Thermochemical analysis of 1-methylamino-1-methylthio-2-nitroethene synthesis

A. Koshy, M. Surianarayanan, K.V. Raghavan*

Central Leather Research Institute, Adyar, Madras 600 020, India

Received 1 October 1994; accepted in revised form 25 February 1995

Abstract

The synthesis of 1-methylamino-1-methylthio-2-nitroethene (MMN), an important intermediate in the production of the drug 'Ranitidine', is found to be hazardous. While the reaction itself was found to be endothermic, the reactants and product are found to thermally decompose. The overall hazard potential of this reaction system is, therfore, of unknown magnitude. In the present investigation, kinetic and thermodynamic parameters such as activation energy, exothermic onset temperature, heat of reaction and time available before explosion have been estimated employing microcalorimetric techniques. Important issues related to the overall safety of the process are discussed.

1. Introduction

Thermal explosion has been a major cause for accidents in chemical reactors [1–3]. A number of factors [4–7] such as reaction kinetics, autocatalytic effects, temperature and pressure effects, presence of highly volatile constituents, hazardous nature of chemicals and their incompatible combinations that trigger undesirable side reactions, etc. have been found to be responsible for the hazardous behaviour. Recent developments in microcalorimetry have provided useful tools for safety analysts to identify and quantify reaction hazards [4, 8–10]. Their deployment at the process development stage will ensure intrinsic safety of thermally sensitive reaction systems.

This paper examines in detail the thermochemical aspects of the synthesis of 1-methylamino-1-methylthio-2-nitroethene(MMN), an important intermediate in the production of the highly potent drug 'Ranitidine'. Although the basic reaction is endothermic, the nitromethane used in this reaction is a known hazardous chemical and there is a total lack of thermal information on the other reactant and the product. The overall hazard potential of the reaction system is therefore of unknown magnitude.

---

* Corresponding author.

2. Process

The method of preparation of MMN involves the reaction of *n*-methylcar-bonimidodithioic acid dimethyl ester (CAD) with nitromethane (NM) at 103–105 °C in the presence of solid zeolite catalyst under reflux conditions. The reaction time required for 50% conversion is about 48 h. The details of the synthesis of MMN have been reported by Rakeeb et al. [9]. The main advantages of this reaction are (i) the catalyst can be recovered and reused, (ii) the product is not contaminated with the unwanted 1,1-bismethyl amino-2-nitroethylene and (iii) the product is more than 99% pure.

3. Experimental

High pressure DSC (Dupont 2910), TGA (Dupont 2900), RC (Mettler, Switzerland) and ARC (CSI, USA) were employed for the thermal analysis. The sample size was typically 5–10 mg. A heating rate of 10 °C/min in N_2 atmosphere was employed for DSC and TGA. The energy measurement sensitivity of the DSC cell was calibrated using indium metal standard. The microbalance of the TGA was calibrated with M class standard weights employing weight calibration software. Reaction conditions were simulated in the RC to study the effect of process parameters on thermal behaviour of the system. The main and decomposition reactions were studied under adiabatic conditions in ARC.

4. Results of thermal analysis and discussion

DSC/TGA studies were carried out for reactants (NM and CAD), product (MMN) and fresh and regenerated catalyst samples to identify the temperatures of transition and onset of exothermicity. The results of DSC and TGA studies for reactants (NM and CAD) and product (MMN) alone are given in Table 1.

The DSC and TGA thermograms of MMN are shown in Fig. 1. It can be noticed that a significant weight loss for MMN had occurred around 125 °C. This falls within the exothermic region observed in the DSC study. The DSC plots for the regenerated

