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KINETIC INVESTIGATION OF SOME STEROIDS BY THERMOGRAVIMETRY

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The kinetic values of thermal degradation of some steroids were calculated by using TG and DTG curves and the Freeman-Carroll and the Jeres methods. The n and E_a values calculated by the Jeres method are more reasonable. The kinetic thermal stabilities of the simple functional groups of the steroids were compared by using the E_a values of Jeres, and the following sequences were found: 17β-OH > 17-octyl > 17-Ac-CHO > 17-keto; 3β-OH > 3-keto > 3α-OH; and 5α-H > 5 β-H > $\Delta^{5(6)}$ > Δ^4. The k, Z, ΔH^*, ΔS^* and ΔG^* values were calculated at the maximum decomposition rate temperatures by using the Jeres values. The ΔS^* values are negative and suggest a high ordering of the transition state. The ΔH^* and ΔG^* values are positive, as expected.

The thermal degradation of steroids is a nonisothermal process involving mass loss:

$$A_s \rightarrow B_s + C_g \tag{1}$$

where A_s = original solid reactant; B_s = solid residue, which may or may not be present, and C_g = gaseous product evolved. Thus, the activation energy of the activated complex and the order of the degradation reaction can be found by the Freeman-Carroll [1] and the Jeres [2] methods.

The Freeman-Carroll method is the most widely used method for the kinetic analysis of nonisothermal decomposition processes despite the great number of other methods proposed. The advantages of this method are that considerably fewer experimental thermogravimetric data are required than in the isothermal method, and that the kinetics can be obtained in a continuous manner over an entire temperature range without any missing regions [3]. In general, the Freeman-Carroll method postulates a kinetic equation of the type

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$$-\frac{dx}{dt} = kx^n \tag{2}$$

and good agreement should be expected for those processes whose kinetics can be expressed by Eq. (2), where x = the amount of the substance still to decompose at time t, n = the order of reaction, and k = the temperature-dependent rate constant. The temperature-dependence of k is given by the Arrhenius equation:

$$k = Z e^{-Ea/RT} \tag{3}$$

where Z = pre-exponential factor, E_a = activation energy of the reaction, R = ideal gas constant and T = absolute temperature. From Eq. (2), if a linear dependence of temperature with time is assumed, a linear equation

$$Y = -\frac{E_a}{R} X + n \tag{4}$$

can be derived, where

$$Y = \frac{\Delta \ln(dc/dt)}{\Delta \ln(1-c)} \quad \text{and} \quad X = \frac{\Delta (1/T)}{\Delta \ln(1-c)}$$

and c is the mass fraction reacted.

Jeres proposed that this method has a disadvantage that results directly from the mathematical treatment of the data and is independent of the validity of the kinetic equation proposed. An analysis of the mathematical treatment employed in the Freeman-Carroll method showed the existence of large errors in the determination of the order of the kinetic equation, and Jeres proposed a modification which allows a reduction of this error. According to the Jeres method, n and E_a are given as

$$n = \frac{\bar{Y}}{1 - Q\bar{X}} \tag{5}$$

$$E_a = \frac{RQ\bar{Y}}{1 - Q\bar{X}} \tag{6}$$

where $\bar{X}$ and $\bar{Y}$ are mean values of X and Y, and Q is given as

$$Q = \left[\frac{c' T^2}{(1-c)}\right]_{c'=\max} = \frac{Ea}{nR} \tag{7}$$

Here, $c' = \frac{dc}{dT} = \frac{1}{B}\frac{dc}{dt}$ and B is the heating rate. This treatment allows bypassing of the unanswerable question of which is the best-fitting straight line.

According to the transition state theory, the degradation reactions can be represented as

$$\text{solid reactants} \xleftrightarrow{K^*} \text{intermediates}^* \xrightarrow{k^*} \text{products}$$

