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Article

Thermal Stability Evaluation of Nitroalkanes with Differential Scanning Calorimetry

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ABSTRACT: The thermal stability of a set of aliphatic nitroalkanes, comprising primary and secondary nitroalkanes, with short and long linear chains or cyclic, was tested by differential scanning calorimetry (DSC) analysis, for comparative purposes. An exothermic decomposition phenomenon of a high entity occurred for all compounds, and no significant difference was observed to depend on the structure of the compounds tested. A maximum recommended process temperature (T_{D24}) to avoid decomposition is estimated for the studied compounds. Although estimated T_{D24} values are difficult to access under normal conditions of handling and storage in R&D labs, the decomposition energy for all the compounds is higher than 500 J/g, and thus, attention should be paid, especially for transportation, storage, and handling. Yoshida correlation and a more conservative modified correlation developed by Pfizer were applied to the DSC data to predict shock sensitivity and explosive propagation. With the most used Yoshida correlation, some nitroalkanes are predicted to be potentially shock sensitive and explosive as neat substances. Pfizer-modified correlation flags all the compounds to be potentially explosive or shock-sensitive. The information provided herein indicates the inherent reactivity of these compounds and could provide suggestions about precautions for storage and handling in a R&D laboratory. In light of this information, it is advisable to run accelerating rate calorimetry evaluation and experimental explosive testing to complete the hazard assessment before employment on an industrial scale.

KEYWORDS: *nitroalkanes, stability, differential scanning calorimetry, decomposition*

INTRODUCTION

Nitroalkanes are a highly versatile class of molecules due to the strong effect of the nitro group as an electron-withdrawing group. In fact, these molecules are prone to allow, under basic conditions, the formation of stabilized carbanions (nitronate anion) used as nucleophiles leading to C−C single[1−3] and C═C double[4] bond formation, mainly via Michael or Henry reactions. In addition, after the C, C bond is formed, the aliphatic nitro group can be transformed into other functionalities such as carbonyls (Nef reaction),[5,6] amines,[7] oximes,[8] and so forth. The high chemical versatility makes nitroalkanes one of the most useful, versatile, and employed classes of molecules in organic synthesis. Indeed, literature continuously reports progress in their chemical reactivity and in their use as key starting materials for the preparation of a large variety of fine chemicals and target molecules, including natural products and pharmaceuticals.[9−16]

Because of the growing employment of this class of molecules, the goal of this communication is to develop preliminary studies on the hazard, in calorimetric terms, and to provide some insights into their handling. Indeed, nitro-substituted compounds and nitroalkanes are high-energy materials, typically highly flammable and strong oxidizing agents. Thus, a general understanding of their thermal hazards can significantly contribute to improving process safety and the safe storage of these chemicals. In this work, we report differential scanning calorimetry (DSC) analysis of nitroalkanes **1**−**8** (Figure 1).

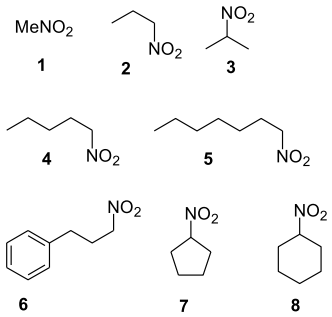

Figure 1. Nitroalkanes **1**−**8** tested in this study.

Nitroalkanes **1**−**8** are representative of a variety of categories, such as (i) primary (**1**, **2**, **4**−**6**) and secondary (**3**, **7**, **8**) nitroalkanes, (ii) nitroalkanes with short (**1**−**3**) and long (**4**−**8**) carbon chain, (iii) linear (**4**−**6**) and cyclic (**7**, **8**) nitroalkanes, (iv) nitroalkanes with long chain with (**6**) or without (**4**, **5**) an aromatic ring. Therefore, comparisons from these groupings can be made.

