THERMAL AND KINETIC STUDIES ON THE STABILITY OF SOME UREIDO-SULFON-AMIDE DERIVATIVES
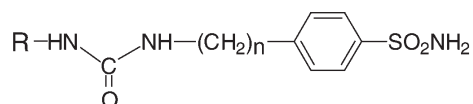
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Abstract

The kinetic and thermal behaviour of the following compounds:

$$R-HN-\underset{\underset{O}{\|}}{C}-NH-(CH_2)_n-C_6H_4-SO_2NH_2$$

where R=3,4-dichlorophenyl, phenyl, cyclohexyl; n=0, 1, 2 were studied by TG and DTA techniques.

The compounds decompose in many steps; the last one corresponding to the burning of $H_2N-S-C_6H_4-C_6H_4-S-NH_2$ occurs with comparable reaction rates.

Keywords: non-isothermal kinetics, thermal decomposition, ureido-sulfonamide derivatives

Introduction

The potential chemotherapeutic properties shown by some sulfonamide molecules are increased by complexation with transition ions [1, 2].

Thermal analysis is an appropriate method to characterize this type of complexes, but first it is necessary to elucidate the thermal behaviour of uncomplexed potential ligands. In order to augment the chemical information concerning thermal behaviour of this class of organic solids, our laboratory initiates a study of these compounds, the present paper being the second of this research project.

Thus, we describe both a thermal study on the stability of some ureido-sulfonamides and a kinetic study of some singular steps of decomposition.

Experimental

Apparatus

The heating curves were recorded in static air atmosphere using a Q-1500D (Paulik, Paulik, Erdey) – MOM Budapest, derivatograph in the temperature range 25–800°C at various heating rates (β) between 2.5 and 5 K min^{-1}. DTA curves were recorded using Al_2O_3 as reference compound. Amounts of 90-100 mg of substance were used for the analysis. Experimental data were processed with the computer program VERSA-TILE [3, 4]. Kinetic parameter values were obtained using the integral methods Coats–Redfern [5], Flynn–Wall for constant heating rate [6, 7] and Coats–Redfern modified by Urbanovici and Segal [8].

Samples

The following compounds of the general formula:

R—HN—C(=O)—NH—(CH$_2$)$_n$—⟨phenyl⟩—SO$_2$NH$_2$
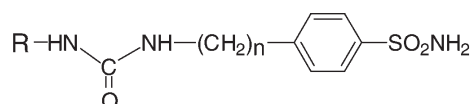
listed in Table 1 were used.

Table 1 List of the investigated compounds

Nr	R	n	Name
1	3,4-Dichlorophenyl	0	N-(4-aminosulfonylphenyl)-N'-3,4-dichlorophenyl-urea
2	3,4-Dichlorophenyl	1	N-(4-aminosulfonylphenylmethyl)-N'-3,4-dichlorophenyl-urea
3	3,4-Dichlorophenyl	2	N-(4-aminosulfonylphenylethyl)-N'-3,4-dichlorophenyl-urea
4	Phenyl	0	N-(4-aminosulfonylphenyl)-N'-phenyl-urea
5	Phenyl	1	N-(4-aminosulfonylphenylmethyl)-N'-phenyl-urea
6	Phenyl	2	N-(4-aminosulfonylphenylethyl)-N'-phenyl-urea
7	Cyclohexyl	0	N-(4-aminosulfonylphenyl)-N'-cyclohexyl-urea
8	Cyclohexyl	1	N-(4-aminosulfonylphenylmethyl)-N'-cyclohexyl-urea
9	Cyclohexyl	2	N-(4-aminosulfonylphenylethyl)-N'-cyclohexyl-urea

Synthesis and structural characterization of these compounds were reported in a previous paper [1].

