Combustion and explosion characteristics of 5-aminolevulinic acid hydrochloride and its intermediate product

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Abstract:

We investigated the combustion and explosion characteristics of new antitumor drug — 5-aminolevulinic acid (5-ALA) hydrochloride and its intermediate of synthesis — 5-nitrolevulinic acid (5-NLA) methyl ester. The results were obtained by experiments and by calculations. Differential scanning calorimetry data obtained at different heating rates and the Kissinger method calculations were used to determinate the kinetic parameters of the thermal decomposition for 5-NLA methyl ester. It was found that 5-NLA methyl ester belongs to a substances prone to explosive transformation. The data obtained during experimental period were transferred to the manufacturer — that would help to create a proper explosion protection for work environment and to design technological processes taking into consideration the required precautions.

Keywords: 5-ALA hydrochloride; 5-NLA methyl ester; flammable properties; explosive characteristic.

1 Introduction

The research concerns to the definition of flammable and explosive properties of the new antitumor drug — 5-aminolevulinic acid hydrochloride (further in the text 5-ALA hydrochloride) and its intermediate of synthesis – 5-nitrolevulinic acid methyl ester (further in the text 5-NLA methyl ester) using calculated and experimental methods.

The work was done in the frame of the implementation of the research program for substances, synthesized while fulfilling the strategy for the development of the Russian pharmaceutical industry for the current period up to 2025 [1]. We continue the series of publications started by the Ref. [2] and Ref. [3].

The flammable and explosive properties were determined on the standard equipment by the method of GOST 12.1.044-89 [4]. Lower explosion limit (LEL) for 5-ALA hydrochloride was determined using a blasting cylinder made of hardened glass. The very essence of the measurement method is the ignition of an air-dust mixture having a predetermined concentration in the volume of a reaction vessel and the subsequent evaluation of the results of ignition. When determining the LEL, a concentration regime is identified in which the possibility of ignition is entirely probable (so called “unstable ignition regime”). The ignition and autoignition temperatures were determined using the device described in the GOST – OTP device. With its help, the specified mass of matter is heated with a periodic attempt to ignite evolved vapor (ignition source is not used if we need to determine the T_{flash}, which is the lowest temperature at which dust can ignite, when given an ignition source) with visual evaluation the ignition results. Another device from GOST (OTM) allowed to determine a group of flammability for the 5-NLC hydrochloride. The simultaneous thermal analyzer NETZSCH TG/DSC STA 449 F3 Jupiter was used to obtain the thermal characteristics of the samples.

2 Experimental

Before the start of the experiments and calculations the chemical structure of the substances was confirmed using the IR spectroscopy method. The data were obtained with a Nicolet 380 FT-IR spectrometer. The references of the spectra were carried out using [5] and [6]. The presence of appropriate absorption bands proved the chemical structure of matter.

For the 5-NLA methyl ester there were found the absorption bands of the nitro group O_2N— (1211 and 1368 cm^{-1}), as well as the characteristic elements of the structure —CH_2—C(O)—CH_2 (1731 cm^{-1}) and C–O–C (1173 cm^{-1}). For the 5-ALA hydrochloride in addition to bands of structural groups, characteristic amino acid absorption bands were found (2555 cm^{-1}, 2580 cm^{-1} and 1311 cm^{-1}), as well as absorption band of hydroxyl group (951 cm^{-1}), for the previously mentioned group that is shared by both substances —CH_2—C(O)—CH_2 (1727 cm^{-1}) and for the —CH_2—COOH (1739 cm^{-1}).

The study of temperature characteristics of the 5-ALA hydrochloride by the DSC method showed (Figure 1) that at a temperature range (167-210) °C there was a mass-loss jump (27% by weight) which is accompanied by endothermic event – presumably there an act of starting decomposition takes place, which manifests itself in the form of detachment of a highly toxic group HCl(g) (points A-B).

Exothermic event starts at 291 °C – apparently, due to thermal oxidation of the organic part of the molecule. The maximum of exothermic event is observed at 565 °C (point C), what practically coincides with the kindling point of the substance (575 °C).