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In general, various parameters and methods are currently used to characterize the thermal hazards of reactive substances,[17] with the aim of predicting and reducing thermal risks and improving process safety and chemical storage, thus preventing fire and explosion incidents, both at the R&D level and, more importantly, at the industrial level. During the past decades, much effort has been dedicated to the study of thermal stability properties and in the assessment of thermal hazards of nitro aromatics[18−21] due to their employment in industrial processes and to their involvement in industrial accidents.[22−24] However, information about the thermal stability of nitroalkanes is still scarce or not easily accessible probably because nitroalkanes are less involved in industrial processes compared to nitroaromatics. Thanks to its commercial applications as a solvent and high-energy fuel, nitromethane is the only nitroalkane to have been extensively studied.[25−27]

Theoretical studies of thermal decomposition of nitromethane and nitroalkanes have been reported starting from the last century[28−30] and throughout the current century.[31] The calculation of bond dissociation energy and the understanding of the mechanism of decomposition for the determination of the formation enthalpies of reactive species have been fundamental for these methods.[32] However, even for nitromethane (**1**), which is the simplest nitroalkane, the primary reactions involved in decomposition have been long debated.[33−36] Computational methods, such as the Hartree−Fock and density functional theory (DFT) ab initio methods,[37−41] have promoted the notion that the C−N bond dissociation with NO_2 elimination is the primary reaction of the thermal decomposition of nitromethanes.[34,42]

Further studies have indicated that isomerization of nitromethane into nitrite should be taken into consideration, as well as the secondary reactions of the nitro-substituted radicals and the contribution of other primary unimolecular reactions, like isomerization to nitrites and aci-forms.[43] In addition to those methods, the latest development of molecular simulation as a predictive tool, such as, quantitative structure−activity/property relationships, represents an alternative way of predicting physical and chemical properties of energetic materials, like decomposition enthalpies (theoretical decomposition enthalpies).[44,45]

Together with theoretical and computational methods, experimental methods are used to characterize the thermal properties of chemicals, especially for compounds involved in industrial processes. In this context, DSC is one of the most commonly employed techniques to determine inherent chemical reactivity especially because it allows the collection of data with low amounts of material (milligram scale). DSC thermograms provide initial exothermic onset temperature (Tonset) and enthalpy change, thus giving information about the thermal risk associated with chemicals. The onset temperature describes how easily a chemical can decompose, while the heat of decomposition describes the amount of energy released during decomposition. When the analysis is performed with the same experimental procedure and with the same processing methods, results should be comparable and pattern recognition and model development could be obtained from DSC datasets.[46,47] However, major differences can be observed depending on the experimental setup: the temperature determined in a DSC experiment depends on the experimental condition, on the heating rates, and on the sample mass used.[48] The crucible is very important for DSC analysis: among the critical factors are the material of the crucible (chemical compatibility with the chemical to analyze) and its specification of maximum pressure tolerated (open crucibles could influence the physical changes in state of the sample).

One of the most comprehensive studies with DSC analysis has been reported in 1991 by Ando et al.[49] with more than 800 compounds, classified into 28 types according to their functional groups as peroxides, nitrocompounds, ketones, alcohols, and so forth. In particular, among the 115 nitrocompounds tested, 98% of the compounds showed exothermic behavior with an average Tonset of 300 °C and an average heat of decomposition of 506 cal/g (2118.5 J/g). The majority of nitrocompounds tested were nitroaromatics and, although included in the experiment lists, data for nitromethane and nitropropane have not been reported probably due to substance evaporation in the aluminum pinhole crucible. DSC analysis has been reported in 1997 by Duh and co-workers for nitromethane, together with its incompatibility with strong bases and acids.[50] Among the fundamental information, these experiments, performed in high-pressure crucibles, revealed a dramatic lowering of the Tonset of 200 °C for nitromethane in the presence of HCl 6 M and a lowering of the Tonset of 240 °C for nitromethane in the presence of NaOH 6 M, compared to pure nitromethane.[50] Here, we present a thermal stability analysis of nitroalkanes **1**−**8** by DSC with a clear indication of the experimental setting and methods used useful for the academic and industrial chemists. The decomposition energy for all compounds is more than 500 J/g, highlighting their potential hazard. Furthermore, the Yoshida correlation is applied to the DSC data to predict the shock sensitivity and explosivity of the tested nitroalkanes. Some of them are predicted to be explosive and shock sensitive. A more conservative correlation developed recently by Pfizer indicates all the compounds to be potentially explosive and shock sensitive. The implications of these results and predictions are that (1) caution should be used when handling these chemicals at the R&D laboratory scale and (2) accelerating rate calorimetry (ARC) evaluation and experimental explosive testing should be performed before scaling-up and for nitroalkane employment at the industrial scale.