Results and discussions

N-(4-Aminosulfonylphenyl)-N'-3,4-dichlorophenyl-urea (β=5 K min^{-1})

TG curve shows that the decomposition process begins in solid state, before melting (255–257°C).
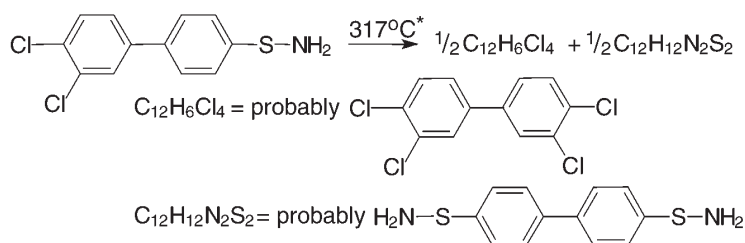
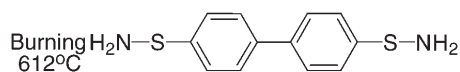There are 3 decomposition steps, which can be assigned to the following reactions, according to their mass loss:

I.
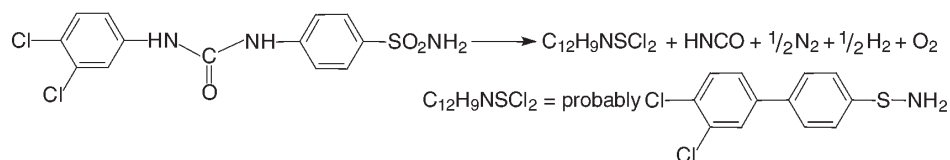
In this step, the mass loss is: $\Delta m_{exp.}=24.3\%$; $\Delta m_{calc.}=25.0\%$

II.

Mass loss: $\Delta m_{exp.}=39.4\%$; $\Delta m_{calc.}=40.6\%$

III.

Mass loss: $\Delta m_{exp.}=34.3\%$; $\Delta m_{calc.}=34.4\%$

The calculated kinetic parameters for this last step, representing the burning of the fragment described above are:

Table 2 Kinetic parameter values for the IIIrd step of decomposition of N-(4-aminosulfonyl-phenyl)-N'-3,4-dichlorophenyl-urea
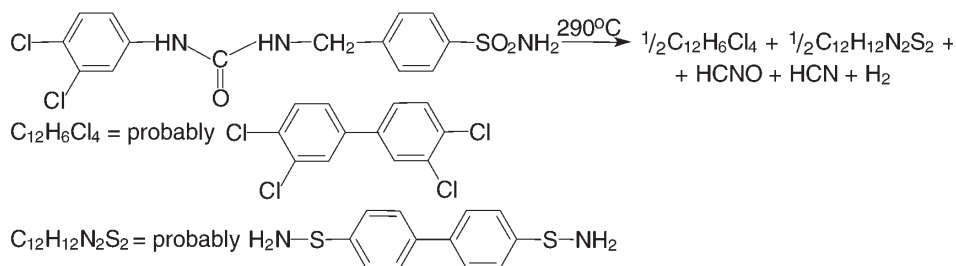
Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$1.75 \cdot 10^6$	$5.91 \cdot 10^6$	$3.86 \cdot 10^7$
Activation energy/kJ mol^{-1}	136.3	141.9	139.6
Reaction order	1.2	1.2	1.2
Correlation coefficient	−0.9866	−0.9889	−0.9864

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*   All temperatures indicated on the arrows correspond to the maximum reaction rate

N-(4-aminosulfonylphenylmethyl)-N'-3,4-dichlorophenyl-urea ($\beta=5$ K min^{-1})

Decomposition process starts before melting (212–214°C):

I.

$$C_{12}H_6Cl_4 = \text{probably}$$

$$C_{12}H_{12}N_2S_2 = \text{probably}$$

Mass loss: $\Delta m_{\text{exp.}}=64.9\%$, $\Delta m_{\text{calc.}}=66.8\%$
Kinetic parameter values for this step are:

Table 3 Kinetic parameter values for the Ist step of decomposition of N-(4-aminosulfonyl-phenylmethyl)-N'-3,4-dichlorophenyl-urea

Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$3.86 \cdot 10^7$	$4.15 \cdot 10^7$	$2.19 \cdot 10^7$
Activation energy/kJ mol^{-1}	108.1	107.7	105.5
Reaction order	2.0	1.9	1.9
Correlation coefficient	−0.9863	−0.9883	−0.9866