Table 1

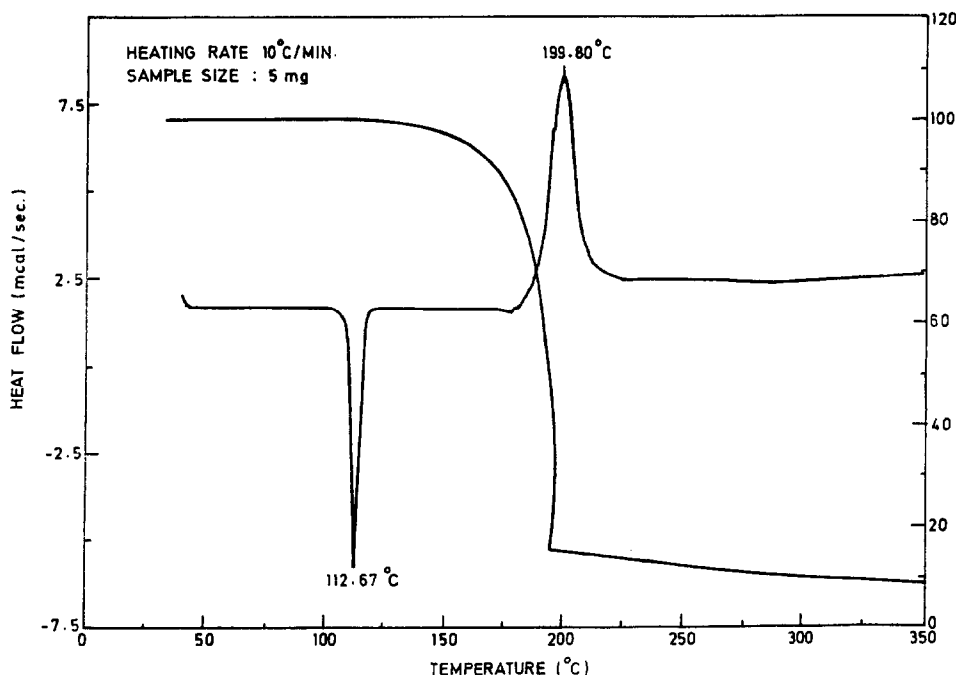| Sample	Onset of exotherm	Heat of reaction (cal/g)	Remarks
CAD	152	—	At 700 psi (N_2)
NM	200	—	At 700 psi (N_2)
MMN	170	126.9	MP: 112 °C highly exothermic

Fig. 1. DSC, TGA plots for MM-2-nitroethene.

catalyst samples washed with ethylene dichloride (EDC), methanol (MeOH) and H_2O respectively are given in Fig. 2. Mild exothermic peaks were observed for catalyst samples washed with EDC and MeOH whereas the water washed catalyst samples exhibited a behaviour similar to that of the unwashed catalyst. The TGA studies for the catalyst showed a weight loss of 20% up to a temperature of 500 °C for the freshly prepared catalyst; while the MeOH washed catalyst sample exhibited maximum weight loss and the EDC and water washed catalyst samples suffered minimum loss.

4.1. Reaction calorimetry (RC)

The process was simulated in the RC to identify the thermally sensitive parameters of the reaction. It is found to be endothermic in nature and the heat of reaction is experimentally found to be 25.15 kJ/mol.

4.2. Accelerated rate calorimetry (ARC)

The samples which exhibited exothermicity in DSC screening were selected for ARC studies to evaluate thermal parameters like self-heat rate, onset of exothermicity, temperature/pressure vs. time, and pressure vs. temperature behaviour.
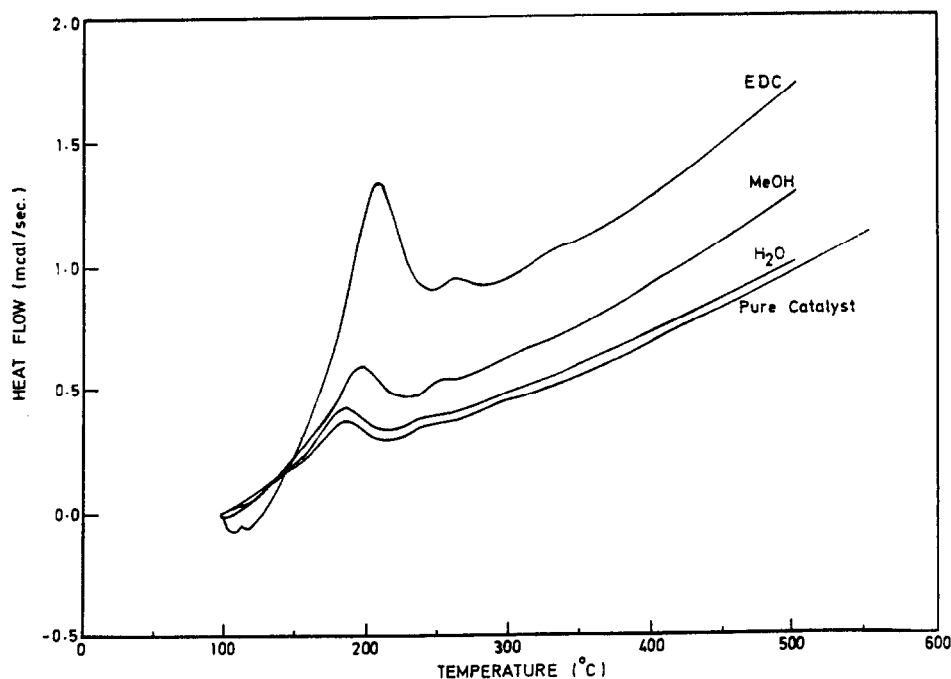
Fig. 2. DSC plot for regenerated catalyst sample washed with H_2O, MeOH and EDC.