RESULTS AND DISCUSSION

In this work, thermal stability data of nitroalkanes **1**−**8** have been collected by means of DSC analysis. All compounds used are liquid and were loaded in a high-pressure golden crucible sealed under nitrogen. The golden crucible ensures chemical inertness, and the nitrogen atmosphere ensures the accurate observation of the decomposition phenomenon also for hypergolic mixtures. Furthermore, in these conditions, compound evaporation is suppressed, allowing the observation of the sole thermal decomposition process. DSC curves have been acquired at three different heating rates described in the Materials and Methods section (method A: 1 °C/min; method B: 5 °C/min; method C: 10 °C/min) and for each set, averaged values are reported in the tables. Although the decomposition beginning is visible for all experiments, the exothermic phenomenon is complete for all of the studied compounds only for DSC experiments at 1 °C/min heating rate. Only these data have thus been included to report decomposition energies and to estimate T_{D24} and Yoshida shock sensitivity and explosive propagation. As visible from the DSC curves (Supporting Information), a sudden exothermic

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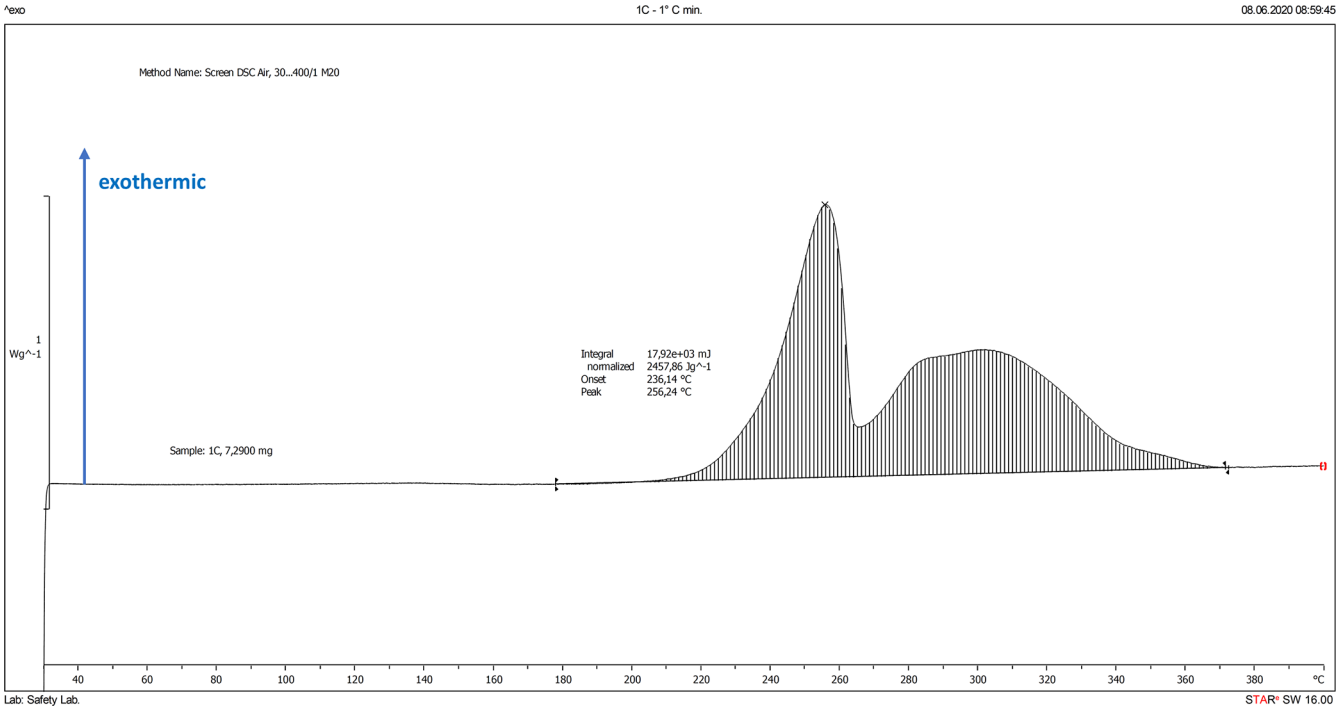
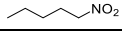
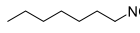


