °C.¹² In contrast, the trimethylsilyl-containing analog **6** was considerably more stable and less prone to decomposition during routine handling. This observation is consistent with its DSC behavior (Figure 1), which showed a remarkably higher onset temperature of 231 °C. The exact pathway for decomposition of substrates such as **2** and **6** is not known. Attempts to elucidate these processes by determination of the structure or physical properties of the products, formed either as a result of the DSC heating process (cf. below) or from the slower decomposition of **2** as handled under ambient conditions, have been unsuccessful. Instead dark-colored, essentially insoluble, soot-like material is formed, which is similar to the outcomes of HDDA cyclizations performed in the absence of an efficient trapping agent.^{6a,13} In those instances, we speculate that decomposition is initiated by bimolecular events in which the intermediate benzyne reacts with another molecule of the substrate polyyne.

The behavior of a second pair of relatively simple diynes **7** and **8** (Figure 2) provides different insights. In each, the

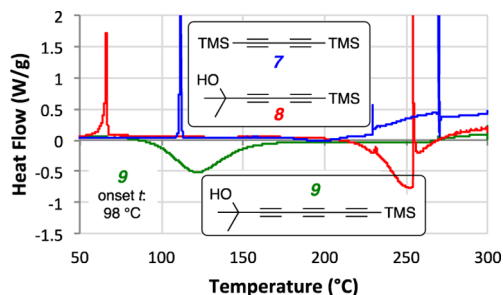


Figure 2. DSC traces for 1,3-diyne **7** and **8** and 1,3,5-triynyl-substituted diyne **9**.

butadiyne is capped on both ends with a quaternized substituent that provides considerable steric shielding. The DSC trace of each of these crystalline solids indicates a sharp endotherm characteristic of the melting point for each (**7**: mp 112–113 °C;^{14a} **8**: mp 62–64 °C^{14b}). Incidentally, the samples of all of the other polyynes for which DSC data are

reported in this paper are viscous oils at ambient temperature. No other change was observed for **7** or **8** until well over 200 °C. It is tempting to speculate that the small endotherm at 229 °C might reflect the boiling point of diyne **7**.¹⁵ However, we are reluctant to overinterpret the high temperature DSC behavior in these studies because of potential complications from events such as bulging of the sealed DSC pan and unidentified decomposition and volatilization of low boiling fragments. Such processes can lead to anomalous behavior at those extreme temperatures. In this regard, it is interesting to note that a number of alkynes containing the Me₂(HO)C– moiety, like that present in **8**, are reported to fragment and liberate the terminal alkyne upon thermolysis at high temperatures (175–275 °C).¹⁶ However, it can be concluded with confidence that neither of these bulky diynes shows any significant sign of reactivity below ca. 220 °C.

In contrast, the DSC scan of the conjugated (noncrystalline) triyne **9** showed a broad exotherm characteristic of a reaction and having a relatively low onset temperature (of 98 °C). This presumably reflects the combined greater steric accessibility of the internal alkyne moiety in **9** vis-à-vis that in **7** or **8**, which allows for bimolecular association and reaction, as well as the additional electronic perturbation present in the more highly conjugated triyne **9**. In the course of studying the longest discrete polyyne known to date (a doubly capped docosayne), Tykwinski and co-workers have observed lower DSC onset temperatures with increasing chain length of the polyyne.^{9b}

The DSC data for four triyne substrates, each known to undergo HDDA cyclization and trapping efficiently in solution,⁷ are shown in Figure 3. The measured half-life as well as the energy of activation¹⁷ for cycloisomerization is shown under the structure of each substrate. The relative rates of cyclization of these four triynes span a factor of >10⁴.⁷ Each gives the tetracyclic product indicated at the bottom right of Figure 3 (and cf. **5**, Scheme 1). The DSC onset

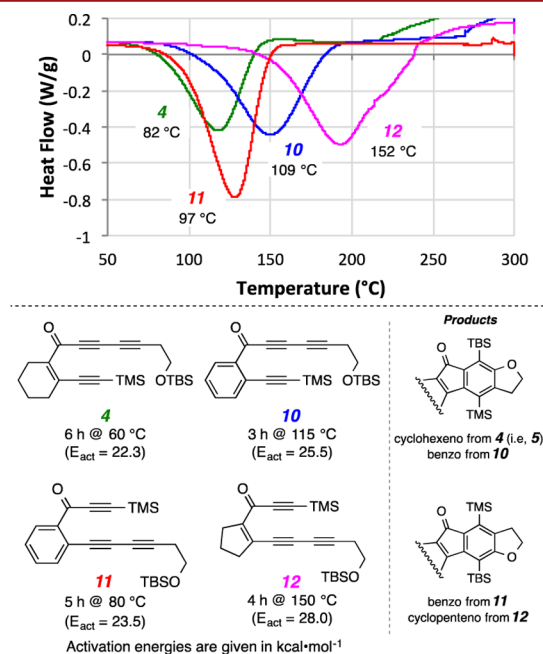


Figure 3. DSC traces for HDDA substrates **4** and **10** (diynes) and **11** and **12** (monoyne).

assessed for preliminary insight about the reaction temperature required for their cycloisomerization in solution. DSC investigation of other classes of thermal reactions has the potential to provide new insights and understanding.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterization data, copies of ^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: hoye@umn.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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