Thermochimica Acta, 178 (1991) 75–79
Elsevier Science Publishers B.V., Amsterdam

DECOMPOSITION KINETICS OF β-CYCLODEXTRIN AND INCLUSION COMPLEX OF β-CYCLODEXTRIN WITH IBUPROXAM, 2-(4-ISOBUTYLPHENYL)PROPIOHYDROXAMIC ACID

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(Received 19 June 1990)

ABSTRACT

The kinetics of the thermal decomposition of β-cyclodextrin and of the inclusion complex of β-cyclodextrin with ibuproxam have been studied by isothermal thermogravimetry between 250 and 275 °C. The isothermal curves of β-cyclodextrin and the inclusion complex up to mass losses of 58.1% and 62.0% respectively have been used in the kinetic calculations. The first half of the mass loss obeys nucleation mechanism A2 and the second half obeys a first order F1 mechanism. Activation energies have been calculated.

INTRODUCTION

Complexation of active substances with β-cyclodextrin is often used in pharmacy in order to increase the solubility of the drug and to improve its stability [1]. Determination of the stability of drugs can take several months; however, the use of thermal analysis can shorten this time significantly. Thermal decomposition of the pure substance and its inclusion complex usually takes place via different mechanisms and leads to different decomposition products [2]. The degradation of ibuproxam has already been studied by analysis of its decomposition products [3], as well as by isothermal kinetics [4]. In this work we studied the isothermal decomposition of β-cyclodextrin and its inclusion complex with ibuproxam.

EXPERIMENTAL

The isothermal weight changes were determined by means of a Mettler 2000C thermoanalyzer connected to a microcomputer for data storage. Experimental conditions were: platinum crucibles, sample weight 10.0 mg, heating rate to isothermal temperature 15 °C min^{-1}, atmosphere of dry air with 35 ml min^{-1} flow rate. The inclusion complex contained 14.0% of

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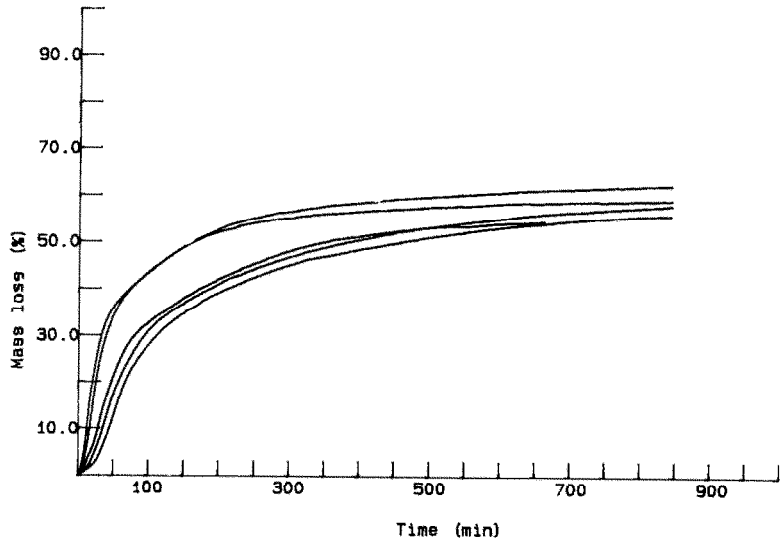

Fig. 1. Isothermal decomposition of β-cyclodextrin

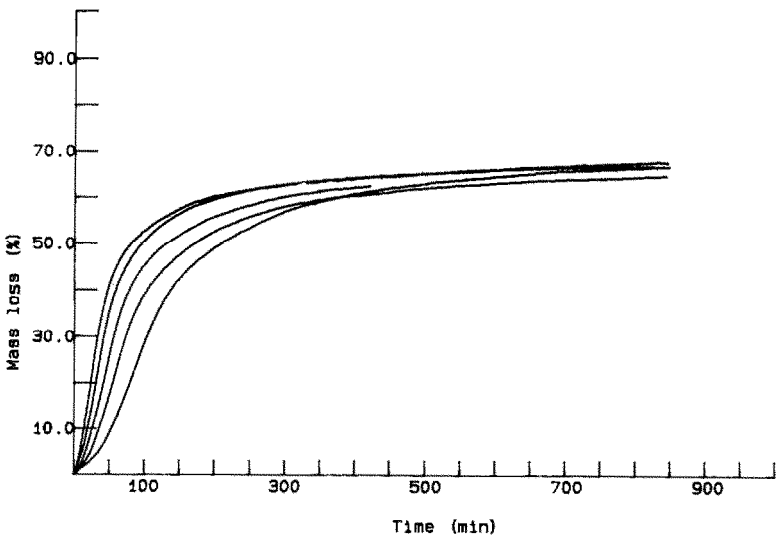

Fig. 2. Isothermal decompositon of inclusion complex

TABLE 1
Activation energies (kJ mol^{-1}) and correlation coefficients (in parentheses)

