THERMAL AND KINETIC STUDY OF CHOLIC ACID BY TG, DTG, DTA AND DSC METHODS

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In the present paper the thermal decomposition of cholic acid, a biologically active substance having a cyclopentane-phenantrene nucleus was performed by thermal analysis methods. The TG, DTG and DTA thermal curves reveal three endothermic processes: decarboxylation, dehydration and thermal decomposition, while the DSC thermal curves show one more process, an exothermic one.

The kinetic study of the decomposition stage shows that the process is a first order reaction with an activation energy of 114 kJ/mol and a preexponential factor of 10^8 s^{-1}.

Introduction

It is well known that cholic acid is the basic nucleus in the synthesis of corticosteroides and of the estrogene hormons. Cholic acid is a trihydroxymonocarboxilic acid, with the following structure:
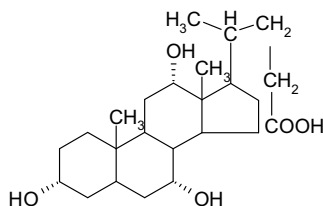

Fig. 1: *The cholic acid structure.*

It belongs to the billiary acids class. Sodium salts of conjugate cholic acids have the property of solubilizing the water insoluble substances thus making possible their passage through the intestinal mucous membranes and their resorption.

The present study reveals the decomposition stages of the cholic acid, the intermediate products formed, and establishes the stability conditions of the substance.

Experimental

Experiments were carried out using a Merk cholic acid of 99% purity.

The thermal analysis curves TG, DTG and DTA were plotted at a 5 K/min heating rate in air static atmosphere using a computer controlled C.MOM Budapest Derivatograph,

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Paulik-Erder type. The powdered samples, of 26 mg weight, and α-Al_2O_3 as inert reference material were used. The powdered samples, of 26 mg weight, and α-Al_2O_3, as inert reference material were used. The samples were heated in a static air atmosphere with a heating rate of 5 K/min.

The DSC thermal curves were drawn at a 20 K/min scan rate in Ar atmosphere, using a Perkin-Elmer DSC-2. Experiments were conducted with samples encapsulated in sealed aluminum pans and weighing 1÷2 mg each. The measurements were carried out in the 330÷550 K range.

Results and Discussions

It is well known that the thermal stability of any molecular compound is determined by the temperature at which the TG curve exhibits deviations from the base line.

The analysis of the thermal curves in Fig. 2 reveals that, at the heating rate of 5 K/min, the initial temperature at which the weight starts to decrease is $T = 171^{o}C$.
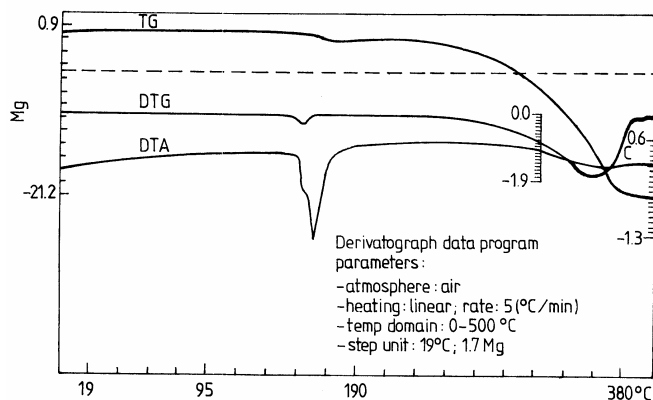

Fig. 2: *The TG, DTG and DTA thermal curves of cholic acid.*

In fact, the thermal decomposition of the cholic acid is a complex one. The DTA derivatogram shows that the process is not a unique one and consists in three steps.

The first step of degradation reveals a endothermic effect. The light gas product, CO_2, was obtained in the monoxydative decarboxylation.

The second step is an oxydative dehydration.

The two light gas products (H_2O and CO_2) result from the breaking of the weaker bonds and the process is characterized by low activation energy value.