II.
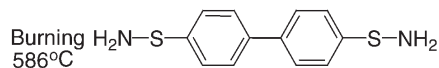
Mass loss: $\Delta m_{\text{exp.}}=32.5\%$; $\Delta m^{\text{calc.}}=33.2\%$
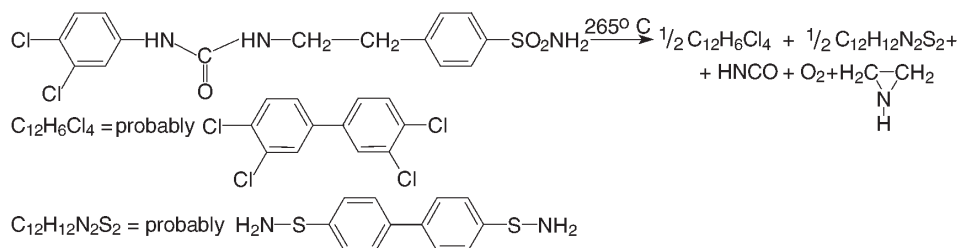For this last step, the burning, kinetic parameter values are:

Table 4 Kinetic parameter values for the IInd step of decomposition of N-(4-aminosulfonyl-phenylmethyl)-N'-3,4-dichlorophenyl-urea

Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$2.79 \cdot 10^3$	$1.75 \cdot 10^4$	$1.02 \cdot 10^4$
Activation energy/kJ mol^{-1}	106.8	114.9	114.2
Reaction order	1.1	1.1	1.2
Correlation coefficient	−0.99401	−0.9954	−0.98408

N-(4-aminosulfonylphenylethyl)-N'-3,4-dichlorophenyl-urea (β=5 K min⁻¹)

In this case, the process of decomposition starts before melting (200–202°C):

I.

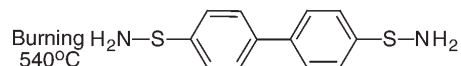Mass loss: $\Delta m_{exp.}$=69.2%; $\Delta m_{calc.}$=68.0%
Kinetic parameter values for this step are:

Table 5 Kinetic parameter values for the Iˢᵗ step of decomposition of N-(4-aminosulfonyl-phenylethyl)-N'-3,4-dichlorophenyl-urea

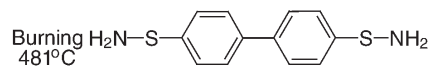| Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s⁻¹	$2.46 \cdot 10^5$	$5.24 \cdot 10^5$	$1.64 \cdot 10^5$
Activation energy/kJ mol⁻¹	83.3	84.9	81.5
Reaction order	1.9	1.8	1.8
Correlation coefficient	–0.99698	–0.9976	–0.99703

II.

Mass loss: $\Delta m_{exp.}$=30.8%; $\Delta m_{calc.}$=32.0%
For this last step, kinetic parameter values are:

Table 6 Kinetic parameter values for the IIⁿᵈ step of decomposition of N-(4-aminosulfonyl-phenylethyl)-N'-3,4-dichlorophenyl-urea

Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s⁻¹	$2.99 \cdot 10^4$	$1.37 \cdot 10^5$	$1.09 \cdot 10^5$
Activation energy/kJ mol⁻¹	113.6	120.1	120.6
Reaction order	0.5	0.5	0.6
Correlation coefficient	–0.9915	–0.9932	–0.9920

N-(4-aminosulfonylphenyl)-N'-phenyl-urea (β=2.5 K min^{-1})

For this compound, decomposition begins in solid state, before melting (227–229°C). The only interpretable decomposition step is the last one, which represents the burning of the H_2N–C_6H_4–C_6H_4–NH_2 fragment, as the other compounds presented:

Mass loss: $\Delta m_{exp.}$=41.9%; $\Delta m_{calc.}$=42.6%
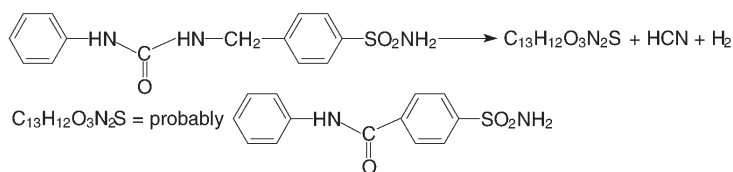Kinetic parameter values for the burning reaction are:

Table 7 Kinetic parameter values for the last step of decomposition of N-(4-aminosulfonyl-phenyl)-N'-phenyl-urea

| Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$8.19 \cdot 10^4$	$1.58 \cdot 10^5$	$1.36 \cdot 10^5$
Activation energy/kJ mol^{-1}	111.4	113.0	113.7
Reaction order	1.0	0.9	1.0
Correlation coefficient	−0.9858	−0.9885	−0.9861

N-(4-aminosulfonylphenylmethyl)-N'-phenyl-urea (β=5 K min^{-1})

The decomposition process starts in solid state; during melting (210–212°C) the reaction rate decreases probably due to a local cooling process because of the endothermic effect of melting. The amount of compound decomposed in solid state represents only 2.6% of the total amount. Between the steps I, II and III the TG curve shows no distinct separation regions, the following decomposition reaction starting before the end of the previous one. That is the reason for processes I, II and III will be presented globally:
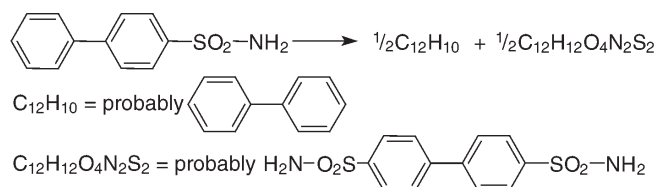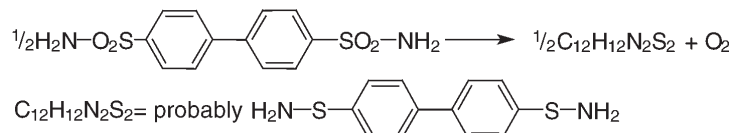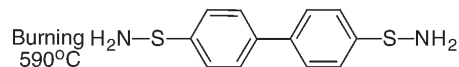
I.

II.

III.

$$C_{12}H_{10} = \text{probably}$$

$$C_{12}H_{12}O_4N_2S_2 = \text{probably } H_2N{-}O_2S{-}\text{...}{-}SO_2{-}NH_2$$
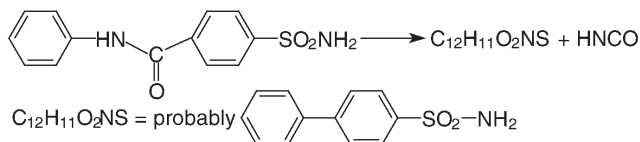
Globally for the steps I, II and III:
Mass loss: $\Delta m_{exp.}=51.4\%$; $\Delta m_{calc.}=48.9\%$

IV.

$$C_{12}H_{12}N_2S_2 = \text{probably } H_2N{-}S{-}\text{...}{-}S{-}NH_2$$

Mass loss: $\Delta m_{exp.}=10.8\%$; $\Delta m_{calc.}=10.5\%$

V.

Mass loss: $\Delta m_{exp.}=38.8\%$; $\Delta m_{calc.}=40.7\%$
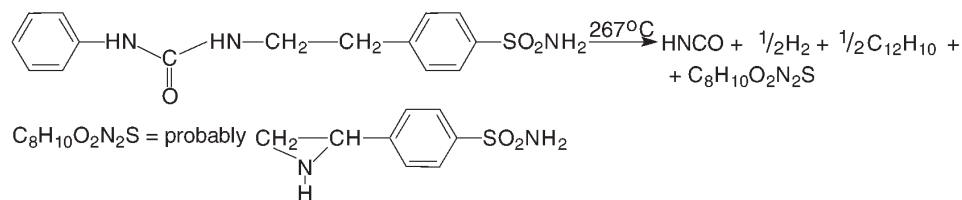Kinetic parameter values, for this last step, are:

Table 8 Kinetic parameter values for the Vth step of decomposition of N-(4-aminosulfonyl-phenylmethyl)-N'-phenyl-urea

Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$2.96 \cdot 10^4$	$1.32 \cdot 10^5$	$4.62 \cdot 10^4$
Activation energy/kJ mol^{-1}	120.6	127.4	122.9
Reaction order	0.8	0.8	0.8
Correlation coefficient	–0.9956	–0.9964	–0.9957

N-(4-aminosulfonylphenylethyl)-N'-phenyl-urea ($\beta=2.5$ K min^{-1})

The decomposition process starts in solid state; during melting (202–203°C) the reaction rate decreases probably due to a local cooling process because of the endothermic effect of melting. The amount of compound decomposed in solid state represents only 2.1% of the total amount. This led to the evaluation of the kinetic parameter values for the liquid state decomposition process.
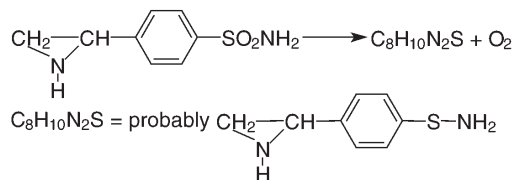
I.

Mass loss: $\Delta m_{exp.}$=36.1%; $\Delta m_{calc.}$=37.2%
Kinetic parameter values are:

Table 9 Kinetic parameter values for the Ist step of decomposition of N-(4-aminosulfonyl-phenylethyl)-N'-phenyl-urea

Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$2.93 \cdot 10^{10}$	$4.69 \cdot 10^{10}$	$4.28 \cdot 10^{10}$
Activation energy/kJ mol^{-1}	134.6	136.3	136.0
Reaction order	1.8	1.8	1.8
Correlation coefficient	–0.98461	–0.9864	–0.98463

II.

Mass loss: $\Delta m_{exp.}$=10.5%; $\Delta m_{calc.}$=10.0%

III.

Mass loss: $\Delta m_{exp.}$=13.6%; $\Delta m_{calc.}$=13.2%

IV.

Burning H$_2$N—S———————————————S—NH$_2$
546°C

Mass loss: $\Delta m_{exp.}$=39.8%; $\Delta m_{calc.}$=38.9%

For this last step, representing the burning of the fragment described above, the kinetic parameter values are:

Table 10 Kinetic parameter values for the IVth step of decomposition of N-(4-aminosulfonyl-phenylethyl)-N'-phenyl-urea
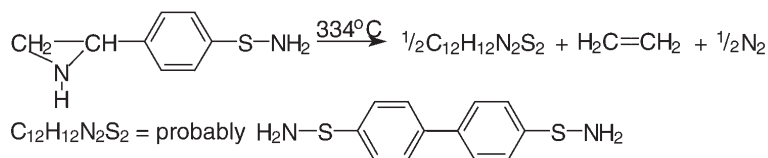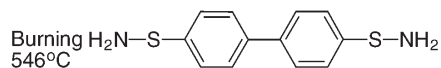
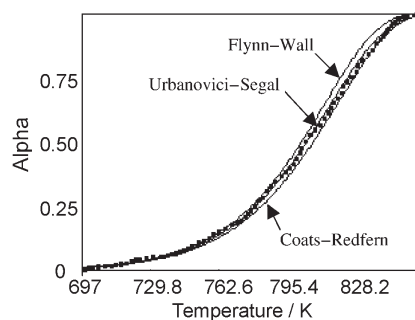| Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$4.4 \cdot 10^7$	$1 \cdot 10^8$	$1.5 \cdot 10^8$
Activation energy/kJ mol^{-1}	165.4	169.5	172.4
Reaction order	0.8	0.8	0.9
Correlation coefficient	−0.9980	−0.9983	−0.9979

Fig. 1 Superposition of simulated curves (Coats–Redfern, Flynn–Wall and Urbanovici–Segal) with the experimental points for the IVth step of decomposition of (4-aminosulfonylphenylethyl)-N'-phenyl-urea

N-(4-aminosulfonylphenyl)-N'-cyclohexyl-urea (β=5 K min^{-1})

Decomposition process starts in solid state, before melting (223–225°C):

I.