The reaction rate is governed by the rate of decomposition of the intermediates, and the rate of formation of the intermediates is assumed to be so rapid that they are present in equilibrium concentrations at all times [4]. Here, the product of K^* and k^* gives k_2, which is given by the following equation:

$$k_2 = e\left(\frac{kT}{h}\right) e^{\Delta S^*/R} e^{-Ea/RT} \tag{8}$$

Hence,

$$Z = \left(\frac{kTe}{h}\right) e^{\Delta S^*/R}$$

or

$$\Delta S^* = R\left[\ln\left(\frac{hZ}{kT}\right) - 1\right] \tag{9}$$

where k = Boltzmann's constant, h = Planck's constant, and ΔS^*= the entropy of activation. The enthalpy of activation, ΔH^*, for solids and liquids, is related to the activation energy, E_a, by the following equation:

$$\Delta H^* = E_a - RT \tag{10}$$

and consequently the expression for the Gibbs function of activation, ΔG^*, is given as

$$\Delta G^* = \Delta H^* - T\Delta S^*. \tag{11}$$

Experimental

TG and DTG measurements were made simultaneously with a Shimadzu DT-30 thermal analyser. Platinum sample pans were used in a nitrogen atmosphere at a flow rate of 25 ml min^{-1}. Samples were heated up to 600^{0} at a heating rate of 10 deg min^{-1}.

Pure steroids (Merck and Sigma) were used.

Results and discussion

The nonisothermal thermal degradation of the investigated steroids (Fig. 1) usually takes place in one stage, as indicated by the mass loss, accompanied by a peak in the DTG curve. TG and DTG curves are given in Fig. 2.

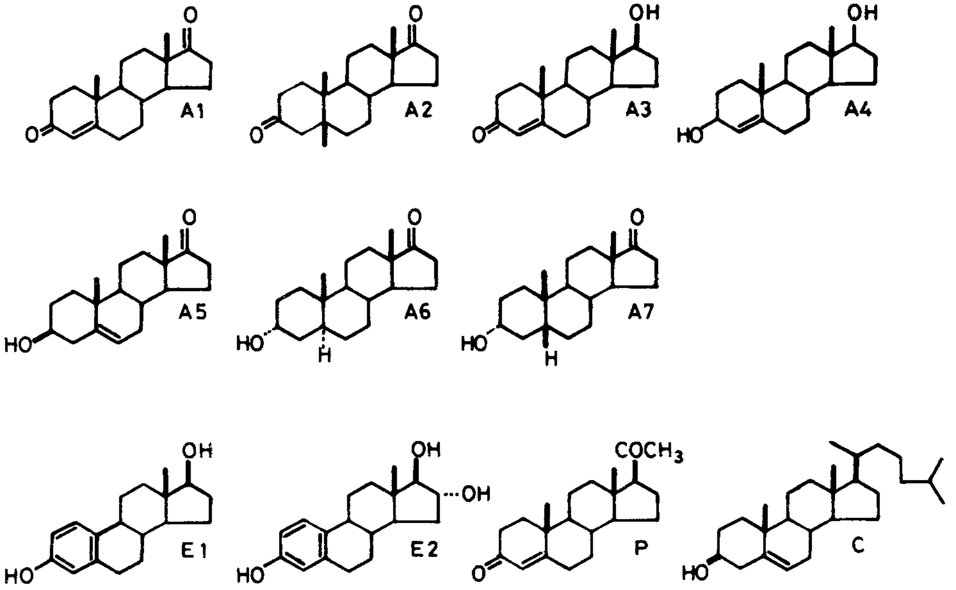

Fig. 1 Investigated steroids. Androgens: A1 androstenedione, A2 5β-androstenedione, A3 testosterone, A4 androstenediol, A5 dehydroepiandrosterone, A6 androsterone, A7 aetiocholanolone; Estrogens: E1 estradiol, E2 estriol;P: progesterone, C: cholesterol

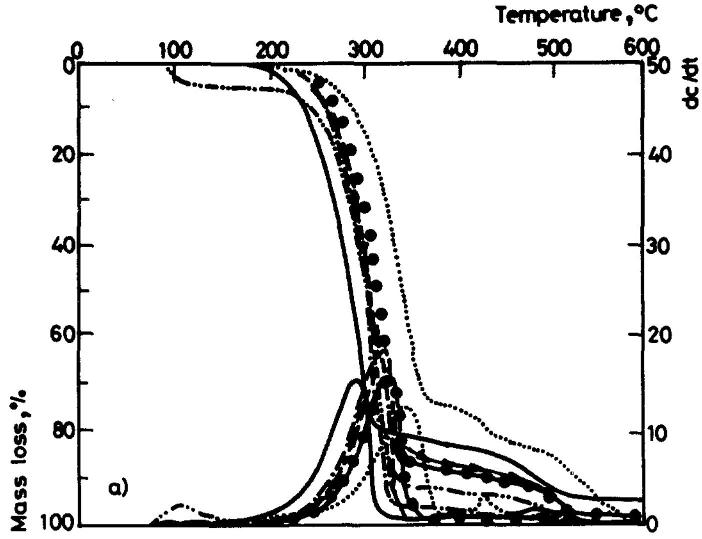

Fig. 2a TG and DTG curves of androgens; ······A1, ➤➤➤ A2, —— A3, —··—·A4, -●-●-●-●- A5, – – – A6, —·—·–A7