As shown on Figure 2 and Table 1, 5-NLA methyl ester initially melts and evaporates when heated, further at (242-269) °C starts exothermic event (point A), which happens apparently due to the separation of the group NO_2 (a rather weak bond C-NO_2). Thermooxidation of the matter decomposition products with the maximum of exothermic event begins at (450-510) °C. This range coincides with the value of the substance kindling point (495 °C).

3 Results and discussion

Values of ln (φ/T^2_{max}) and 1/T were also calculated to draw a straight line. Derivation of the equation for this line (as well as its drawing) were performed with Microsoft Excel by the method of linear approximation (Figure 3).Slope of such line is E_a/R where's E_a is activation energy and thereby we can easily highlight it. The free term in the equation is ln (AR/E_a) from which we can determine lg A.

As a result of calculations using the Kissinger method, the following kinetic parameters were obtained: E_a = 171 kJ/mol, lg A = 14,2 s^{-1}.

Software package REAL [12] was used to calculate parameters of explosive transformation of 5-NLA methyl ester (heat of explosion for example). The magnitude of 5-NLA methyl ester heat of explosion was 713 kJ/kg.

Estimated T_{flash}, or temperature, at which the exponential growth of the explosive reaction rate starts, were carried out according to a formula that follows from the solution of the problem of thermal explosion in convective heat exchange with the surrounding medium [13]. Consideration of this problem is an integral part of the combustion and explosion theory [14]. See equation 1.

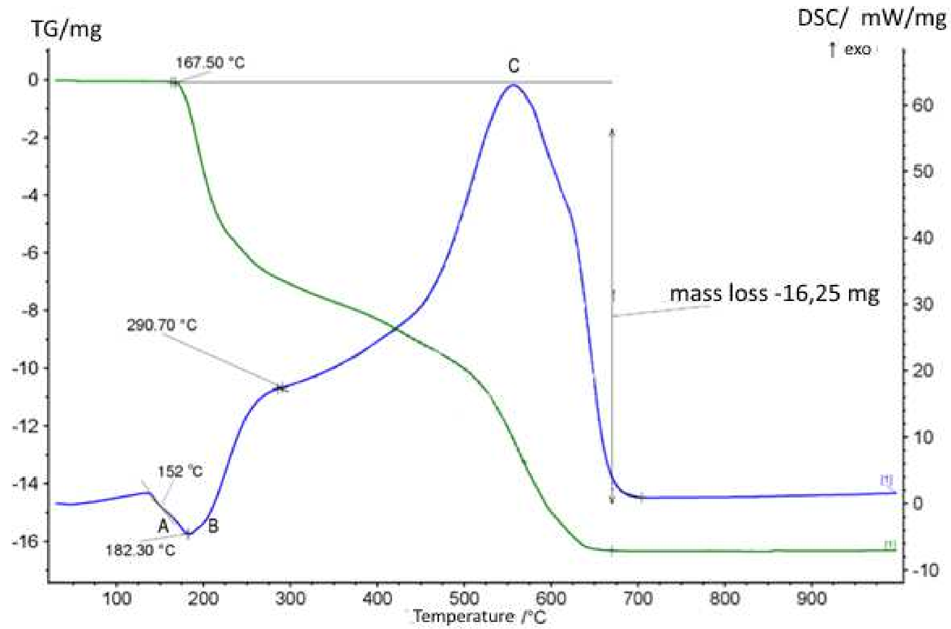

Figure 1: Thermogram of 5-ALA hydrochloride (heating rate 20 ºC per minute).