C$_7$H$_9$O$_3$N$_3$S = probably H$_2$N—C—NH———SO$_2$NH$_2$
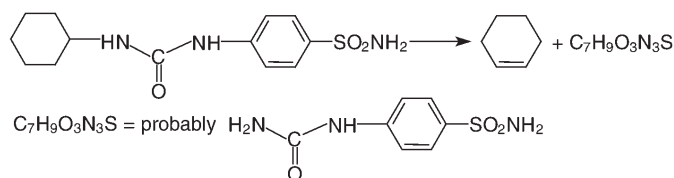
Mass loss: $\Delta m_{exp.}$=27.2%; $\Delta m_{calc.}$=27.6%

II.
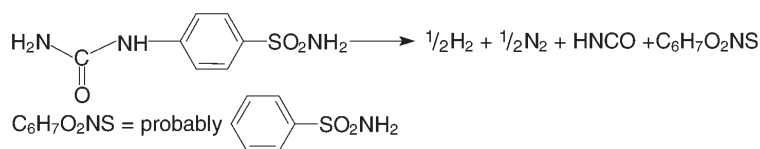
Mass loss: $\Delta m_{exp.} = 18.7\%$; $\Delta m_{calc.} = 19.5\%$

III.
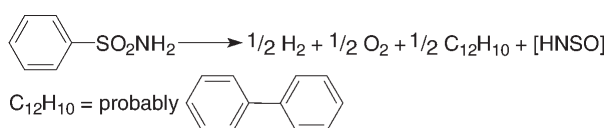
Mass loss: $\Delta m_{exp.} = 31.1\%$; $\Delta m_{calc.} = 31.6\%$

IV.

This step consists in the burning of a hypothetical fragment, [HNSO], (molecular mass close to 63)

Burning[HNSO]
579°C

Mass loss: $\Delta m_{exp.} = 21.0\%$; $\Delta m_{calc.} = 21.2\%$

For this last step, representing the burning of the fragment described above, the kinetic parameter values are:

Table 11 Kinetic parameter values for the IVth step of decomposition of N-(4-aminosulfonyl-phenyl)-N'-cyclohexyl-urea

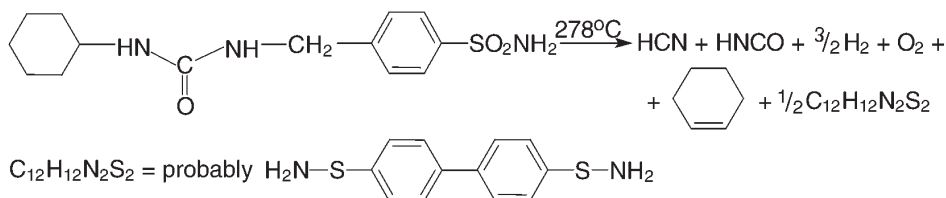| Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$1.69 \cdot 10^4$	$3.98 \cdot 10^4$	$2.67 \cdot 10^4$
Activation energy/kJ mol^{-1}	112.6	114.9	114.8
Reaction order	1.1	1.0	1.1
Correlation coefficient	−0.9942	−0.9955	−0.9942

N-(4-aminosulfonylphenylmethyl)-N'-cyclohexyl-urea ($\beta = 5$ K min^{-1})

Similarly to the compound 6, the decomposition process starts in solid state; during melting (202–203°C) the reaction rate decreases probably due to a local cooling process because of the endothermic effect of melting. The amount of compound decomposed in solid state represents only 0.8% of the total amount. This led to the evaluation of the kinetic parameter values for the liquid state decomposition process.

I.