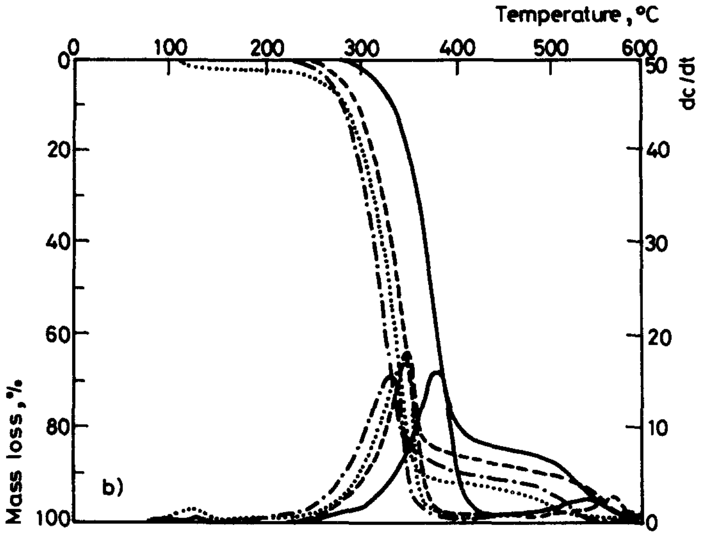

Fig. 2b TG and DTG curves of estrogens progesterone and cholesterol; —— E1, ····· E2, ·—·—P, – – – C

The initial decomposition temperatures, IDT, and the temperature ranges for which E_a values are calculated are taken from the TG and DTG curves, respectively. IDT values and T ranges are given in Table 1 with n and E_a values calculated via both the Freeman-Carroll (FC) and Jeres (J) methods.

Table 1 Kinetic parameters of thermal degradation of steroids

Steroid	IDT, °C	T range, °C	n_{FC}	n_J	E_{aFC}, kJ mol^{-1}	E_{aJ} kJ mol^{-1}
A1	190	210–350	-1.78	0.008	69.8	73.3
A2	194	210–320	0.66	0.006	93.2	84.9
A3	180	230–350	2.07	0.006	103.2	90.5
A4	80	210–310	–0.13	0.005	110.3	110.7
A5	210	210–330	2.09	0.006	112.4	104.4
A6	205	210–330	1.37	0.003	112.4	103.9
A7	190	190–310	-2.23	0.003	63.7	70.0
E1	95	210–350	–0.81	0.004	63.0	67.9
E2	260	270–370	-1.95	0.006	79.0	91.2
P	226	230–340	0.07	0.004	81.1	80.4
C	250	270–370	1.87	0.006	142.8	118.1

FC: Freeman-Carroll, J: Jeres

While the n_{FC} values vary between about +2 and -2, the n_J values are zero for all steroids. The zero order is reasonable for the degradation of steroids, because the rate of degradation is independent of the amount of unreacted solid material according to the transition state theory explained in the introduction. Further, the similar structures of the steroids predict similar degradation reactions, which leads to the same order for all of them.

All conversion reaction probabilities for the investigated steroids ($S_x \rightarrow S_y$) were examined theoretically, and it was found that 13 simple functional group conversions (SFGC) are probable. These SFGC with the sample reactions including them and the ΔE_a values calculated for them are given in Table 2. The ΔE_a value of a SFGC reaction will be equal to the ΔE_a value of a conversion reaction between the two steroids which differ only in one functional group. Conversions 1, 2, 3, 5, 9, 11, 12 and 13 are of this type. The ΔE_a value of a sample reaction which has more than one SFGC will be equal to the sum of the ΔE_a values of these SFGC. Hence, the unknown ΔE_a values can be calculated from the known ones. The ΔE_a values of the SFGC of types 4, 6, 7, 8 and 10 were calculated in this way. Through the results of the calculations, the kinetic thermal stabilities of these functional groups of the investigated steroids can be compared. A steroid or functional group with a high activation energy is undoubtedly more stable than one with a low one.