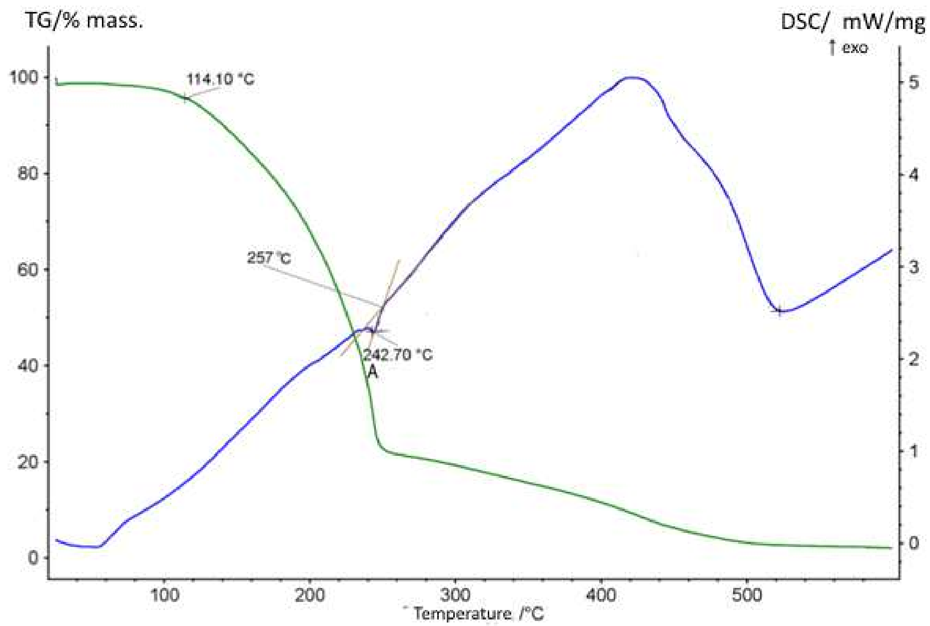

Figure 2: Thermogram of 5-NLA methyl ester (heating rate 2 ºC per minute).

Table 1: Results of thermograms decoding for 5-NLA methyl ester.

Heat rate, °C/min	Melting point, °C	Initial temperature of exothermic process, °C	Maximum temperature of exothermic process, °C	Exothermic process maximum peak at, °C
2	44	242,7	257	450
5	47	260,6	273	475
10	50	263	282	510
20	40	268,7	287	490

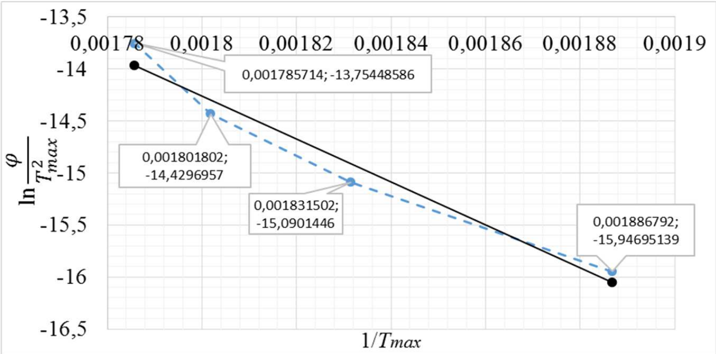

Figure 3: Straight relationship between $\ln\frac{\varphi}{T_{max}^2}$ and $\frac{1}{T_{max}}$ for 5-NLA methyl ester.

$$T_{flash} = \frac{E}{R\cdot\ln\frac{e\cdot V\cdot d\cdot B\cdot E\cdot Q}{S\cdot Nu\cdot k\cdot R\cdot T_*^2\cdot c_V}}, \quad (1)$$

where: T_{flash} – flash temperature, K; E – activation energy, cal/mole; R – universal gas constant e – base of natural logarithms (critical value of the N.N. Semenov's criterion); d – spherical vessel diameter, cm; V – volume of the vessel in which the flash occurs (taken as a sphere), cm^3; B – pre-exponential factor, Q = 0.5·Q_v heat of decomposition (half the heat of explosion at a constant volume), cal/g; S – cooling surface area of the vessel, cm^2; Nu – Nusselt number, κ – coefficient of thermal diffusivity, cm^2/s; c_v – heat capacity at constant volume, cal/(g·K).

It was assumed that the experiment is carried out in a test tube with a 15 mm diameter (d). For organic matter c_v = 1,255 J/(g·K) = 0,3 cal/(g·K), $\kappa = 10^{-3}$ cm^2/s.