	β-Cyclodextrin	Inclusion complex
A2 mechanism	152 (0.955)	131 (0.999)
F1 mechanism	122 (0.921)	70 (0.841)

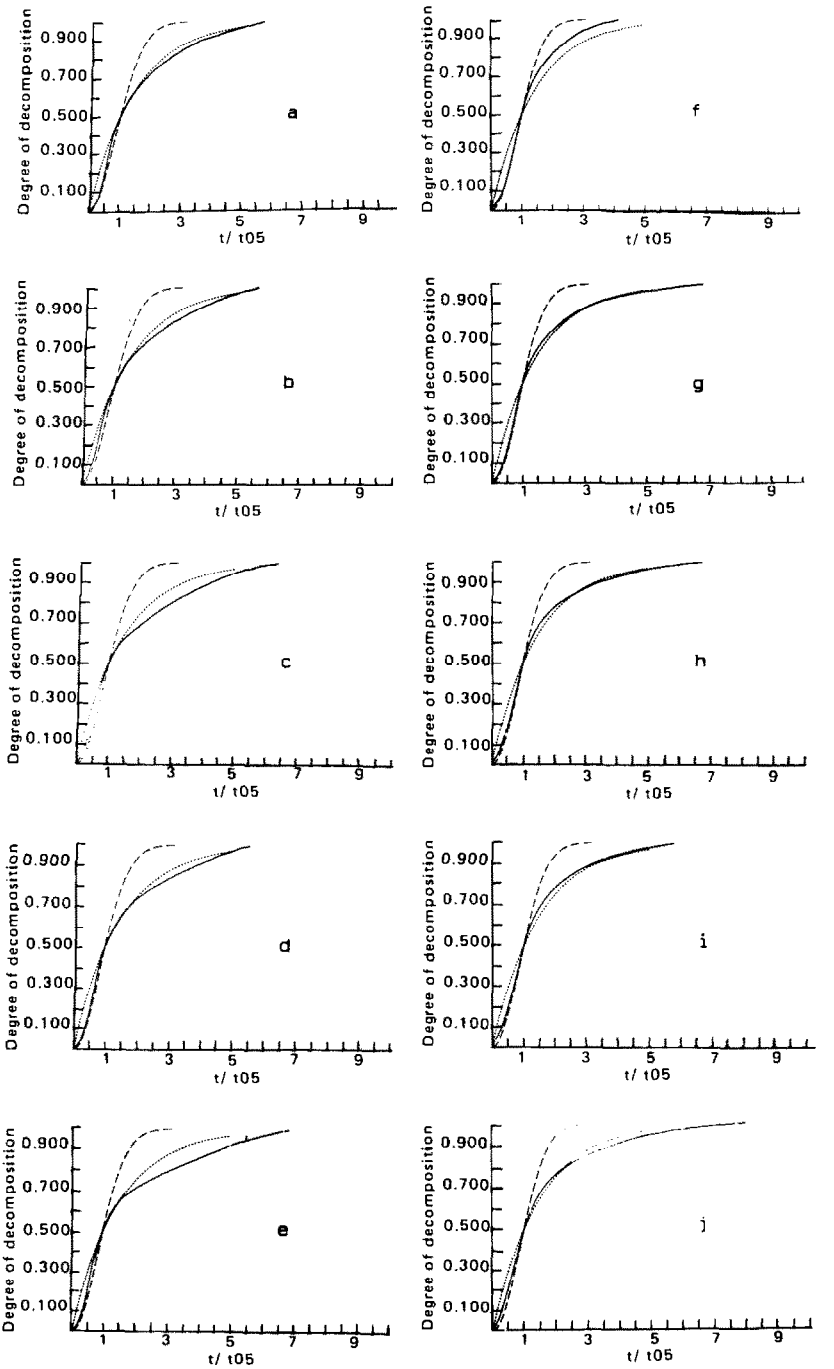

Fig. 3. $t/t_{0.5}$ test for the decompositon of β-cyclodextrin up to a mass loss of 58.1%: solid line, experimental curve; dashed line, A2; dotted line, F1 (a, 255 °C; b, 260 °C; c, 265 °C; d, 270 °C; e, 275 °C); and $t/t_{0.5}$ test for the decomposition of the inclusion complex up to a mass loss of 62.0%: solid line, experimental curve; dashed line, A2; dotted line, F1 (f, 250 °C; g, 255 °C; h, 260 °C; i, 265 °C; j, 270 °C).

ibuproxam. Pure β-cyclodextrin contained 12.0% of water, which was removed by heating the substance at 100 °C for 15 min before isothermal decomposition.