Table 2 Functional group conversions of steroids and related ΔE_a values

Type	Simple functional group conversions (SFGC)	SR $Sx \xrightarrow[o]{SFGC} Sy$	ΔE_a, kJ mol^{-1} FC	ΔE_a, kJ mol^{-1} J	More stable group
1	17-keto → 17β-OH	$A1 \xrightarrow{1} A3$	+33.4	+17.2	17β-OH
2	3-keto → 3β-OH	$A3 \xrightarrow{2} A4$	+7.1	+20.2	3β-OH
3	3-keto → 3α-OH	$A2 \xrightarrow{3} A7$	-29.5	-14.9	3-keto
4	$\Delta^4 \rightarrow \Delta^{5(6)}$	$A1 \xrightarrow[4]{4+2} A5$	+42.6 +35.5	+31.1 +10.9	$\Delta^{5(6)}$
5	$\Delta^4 \rightarrow$ 5β-H	$A1 \xrightarrow{5} A2$	+23.4	+11.6	5β-H
6	$\Delta^4 \rightarrow$ 5α-H	$A1 \xrightarrow[6]{6+3} A6$	+42. 6 +72.1	+30.6 +45.5	5α-H
7	$\Delta^{5(6)} \rightarrow$ 5β-H	$A5 \xrightarrow[7]{7-2} A2$	-19.2 -12.1	-19.5 +0.7	$\Delta^{5(6)}$(FC) 5β-H (J)
8	$\Delta^{5(6)} \rightarrow$ 5α-H	$A5 \xrightarrow[8]{8-10} A6$	0.0 +36.6	-0.5 +34.6	5α-H
9	5α-H → 5β-H	$A6 \xrightarrow{9} A7$	-48.7	-33.9	5α-H
10	3α-OH → 3β-OH	$A6 \xrightarrow[10]{10+1-6} A4$	-2.1 +36.6	+6.8 +35.1	3β-OH
11	17-keto → 17-Ao-CHO	$A1 \xrightarrow{11} P$	+11.3	+7.1	17-Ac-CHO
12	17-keto → 17-octyl	$A5 \xrightarrow{12} C$	+30.4	+13.7	17-octyl
13	16-ringH → 16α-O	$E1 \xrightarrow{13} E2$	+16.0	+23.3	16α-OH

SR: Sample reactions which involve one or more of these simple functional group conversions

For all SFGC (1, 11, 12) between the functional groups at C-17, the 17-keto group is on the left side. Since $\Delta E_a(1) > \Delta E_a(12) > \Delta E_a(11)$(the same for both FC and J), the sequence of kinetic thermal stabilities of these groups will be

$$17\beta\text{-OH} > 17\text{-octyl} > 17\text{-Ac-CHO} > 17\text{-keto}.$$

For the SFGC (2, 3) between the functional groups at C-3, the 3-keto group is on the left side. Since $\Delta E_a(2) > \Delta E_a(3)$ (the same for both FC and J), the sequence of kinetic thermal stabilities of these groups will be

$$3\beta\text{-OH} > 3\text{-keto} > 3\alpha\text{-OH}.$$

According to reaction 10, the stability of 3β-OH is greater than that of 3α-OH, which is in accordance with the sequence.

The SFGC between the double bonds and the hydrogen atoms at C-5 are 4, 5, 6, 7, 8 and 9. On analogy with the C-17 and C-3 groups, the sequences will be

$$5\alpha\text{-H} > \Delta^{5(6)} > 5\beta\text{-H} > \Delta^4 \quad \text{(for FC)}$$
$$5\alpha\text{-H} > 5\beta\text{-H} > \Delta^{5(6)} > \Delta^4 \quad \text{(for J).}$$

According to FC, $\Delta^{5(6)}$ is more stable than 5β-H, whereas the reverse is true for Jeres. Of course, a single bond will be more stable than an olefinic double bond. Thus, it may be concluded that the activation energy values calculated according to the Jeres method are more reasonable.

If the results are summarized:

1. β-OH groups on C-17 and C-3 are generally more stable than keto groups.