Figure 2. DSC curve of 2-nitropropane **3**.

decomposition phenomenon of high entity occurred for all compounds. In general, no endothermic peaks are observed in the thermograms between 30 and 400 °C. A double peak during the exothermic phenomenon is visible (Figure 2) for 2-nitropropane **3** for all experiments at the three different heating rates. DSC thermograms of compounds **2** and **8** also showed the same profile, although less pronounced, at a 1 °C/min heating rate. This behavior could be related to the formation of different species during the decomposition of 2-nitropropane, like radicals or alkenes after rupturing of the C−NO_2 bond and further decomposition or polymerization of those products.

Thermochemical data for compounds **1**−**8** are reported in Table 1. Of note, data for nitromethane are comparable with previous results by Duh et al., previously mentioned.[50]

Table 1. Decomposition Energies of Nitroalkanes 1−8[a]

Compound	M.W:	-ΔH (J/g)	-ΔH (cal/g)	-KJ/mol
(1) $MeNO_2$	61.0	3975.1	950.1	242.6
(2) 	89.1	2466.5	589.5	219.7
(3)	89.1	2100.0	501.9	187.1
(4) 	117.2	1776.0	424.5	208.1
(5) 	145.2	1194.7	285.5	173.5
(6) 	165.2	1007.3	240.7	166.4
(7) 	115.2	1623.9	388.1	187.0
(8) 	129.2	1429.3	341.6	184.6

[a]Values are given with the most used units of measurement (J/g, cal/g, and kJ/mol) and refer to DSC runs acquired at 1 °C/min heating rate. Average results $n \geq 2$.

The dependence of enthalpy changes (heat of decomposition) for compounds **1**−**8** in J/g with increasing molecular weight is reported in Figure 3.

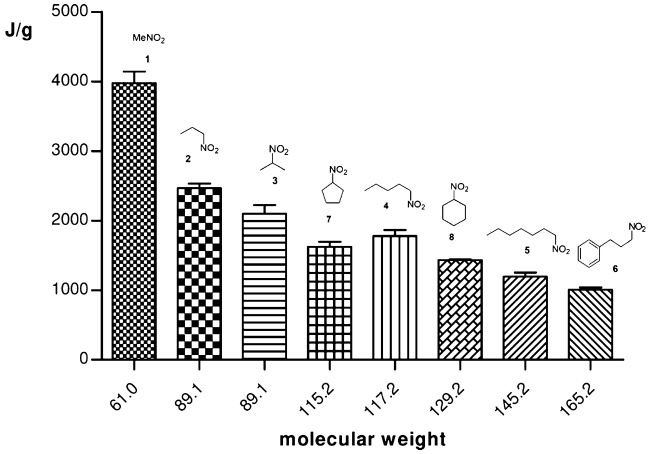


Figure 3. Histogram showing the heat developed (J/g) with increasing molecular weight.

As shown in Figure 3, the dilution effect with molecular weight is clearly visible since the heat developed (J/g) decreases with increasing molecular weight.

In the light of the dilution effect and in the absence of other effects on the decomposition, the heat developed can be normalized by building the kJ/mol plot, which represents the heat developed by 1 mol of compound (Figure 4). No significant variation of the normalized thermal stability is visible for the compounds studied.