The self-heat rate vs. temperature plot for NM shows the onset of exotherm due to its decomposition occurring at 250 °C (Fig. 3). The pressure vs. temperature plot shows a pressure rise exceeding 540 psi (Fig. 4) at 325 °C. The contents of ARC bomb were quenched to prevent further increase in pressure which might otherwise damage the instrument. The CAD exhibited exothermic peaks in the temperature range of 230–250 °C (Fig. 3). A maximum heat generation rate of 1 °C/min was recorded at 230 °C. The pressure vs. temperature curve (Fig. 4) showed a profile similar to that of NM.

All catalyst samples (freshly prepared and regenerated ones) showed no exothermic behaviour up to 450 °C. A small increase in pressure was however observed for the regenerated catalyst samples. The product MMN showed high exothermicity at 110° (Fig. 3). The pressure vs. temperature plot shows an increase of 2300 psi at 149 °C (Fig. 4). The temperature vs. time plot also shows a similar trend.

4.3. Isothermal aging

The reaction mixture, as per the molar proportions prescribed [9] in the process chemistry, was subjected to the isothermal aging at three temperatures, viz. 100, 105 and 110 °C. The reaction mixture kept at 100 °C for 48 h in ARC showed no sign of exothermic behaviour. After isothermal aging, it was subjected to a thermal input
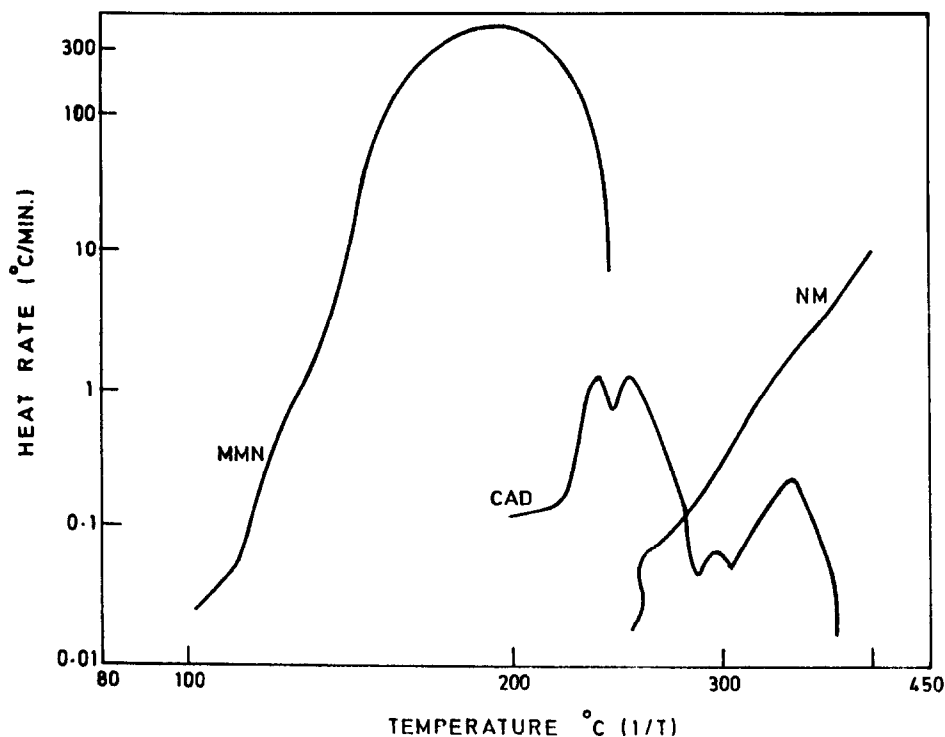
Fig. 3. ARC self-heat rate plot for MMN, CAD and NM.

through heat–wait–search technique. The self-heat rate curve shows an onset of exothermicity at 140 °C (Fig. 5, Plot 1). The reaction mixture kept at 105 °C for 48 h under stirred conditions exhibited no unusual exothermic behaviour at any stage of the reaction. The reaction mixture kept at 110 °C for 48 h in ARC, however, registered exotherm onset at 112 °C (Fig. 5, Plot 2) within 2 h from the start of the experiment. The exotherm exhibited a rapid self-heat rate of 50 °C/min around 280 °C. This was associated with a pressure rise of up to 1600 psi. The reaction mixture was then quenched to protect the ARC facility.