RESULTS

The kinetics of thermal decomposition of β-cyclodextrin and of the inclusion complex of β-cyclodextrin with ibuproxam were studied by isothermal weight changes between 250 and 275 °C (Figs. 1 and 2). In the first part of the isothermal TG curves (up to mass losses of 58.1% for β-cyclodextrin and 62.0% for the complex) the substances decompose at a decreasing rate, and in the second part they decompose at a constant rate, which is much lower than the first.

The mechanism of the first part of the isothermal TG curves was determined with a $t/t_{0.5}$ test [5]. It was not possible to fit the experimental curves with a single mechanism. For the first half, the best fit was obtained for nucleation controlled mechanism A2 [6], which is given by the Avrami equation I: $[-\ln(1-\alpha)]^{1/2} = kt$. The second half could also be described as a random nucleation controlled process, however with the equation $-\ln(1-\alpha) = kt$ (F1 mechanism), which proposes one nucleus on each particle (Fig. 3). The corresponding activation energies were calculated by means of an Arrhenius plot (Figs. 4 and 5) and are given in Table 1.

The rate-controlling processes for thermal decomposition of ibuproxam [4], β-cyclodextrin and their inclusion complex are different. For pharma-

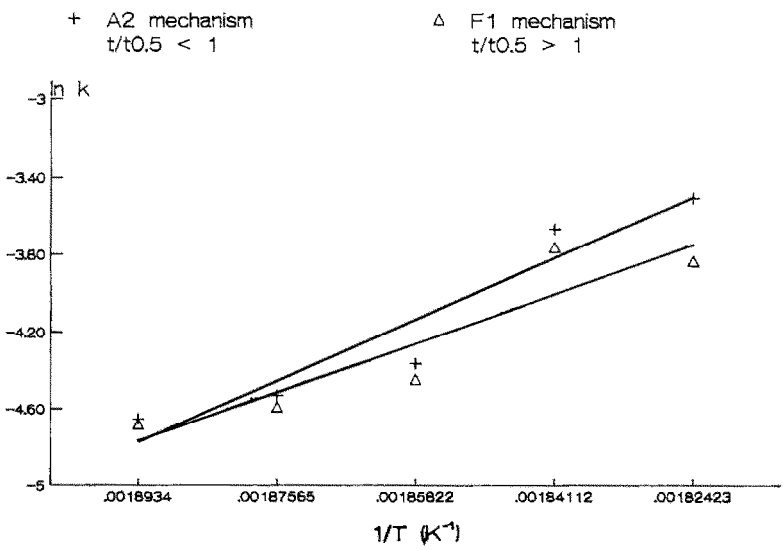

Fig. 4. Arrhenius plot for the decomposition of β-cyclodextrin up to a mass loss of 58.1%.

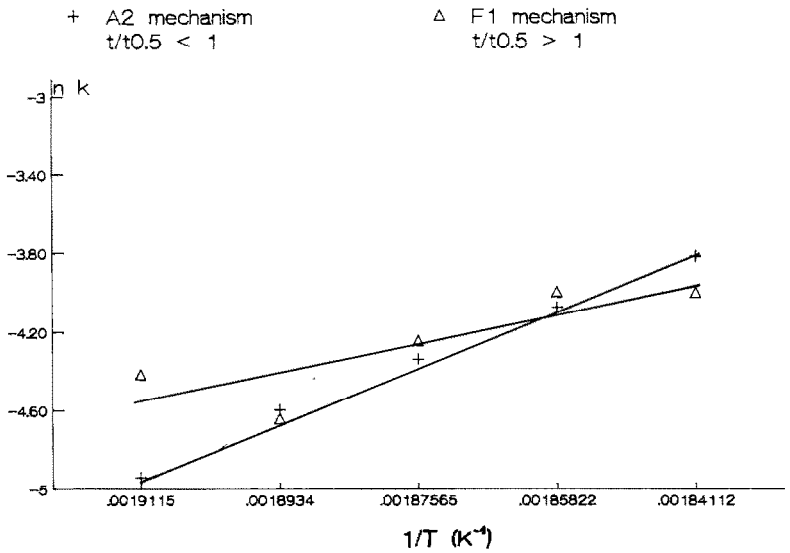

Fig. 5. Arrhenius plot for decomposition of the inclusion complex up to a mass loss of 62.0%.

ceutical technology, however, the stability of the active substance or its complex with the carrier is more important than the formal mechanism of the decomposition. Activation energies for the beginning of the decomposition of ibuproxam (43 kJ mol^{-1}), the inclusion complex (131 kJ mol^{-1}) and β-cyclodextrin (152 kJ mol^{-1}) show significantly enhanced stability for the active substance when bound to β-cyclodextrin.

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