Among the parameters employed to describe the thermal stability of chemicals, the Tonset is the intersection point of the inflectional tangent at the beginning of the exothermic curve with the baseline. However, its capability to accurately

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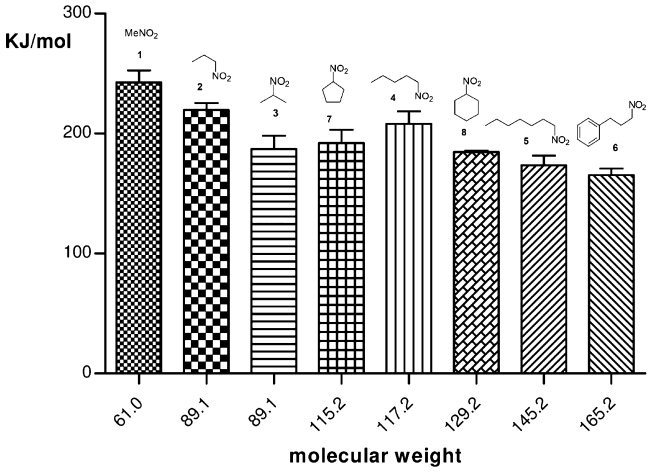

Figure 4. Histogram showing the heat developed by 1 mol of compound (kJ/mol).

represent the thermal hazards has been questioned for several reasons.[51] The first reason is because for broad peaks, the Tonset cannot be precisely identified and it loses its physical meaning. The second reason is because processes with very low activation energies and with slow decomposition kinetics may be difficult to detect via DSC and this can lead to hazard underestimation. For these reasons, the use of Tonsets as single points to set operating temperatures for chemical processes and handling of substance could be risky. Considerable variation in Tonset can be found in the literature also due to different (and often unreported) heating rates, pointing the importance of describing experimental details of DSC results. Another parameter that has been used together with the Tonset is the temperature at the initiation (Tinit) of the detected heat flow variation. Tinit is defined as the temperature at which the heat flow is measured to be >0.01 W g^{-1} from the baseline. The temperature (Tonset and Tinit) determined in a DSC experiment depends on the heating rates, as shown from the values reported in Table 2 for each set of measurements. Among DSC experiments performed in the same conditions, the Tonset and Tinit can be compared to see differences in thermal hazard behaviors among nitroalkanes **1**−**8**.

A graphical comparison between the Tonset and the Tinit among the two series of data 1 and 10 °C/min is shown in Figure 5 for clarity purposes. The lower temperature ramp of 1 °C/min resulted in lower Tinit and Tonset and higher resolution, providing more conservative data to be used for thermal safety evaluation.

To estimate the maximum recommended temperature to avoid unwanted decomposition (T_{D24}), eq 1, developed by Stoessel,[48] was used. T_{D24} is defined as the temperature at which the time to maximum rate under adiabatic conditions (TMRad) becomes >24 h.

$$T_{D24(°C)} = 0.7 \times T_{init(°C)} - 46 \quad (1)$$

Equation 1 was developed by assuming a detection limit of 0.01 W g^{-1}, a specific heat capacity of 1 kJ kg^{-1} K^{-1}, and a zero-order kinetics approximation for the decomposition. The equation is based on the assumptions that at the detection limit of the DSC exotherm, the conversion is close to zero, the heat release rate is equal to the detection limit, and there is a relatively low activation energy (a conservative value of 50 kJ mol^{-1} was used for the formula development). In practice, the equation allows for a conservative first estimation of the safe operating temperature.

Estimated T_{D24} for compounds **1**−**8** are reported in Table 3, together with Tinit and Tonset (reported for clarity purpose in the same table). DSC data from experiments at 1 °C/min were employed for the calculation, and T_{D24} values are given to the nearest 5 °C to account for the limited sensitivity DSC experiments, as described in the literature.[52]

For the nitroalkanes examined, T_{D24} is difficult to access under normal conditions of handling and storage in R&D labs, where small amounts of those reagents are stored. However the decomposition energy for all compounds is high and precautions should be taken, especially for handling and for transportation.[53]

Based on the European Chemicals Agency (ECHA) recommendation,[54] a substance is classified as nonexplosive, without performing any further testing, when the exothermic decomposition energy is less than 500 J/g and the onset of exothermic decomposition is below 500 °C.