(1)

(2)
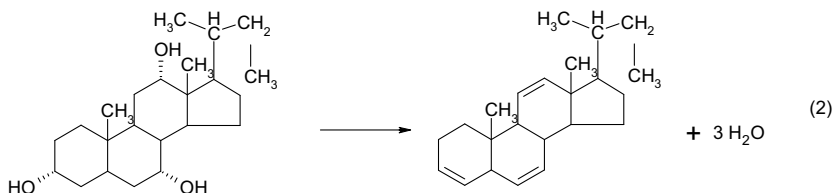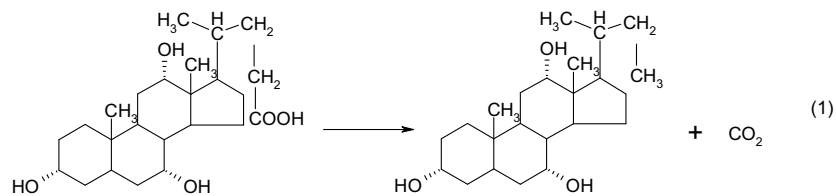
The third step of degradation, starting at 256°C, is also an endothermic one, occurs with higher activation energy and is plotted by reaction:

(3)
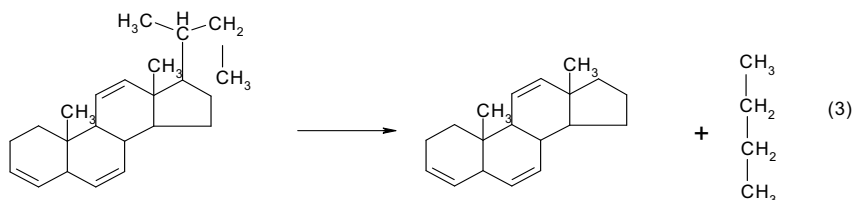
As the third stage is unique, the experimental data can be processed for assesing the kinetic parameters. The reaction rate is expressed by the following equation:

$$\frac{d\alpha}{dt} = A e^{-E/RT} (1-\alpha)^n \qquad (4)$$

where: α is the decomposition degree, t – the time, T – the temperature in K, R – the perfect gases constant, E – the activation energy, A – the preexponential factor correlated with activation entropy, n – the conversion function exponent that, in simple homogenous system is the same with the reaction order. Since the molecule splitting is the limiting step, the simple form of the conversion function was used. After variables separation and equation (4) integration, equation (5) is obtained [1]:

$$\left.\begin{array}{ll} \dfrac{1-(1-\alpha)^{(1-n)}}{(1-n)}; & n \neq 1 \\ \text{and} & \\ -\ln(1-\alpha); & n = 1 \end{array}\right\} = \frac{AEp(x)}{aR} \qquad (5)$$

where: $p(x)$ is the exponential integral, a – the heating rate, and $x = -\dfrac{E}{RT}$.

The calculation methods based on the reaction rate expression (4) are called differentials, whereas those using equation (5) make up the group of the integral methods. The calculation methods can be also distinguished by the approximations they consider.

Another solving method of the differential equation (4), i.e. the elimination of the time variable, is to maintain constant the reaction rate with certain special devices [2,3]. The curve shape, $T = f(\alpha)$, in these conditions, allows the detection of the autocatalytic processes [4]. At the same time, the activation energy can be assessed, irrespective of the form of the conversion function, if two curves are recorded at two different reaction rates.

In the present study, the differential and integral methods, and also the isokinetic one were comparatively used [4]. The nonisothermal kinetic parameters of last step of decomposition are given in Table 1.

Table 1. Values of the kinetic parameters corresponding to reaction (3)
of cholic acid thermal decomposition: δ-standard deviation, *r*-correlation coefficient,
I-integral method, D- differential method, S-special method.

	Calculation method	E (kJ/mol)	$\delta_{(E)}$ (kJ/mol)	A (s^{-1})	$\delta_{(A)}$ (s^{-1})	n	$\delta_{(n)}$	r	Type of meth.
1	Achar [5]	104.93	0.10	1.60106	1.2410	0.90	0.05	0.9775	D
2	Freeman and Carroll [6]	84.26	0.03	1.06104	6.8103	0.77	0.02	0.9582	D
3	Piloyan [7]	62.67	0.16					0.9969	D
4	Coats and Redfern [8]	114.05	0.10	8.72106	6.7105	0.90	0.05	0.9958	I
5	Flynn and Wall [9]	114.25	0.22	6.83108	8.8107	0.80	0.05	0.9965	I
6	van Krevelen [10]	138.34	0.04	1.08109	2.0108	1.00		0.9959	I
7	Urbanovici and Segal [11]	113.93	0.10	8.9106	6.9105	0.80		0.9956	I
8	Fatu and Segal [4]	118.7	0.21	7.8108	8.3106	0.83	0.08		S
9	Average values	106.39	0.12			0.54	0.02	0.98881	

The data were numerically processed with a BASIC [12] and Visual BASIC [13] calculation program.