4.4. Thermokinetics

The ARC self-heat rate curve provided vital information on thermal decomposition kinetics of NM, CAD and MMN. The recent literature reports [11, 12] on thermokinetics are of relevance to the present study. A zero order kinetic model has been applied in the present case as the thermal rate was found to be unaffected by reactant concentration at the initial stages of the reaction. Assuming the rate coefficient to follow Arrhenius type of temperature dependence, the relative reactivity of compounds can be compared by evaluating the activation energy (E_a) by employing the
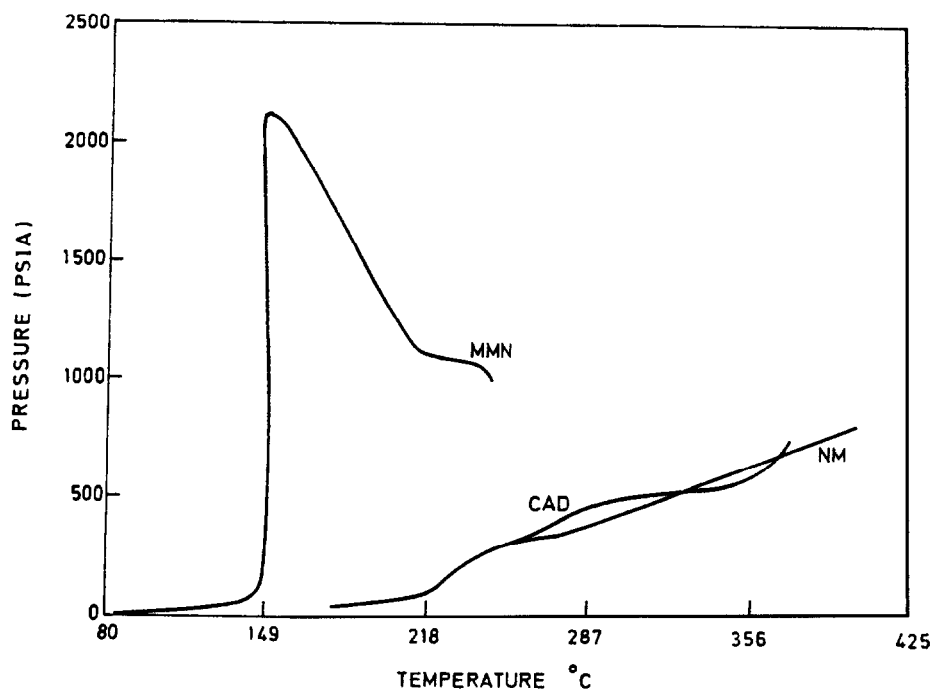
Fig. 4. Pressure vs. temperature, ARC plot for MMN, CAD and NM.

following relationship:

$$R_a = m\Delta H_r A \exp(-E_a/RT).$$

The estimated E_a for MMN, CAD and NM decompositions are shown in Table 2. The smaller the value of E_a, the higher the rate of decomposition. Accordingly, the decomposition of NM is found to be the fastest. It is necessary that the reactor venting facility is adequately designed to counter the thermal decomposition rates of MMM, CAD and NM individually and in combination.

The thermochemical studies have also identified the following:

(a) *Thermal stability*. While the main reaction itself does not exhibit exothermicity, as established by reaction calorimetric studies, the reactants and the product can decompose exothermically. Their relative stabilities, as seen from the onset temperatures, are in the following order:

nitromethane > CAD > MMN.

(b) *Safety margin for temperature excursions*. With less than 10° margin between the reaction and decomposition temperatures of MMN, the possibility of a thermal runaway due to onset of MMN decomposition is high. Past experience with thermal explosions [8, 7, 13] shows a minimum of 50 °C safety margin for most hazardous
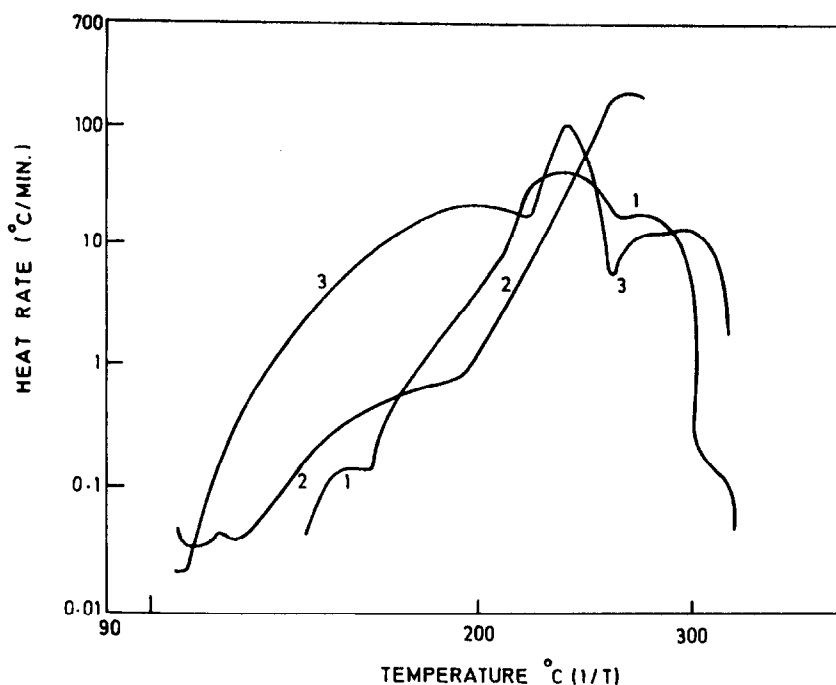
Fig. 5. ARC self-heat rate plot for 1. $CAD + CH_3NO_2 \xrightarrow[\text{iso-aging 100°C}]{\text{zeolite}} \xrightarrow{\text{heat}-\text{wait}-\text{search}}$ 2. $CAD + CH_3NO_2$ $\xrightarrow[\text{iso-aging 100°C}]{\text{zeolite}}$