These limits have been set to prevent the explosive testing procedures from being applied to a large number of organic materials which are not explosive. However, any sample exhibiting an exotherm above 300 J/g may be classed as self-reactive as defined by the United Nations Globally Harmonized System of Classification and Labelling of Chemicals and would therefore be submitted for further testing. Indeed, for explosive substances, experimental explosive testing is recommended for hazard evaluation. In general, the procedure includes UN gap test (a shock test to determine the ability of the substance to propagate a detonation), Koenen test (a test to determine the effect of heating under confinement), a time/pressure test (a test to determine the effect of ignition under confinement), a BAM Fallhammer test (falling weight test to determine sensitiveness

Table 2. Tonset and Tinit Measured at Different Heating Rates: (1, 5, and 10 °C/min)

compound	T_{onset} (°C) 1 °C/min[a]	T_{onset} (°C) 5 °C/min[b]	T_{onset} (°C) 10 °C/min[c]	T_{init} (°C) 1 °C/min[a]	T_{init} (°C) 5 °C/min[b]	T_{init} (°C) 10 °C/min[c]
1	342	332	335	301	298	289
2	291	302	320	225	210	238
3	233	281	309	191	200	216
4	301	312	315	233	231	248
5	259	263	285	208	224	234
6	271	298	294	218	250	246
7	259	282	287	202	224	224
8	270	295	298	217	227	234

[a]Average results with DSC runs ≥2 ($n \geq 2$). [b]$n = 1$. [c]$n = 2$.

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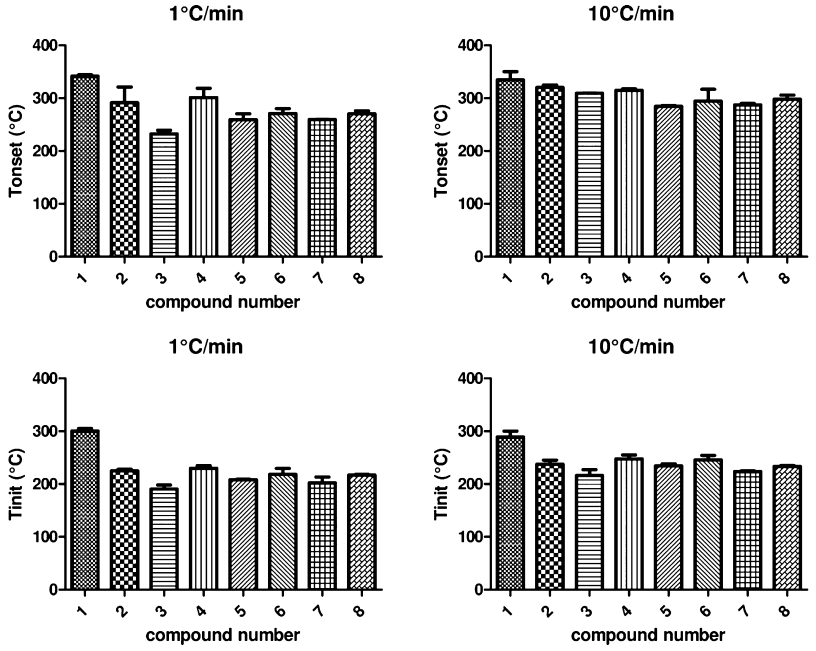
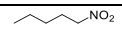
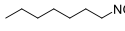
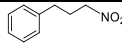


Figure 5. Histograms showing the Tonset and Tinit among the two series of data: 1 and 10 °C/min.

Table 3. Estimated T_{D24} from DSC Data from Method A (1 °C/min)

Compound	Tonset (°C) (1°C/min)	Tinit (°C) (1°C/min)	Estimated T_{D24} (°C)
(1) $MeNO_2$	342	301	165
(2) 	291	225	110
(3) 	233	191	90
(4) 	301	233	120
(5) 	259	208	100
(6) 	271	218	105
(7) 	259	202	95
(8) 	270	217	105

to impact), and a BAM friction test (a test to determine sensitiveness to friction).