$C_{12}H_{12}N_2S_2$ = probably [structure shown]

Mass loss: $\Delta m_{exp.}$=60.3%; $\Delta m_{calc.}$=60.1%
Kinetic parameter values are:

Table 12 Kinetic parameter values for the Ist step of decomposition of N-(4-aminosulfonyl-phenylmethyl)-N'-cyclohexyl-urea

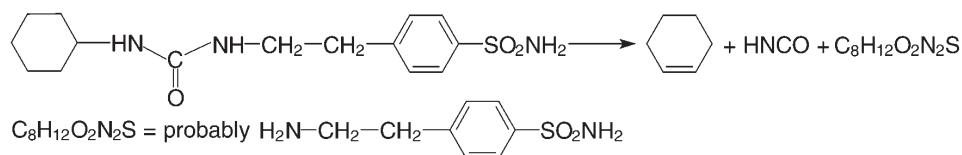| Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$1.55 \cdot 10^{13}$	$1.94 \cdot 10^{13}$	$2.13 \cdot 10^{13}$
Activation energy/kJ mol^{-1}	162.7	163.5	163.8
Reaction order	2.6	2.6	2.6
Correlation coefficient	−0.9894	−0.9905	−0.9897

II.
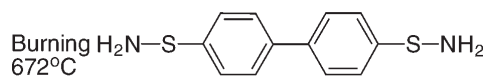
Mass loss: $\Delta m_{exp.}$=40.2%; $\Delta m_{calc.}$=39.9%
For this last step, kinetic parameter values are:

Table 13 Kinetic parameter values for the IInd step of decomposition of N-(4-aminosulfonyl-phenylmethyl)-N'-cyclohexyl-urea

Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	$7.53 \cdot 10^{1}$	$6.9 \cdot 10^{2}$	$1.2 \cdot 10^{2}$
Activation energy/kJ mol^{-1}	90.0	99.4	92.3
Reaction order	0.9	0.9	0.9
Correlation coefficient	−0.9969	−0.9977	−0.9968

N-(4-aminosulfonylphenylethyl)-N'-cyclohexyl-urea (β=2.5 K min^{-1})

The decomposition process starts in solid state; during the melting (211–212°C) the reaction rate decreases probably due to a local cooling process because of the endothermic effect of melting. The amount of compound decomposed in solid state represents only 2.6% of the total amount.

I.

C$_8$H$_{12}$O$_2$N$_2$S = probably H$_2$N–CH$_2$–CH$_2$—◯—SO$_2$NH$_2$

Mass loss: $\Delta m_{exp.}$=38.0%; $\Delta m_{calc.}$=38.5%

II.

H$_2$N–CH$_2$–CH$_2$—◯—SO$_2$NH$_2$ $\longrightarrow$ H$_2$C=CH$_2$ + C$_6$H$_8$O$_2$N$_2$S

C$_6$H$_8$O$_2$N$_2$S = probably H$_2$N—◯—SO$_2$NH$_2$

Mass loss: $\Delta m_{exp.}$=8.9%; $\Delta m_{calc.}$=8.6%

III.

H$_2$N—◯—SO$_2$NH$_2$ $\xrightarrow{336^\circ C}$ H$_2$ + N$_2$ + O$_2$ + $^1\!/_2$ C$_{12}$H$_{12}$N$_2$S$_2$

C$_{12}$H$_{12}$N$_2$S$_2$ = probably H$_2$N—S—◯—◯—S—NH$_2$

Mass loss: $\Delta m_{exp.}$=15.3%; $\Delta m_{calc.}$=14.8%

IV.