Table 2
Activation energies for the thermal decompositions

Material	E_a (J/mol/K)
MMN	279
CAD	731
NM	129

reactions. The present reaction system does not provide this flexibility in the case of temperature excursions.

(c) *Self-acceleration possibilities.* Self-heat rate plots for each of the chemical constituents in the reaction mixture are given in Fig. 4. They show that for a worst thermal situation, viz. in cases when no heat is removed from the reaction system, the decomposition of MMN can initiate a self-propagating mechanism which would finally result in decomposition of nitromethane. The violence of such decomposition

Table 3
Lead time for attainment of self-heat rate

Temperature (°C)	Time		
	MMN	CAD	NM
110	100		
120	60		
140	1		
150	0	100	
180		9	
190		0	
250			700
300			70
350			15
400			0

could have serious consequences. The lead time available before the attainment of self-acceleration of the above decomposition processes can be estimated from ARC data at various temperatures. These are given in Table 3.

A lead time of 100 min is generally favoured for initiating appropriate safety measures leading to reactor venting.

5. Conclusion

Thermochemical analyses of the synthesis of MMN have identified specific process hazards and accident situations which may lead to thermal explosions. This study is of practical utility to recommend appropriate safety measures right at the process development stage for achieving intrinsic safety of such reaction systems.

Acknowledgements

References

[1] T. Kotoyori, J. Loss Prevention, 4 (1991) 120.

[2] L. Brethrick, Handbook of Reactive Chemical Hazard, Butterworths, London, 1987, pp. 267, 273, 429, 543.

[3] Columbia Scientific Industries Corporation, Archives 6, Austin, Texas.

[4] K.V. Raghavan, Proc. CHEMCON, Madras, 1991, Institution of Chemical Engineers India.

[5] W.J. Fenlon, Proc. Int. Symp. on Preventing Major Chemical Accidents, Washington, February 3–7, 1987, pp. 4.69.

[6] D.M. De Faveri, C. Zonato, C. Pagella, A. Vidille and G. Ferraiolo, Proc. Int. Symp. on Runaway Reactions, Massachusetts, March 7–9, 1989, pp. 155.

[7] H.T. Kohlbrand, Proc. Int. Symp. on Preventing Major Chemical Accidents, Washington, February 3–7, 1987, pp. 4.69.

[8] A. Koshy, M. Surianarayanan and K.V. Raghavan, Proc. X Nat. Symp. of Thermal Analysis, Goa, November 1993, pp. 39.

[9] A. Rakeeb, A.S. Deshmukh, T. Indrasena Reddy, Baburao, M. Bhawal, V.P. Shiralkar and S. Rajappa, J. Chem. Soc. Perkin Trans. ISSN 0380-922X, JCPRB4(4) (1990) 1217.

[10] J.C. Cronin, P.F. Nolan and J.A. Barton. Proc. Int. Symp. on Runaway Reactions, Massachusetts, March 7–9, 1989, pp. 633.

[11] T.C. Hofelich, Proc. Int. Symp. on Runaway Reactions, Massachusetts, March 7–9, 1989, pp. 633.

[12] ARC Instruction Manual (P/N 851-9001) of Columbia Scientific Industries Corporation, Austin, Texas.

[13] T.C. Hofelich and R.C. Thomos, Proc. Int. Symp. on Runaway Reactions, Massachusetts, March 7–9, 1989, pp. 74.