5-NLA methyl ester T_{flash}, calculated with Nu=15 (Figure 4) was 496 K (226 °C), which is close to this matter's initial temperature of the exothermic decomposition (515 K or 242 °C).

A detailed description of the T_{flash} calculation for disperse nitro dyes is given in Ref. [15].

Low T_{flash} of 5-NLA methyl ester (185 *°C*) in comparison with initial temperature of exothermic process (458 K or 242 *°C*) can be explained by the high fusibility of the substance — it can be observed at (42-46) *°C*. At this temperatures, intensive evaporation of the substance followed by formation of combustible vapors takes place. The thermal action leads to ignition then.

The obtained data on the flammable and explosive properties of the investigated substances are given in Table 2, from which it can be seen that 5-NLA methyl ester is a combustible substance. LEL was not determined for it experimentally as its melting point is only 42°C. Nevertheless, we calculated it and its magnitude — 48 g/m^3.

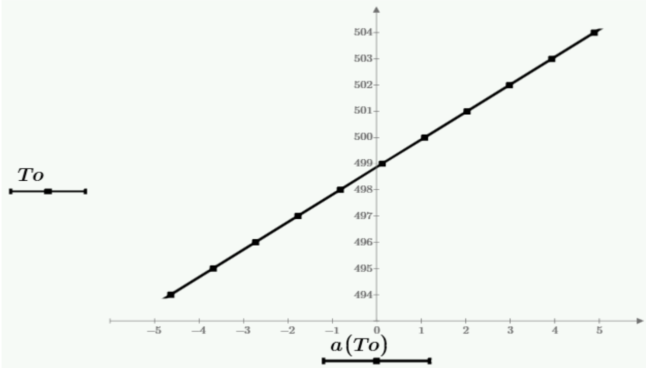

Figure 4: Calculated T_{flash}.

Table 2: Flammable and explosive properties of 5-ALA hydrochloride and 5-NLA methyl ester.

Substance		Properties						
		Initial temperature of exothermic process, °C **	T_{flash}, °C	Autoignition temperature, °C	Maximum explosion pressure P_{max}*, kPa	Maximum rate of explosion pressure rise $(dP/d\tau)_{max}$*, MPa	Lower explosive limit LEL, g/m³	Flammability
1	5-ALA hydrochloride	290,7	305	575	-	-	not found up to 500	Hardly flammable
2	5-NLA methyl ester	242	185	495	671	50,3	48*	Flammable

** – properties obtained by calculation methods [4];*

*** – initial temperature of the intensive exothermic decomposition determined by DSC with heat rates 20°C/min for test subject 1 and 2°C/min for test subject 2.*

Calculation methods were used to determine the enthalpies of formation and combustion of the substances; results are given in Table 3.

Table 3: Enthalpies of formation and flammable properties values for 5-ALA hydrochloride and 5-NLA methyl ester.

Calculation method	Substance	
	5-ALA hydrochloride	5-NLA methyl ester
	$\Delta_f H^{\ominus}$, kcal/mol	
group contribution method	-112,53	-123,2
BGIT	-136,8	-141,2
ChemOffice	-136,2	-138,5
Mean	-128,5 (-155,2*)	-134,3 (-157,55*)
	ΔH°_{comb}, MJ/kg	
Hess law	**-14,49**	**-17,07**
Konovalov-Handrick method	-14,80	-16,81

** – the enthalpy of formation considering phase transitions.*

Enthalpies of combustion calculated by means of Hess law are recommended as more reliable for use as reference values.

4 Conclusions

The study revealed that 5-NLA methyl ester belongs to a group of substances prone to explosive transformation.

The data obtained on the flammable and explosive properties of new organic compounds are of great practical importance. From the pool of research results a report was made for the manufacturer — Federate State Unitary Enterprise "State Science Center "NIOPIK". Authors hope that the results of the research will help entrepreneurs to create a proper explosion safe work environment, design and develop technological processes taking into account the required precautions.

Acknowledgements

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