$\underset{569^\circ C}{\text{Burning}}$ H$_2$N—S—◯—◯—S—NH$_2$

Mass loss: $\Delta m_{exp.}$=37.4%; $\Delta m_{calc.}$=38.2%

For this last step, the kinetic parameter values are:

Table 14 Kinetic parameter values for the IVth step of decomposition of N-(4-aminosulfonyl-phenylethyl)-N'-cyclohexyl-urea
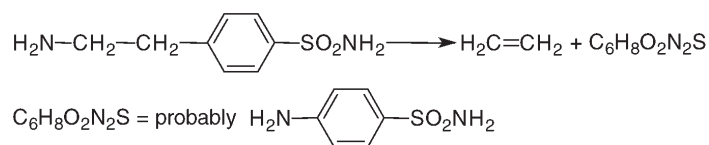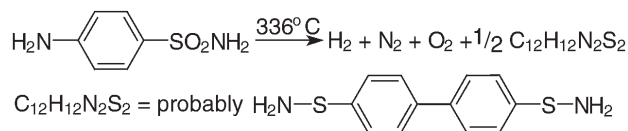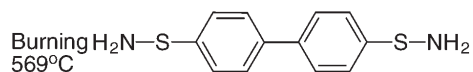
Method	Coats–Redfern	Flynn–Wall	Urbanovici–Segal
Preexponential factor/s^{-1}	5.57·10^9	9.2·10^9	7.7·10^9
Activation energy/kJ mol^{-1}	201.3	204.0	203.0
Reaction order	1.1	1.1	1.1
Correlation coefficient	–0.9932	–0.9940	–0.9931

The final steps, representing the burning of the $H_2N–S–C_6H_4–C_6H_4–S–NH_2$ fragment, occur smoothly in a relatively large temperature-range thus being kinetically workable. For these steps a compensation effect was observed between the values of the preexponential factor and the activation energy, the calculated values for the rate constant at 500°C exhibiting relatively close values:

Table 15 Kinetic parameter values for the steps that represent the burning of $H_2N–S–C_6H_4–C_6H_4–S–NH_2$: (Kinetic constants were calculated with the preexponential factors and the activation energies obtained by Coats–Redfern method)

Compound number	A/s^{-1}	$E_a/kJ\ mol^{-1}$	k_{773K}/s^{-1}	$\Delta G^*/kJ\ mol^{-1}$	$\Delta S^*/J\ mol^{-1}\ K^{-1}$
1	$1.753 \cdot 10^6$	136.268	$1.08 \cdot 10^{-3}$	222.721	–111.84
2	$2.794 \cdot 10^3$	106.796	$1.69 \cdot 10^{-4}$	250.310	–185.66
3	$2.992 \cdot 10^4$	113.564	$6.30 \cdot 10^{-4}$	241.493	–165.50
4	$8.190 \cdot 10^4$	111.377	$2.43 \cdot 10^{-3}$	233.170	–157.56
5	$2.963 \cdot 10^4$	120.646	$2.07 \cdot 10^{-4}$	249.276	–166.40
6	$4.397 \cdot 10^7$	165.412	$2.90 \cdot 10^{-4}$	246.866	–105.37
8	$7.526 \cdot 10^1$	90.026	$6.18 \cdot 10^{-5}$	256.940	–215.93
9	$5.571 \cdot 10^9$	201.292	$1.38 \cdot 10^{-4}$	252.132	–65.77

The close values of the k_{773} are probably due to the oxidation of the same molecular fragment namely $H_2N–S–C_6H_4–C_6H_4–S–NH_2$.

The values for the activation entropy were calculated considering the activation energy equal to the activation enthalpy.

The stranges negative values obtained for the activation entropy may be due to the structural ordering effect of O_2 on the burning reaction's transition state.

As in our previous paper [9], the proposed fragmentation schemes are in agreement with the following literature results:

Studying the thermal behavior of some copper-acetazolamide (5-acetamido-1,3,4-thiadiazole-2-sulfonamide) complexes, Ferrer *et al.* [10] shows that the ligand degradation occurs with the disparition of the IR absorptions of carbonyl and sulfonyl groups, and, for the final step, the sulfur from the copper sulfate originate not only from oxidation of the thiadiazole ring but also directly from the sulfonamido group.

Conclusions

Investigation on the thermal stability of some ureido-sulfonamide derivatives was carried out using a Q-1500D derivatograph.

The decomposition steps were established.

For the kinetically workable steps, the nonisothermal kinetic parameters were evaluated.

The values of the nonisothermal kinetic parameters obtained by the three integral methods are in a satisfactory agreement.

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