Some semiempirical correlations have been developed to predict thermal hazards based on DSC experiments. The Yoshida correlations are mathematical equations (eqs 2 and 3) that correlate a material Tonset and the energy of decomposition from a DSC experiment to its potential ability to propagate an explosion (explosive propagation, EP) or be shock sensitive (shock sensitivity, SS).[55] The limit was developed based on borderline sensitive 1,3-dinitrobenzene (*m*-DNB) and validated for compounds known to propagate an explosion and for compounds that do not have such ability.

$$\mathrm{EP} = \log_{10}(Q) - 0.38 \times \log_{10}(\mathrm{Tonset} - 25) - 1.67 \quad (2)$$

$$\mathrm{SS} = \log_{10}(Q) - 0.72 \times \log_{10}(\mathrm{Tonset} - 25) - 0.98 \quad (3)$$

Q is the decomposition energy of the exotherm expressed in cal/g; Tonset is expressed in °C. If EP or SS $\geq$ 0, the compound is predicted to have the ability to propagate an explosion or to be shock sensitive. Table 4 reports the results obtained by using DSC data with method A (1 °C/min).

Table 4. Yoshida Correlation and Pfizer-Developed Correlation Results for EP and SS

Compound	Yoshida EP	Yoshida SS	Pfizer EP	Pfizer SS
(1) $MeNO_2$	0.36	0.20	0.61	0.68
(2)	0.18	0.04	0.44	0.55
(3)	0.15	0.05	0.40	0.52
(4)	0.03	-0.11	0.30	0.40
(5)	-0.11	-0.23	0.14	0.25
(6)	-0.20	-0.32	0.06	0.17
(7)	0.02	-0.10	0.28	0.40
(8)	-0.04	-0.17	0.21	0.32

This information can be better visualized by plotting $\log_{10}(Q)$ versus $\log_{10}(\mathrm{Tonset} - 25)$ for each compound and verified if the compound is placed above or below the limit line (Figure 6). Values above the line indicate a positive prediction of the property; values below the line indicate a negative prediction.

A more conservative version of these predictive correlations has been developed recently by Pfizer and applied to peptide coupling reagents, as described in eqs 4 and 5.[56] In particular, Pfizer lowered the energy (Q in cal/g) threshold of the Yoshida correlation of 25% and used the Tinit (°C) in place of the Tonset. These correlations have been already used in the

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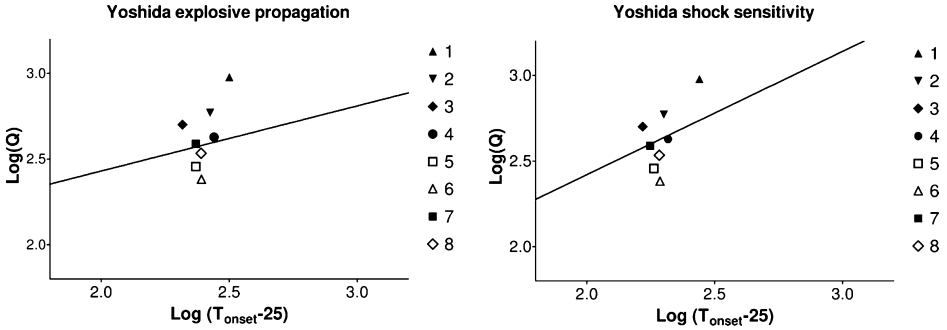

Figure 6. Plot of $\log_{10}(Q)$ vs $\log_{10}(\text{Tonset} - 25)$ for nitroalkanes **1**−**8**. The lines represent the Yoshida EP and SS correlation limits.

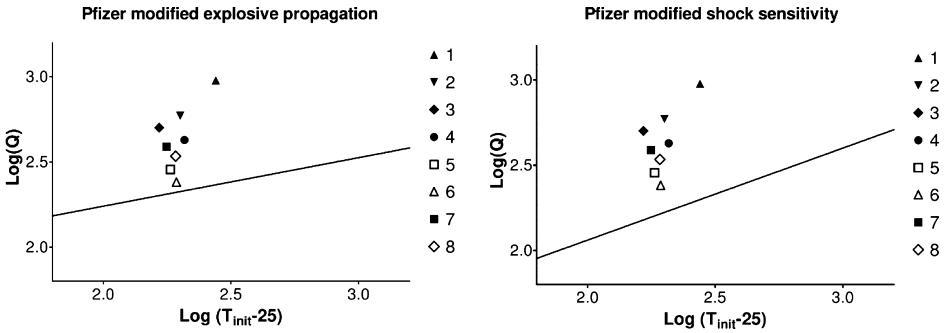

Figure 7. Plot of $\log_{10}(Q)$ vs $\log_{10}(\text{Tonset} - 25)$ for nitroalkanes **1**−**8**. The lines represent the Pfizer-developed EP and SS correlation limits.