2. The 3α-OH group is less stable than the 3-keto group because of the stereochemistry of the steroids, but the 17α-OH should be more stable than the 17β-OH group because it is trans to the 18-methyl group.

3. The 5α-H is more stable than the 5β-H because it *is trans* to the 10-methyl group.

4. Single bonds are also thermally more stable than olefinic double bonds.

These conclusions are in good agreement with the literature findings [5].

According to Jeres, the sequence of kinetic thermal stabilities of the investigated steroids is

$$C > A_4 > A_5 > A_6 > E_2 > A_3 > A_2 > P > A_1 > A_7 > E_1$$

Cholesterol is the most stable compound, as expected, because it is a naturally-occurring steroid.

The k and Z values are calculated by using the n_J and E_{aJ} values at the maximum decomposition rate temperatures, T_{max}, with Eqs (2) and (3) , respectively. The ΔH^*, ΔS^* and ΔG^* values are calculated at T_{max} by using the Jeres values with Eqs (9), (11) and (10), respectively. The T_{max}, k, Z, ΔH^*, ΔS^* and ΔG^* values of the steroids are given in Table 3.

Table 3 Kinetic and thermodynamic properties of the steroids, calculated at T_{max}

Steroid	T_{max}, °C	k, s^{-1}	Zx10^{-7}, s^{-1}	ΔH^*, kJ mol^{-1}	ΔS^* Jmol^{-1} K^{-1}	ΔG^* kJ mol^{-1}
A1	347	0.210	0.03	68.2	–154.1	163.7
A2	323	0.282	0.77	79.1	–127.2	155.7
A3	298	0.335	6.39	85.8	–109.2	148.2
A4	328	0.307	126.40	105.7	–84.8	156.6
A5	332	0.280	21.45	99.4	–99.6	159.7
A6	325	0.315	37.66	99.0	–94.8	155.7
A7	323	0.208	0.03	65.0	–154.7	157.2
E1	345	0.285	0.02	62.7	–160.0	161.6
E2	385	0.270	0.47	85.7	–132.1	172.7
P	336	0.315	0.25	75.3	–136.8	158.7
C	355	0.307	201.45	112.8	–81.3	168.9

The ΔH^* values give the same kinetic thermal stability sequence as the E_a values. The ΔS^* values are negative and this suggests a high ordering of the transition state. No matter how weak the bonds are in the transition state, there will be a net loss in freedom of motion when translations and rotations become vibrations. The energy levels of the complex will be more widely spaced, and the entropy of the complex will be less than that of the two reagent molecules of steroids. The ΔG^* values are positive and this suggests that the formation of activated complex molecules does not proceed spontaneously.

References

1 E. S. Freeman and B. Carroll, J. Phys. Chem., 62 (1958) 394.
2 A. Jeres, J. Thermal Anal., 26 (1983) 315.
3 W. W. Wendlandt, Thermal Methods of Analysis, John Wiley and Sons, New York, 1974.
4 YA. Gerasimov, ed., Physical Chemistry, Mir Publishers, Moscow, 1985.

5 W. Klyne, The Chemistry of Steroids, John Wiley and Sons, New York, 1965.

Zusammenfassung – Ausgehend von TG- und DTG-Kurven wurden mittels des Freeman-Carroll- und des Jeres-Verfahrens die kinetischen Grössen der thermischen Zersetzung einiger Steroide berechnet. Das Jeres-Verfahren ergibt reellere berechnete Werte für n und E_a. Die kinetische thermische Stabilität der einfachen funktionellen Gruppen von Steroiden wurde miteinander verglichen und auf der Grundlage der E_a-Werte nach Jeres folgende Reihenfolge aufgestellt: 17β-OH > 17-Oktyl > 17-Ac–CHO > 17-Keto; 3β-OH > 3-Keto > 3α-OH; 5α-H > 5β-H > $\Delta^{5(6)}$ > Δ^4. Werte für k, Z, ΔH^*, ΔS^* und ΔG^* wurden auf der Basis der Werte nach Jeres für die Temperaturen der grössten Zersetzungsgeschwindigkeit berechnet. ΔS^*-Werte tragen negatives Vorzeichen und deuten auf eine grosse Geordnetheit des Übergangszustandes hin. Wie erwartet waren Werte für ΔH^* und ΔG^* positiv.