The differential method, 1 and 2, in the table above show lower correlation coefficients and are generally more sensitive to the experimental errors. In this case, the reaction rate was calculated by taking the derivative of the TG data. Thus, an additional error is introduced as compared to the integral methods. Method 2 in the Table 1 uses finite differences of some parameters with close values, thus leading to high errors. Method 3 is only applied to the first part of the DTA or DTG curve, so the result cannot be compared with the results given by the previous methods. The narrower the temperature range is, the better the results obtained by method 6 are. The advantage of method 8, used at a constant reaction rate, consists in the elimination of the temperature and weight gradients appearing when certain computer programs are employed. Application of the method 8 depends on how constant the reaction rate can be maintained within an as wide as possible variation range of the

conversion degree. Since this method does not use linear regression, the linear coefficients cannot be calculated.

Therefore, the results obtained by integral methods, from the direct data of the curve TG, are largely used.

Fig. 3 shows the theoretical curve, T using values $E = 114$ kJ/mol, $n = 0.9$ and $A = 9 \cdot 10^7 s^{-1}$.
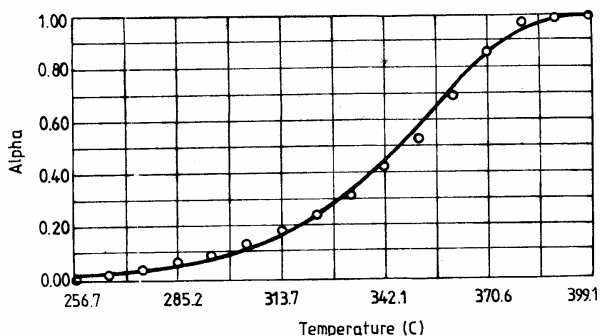

Fig. 3: *The calculated curve $\alpha = \alpha(t)$ of the thermal decomposition.*

As the experimental data are lying close to or on the theoretical curve, the equation (3) kinetic is well described by equation (4). Despite the experimental errors and the transport phenomena, one can consider that process (3) is the first order one.

In the DSC study the same three endothermic stages are obtained, but at 159°C an exothermic phase transition process was noticed. The thermal effect is –15.59 kJ/mol.

The results of DSC measurements are presented in Table 2.

Table 2. The DSC experimental (sensitivity 20.9 mJ/s) and the calculated data: $\Delta^{fus}H$ and $\Delta^{fus}S$.

Sample	Parameters of DSC experiments			$\Delta^{fus}H$ (kJ/mol)	T_{tr} (K)	$\Delta^{fus}S$ (J/molK)
	Scan rate (deg/min)	Sample weight (mg)	Area of curves (sqmm)			
Cholic acid	20	1.79	126.90	14.17	417	39.04
			-139.28	-15.59*	432	-36.07*
			30.95	3.47	453	7.65
			451.00	123.94	475	104.42

*$\Delta^{fus}H$ and $\Delta^{fus}S$, respectively.

In this table, the enthalpies and entropies of processes have been calculated from experimental data [14].

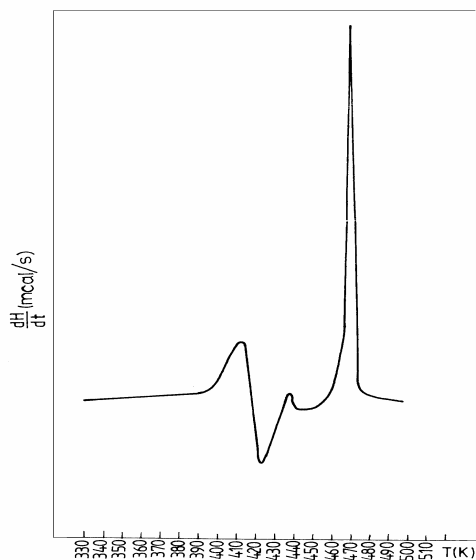Fig. 4: *DSC thermal curve of cholic acid.*

Conclusion

The thermal study of cholic acid, in non-isothermal conditions, consists in: oxidative dehydration, monoxydative decarboxylation and splitting of the intermediary product.

The kinetic study showed that stage (3) is a first order process. The lower values of parameter n (n=0.9) are assigned both to the experimental errors and to the temperature and weight gradients accompanying the heating. The differential method gives higher deviation of the kinetic parameters, as they are more sensitive to the experimental errors than the integral ones.

In the same time DSC allows the checking of the substance purity and calculating of the enthalpies and entropies of processes (1), (2) and (3).

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