literature for reporting the predicted hazard of diazo compounds and diazo transfer reagents.[52]

$$\text{Pfizer EP} = \log_{10}(Q) - 0.285 \times \log_{10}(\text{Tinit} - 25) - 1.67 \quad (4)$$

$$\text{Pfizer SS} = \log_{10}(Q) - 0.54 \times \log_{10}(\text{Tinit} - 25) - 0.98 \quad (5)$$

By applying these correlations to our data, nitroalkanes **1**−**8** are all predicted to be impact sensitive and capable of detonation. Results have been included in Table 4 and Figure 7.

Although it is important to notice that the examined compounds are not necessarily explosive or impact sensitive, both the correlations with their own degree of conservatism are meant to spot for potential danger and avoid false negatives so that any further hazard assessments could be performed before the process undergoes industrial transfer. As a result of this predicted behavior, attention should be paid also in the R&D labs when the compounds are handled or weighed with the spatula or when reagent containers are moved. For reactions performed in a typical R&D lab, the risk of thermal runaway and pressure development is reduced because the reactions are generally conducted on small scales, using dilute concentrations of reagents (more concentrated reaction mixtures could lead to fast heating of the reaction mixture causing solvent evaporation and possible decomposition of nearly neat material). The rate of reagent addition can be carefully adjusted to allow for efficient cooling of the reaction mixture to prevent uncontrolled heat generation. With this in mind, it is advisable before employment at the industrial scale to perform ARC experiments and explosive tests to complete the hazard assessment, as recommended by ECHA and by the United Nations Globally Harmonized System of Classification and Labelling of Chemicals.

MATERIALS AND METHODS

DSC experiments were performed on a Mettler Toledo DSC 3, equipped with FRS 5 + sensor and coupled with a STAR^e 16.00 software for the acquisition of thermal curves and for the analysis of data. Approximately 3−9 mg of each testing sample (liquid compound) was used for the DSC experiments. Each disposable pressure-resistant golden crucible (M20) has an internal volume of 20 μL and can operate at a maximum operating pressure of 217 bar and a maximum operating temperature of 400 °C. Each crucible was sealed manually under a nitrogen atmosphere with a sealing press for crucibles. Method A: samples were heated at 1 °C/min from 30 °C to a maximum temperature of 400 °C. Method B: samples were heated at 5 °C/min from 30 to 400 °C. Method C: samples were heated at 10 °C/min from 30 to 400 °C.

CONCLUSIONS

The study and understanding of the decomposition reaction mechanism of nitrocompounds have been essential steps toward the characterization of thermal safety properties and the estimation of thermal risks of those compounds. Although much effort has been dedicated to nitroaromatic compounds and simple nitroalkanes, such as, nitromethane and nitroethane, information about the thermal stability of nitroalkanes is still scarce or not easily accessible. DSC is one of the most commonly employed techniques to determine thermodynamic properties especially because it allows the collection of data with a low amount of material (milligram scale). The information provided herein by DSC analysis of a set of nitroalkanes indicates the inherent reactivity of those reagents and could provide suggestions about precautions for storage and handling in a R&D laboratory. To complete the characterization of thermal stability, DSC calorimetric data should be integrated with explosive testing, as recommended by ECHA guidelines. Furthermore, data should be always

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integrated by studying in detail the chemical process where the chemicals are involved. Calorimeters, such as the ARC (accelerating rate calorimeter), C80 microscale calorimeter, and compact heat flow calorimeter, could give a broader picture about thermal hazards and, together with gas evolution data and reaction kinetic data, reduce the risks associated with reactive chemical processes.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.oprd.0c00433.

DSC data and thermograms of compounds **1**−**8** (PDF)

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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