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THERMAL BEHAVIOUR OF THE ANTICANCER DRUG CARBOXYETHYLGERMANIUM SESQUIOXIDE

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The thermal behaviour of carboxylethylgermanium sesquioxide (Ge–132) was studied by using DSC, TG and FTIR.

A crystalline-amorphous transition peak and a decomposition peak were observed below 320 °C. The conclusion drawn by Minoru Tsutsai that Ge–132 gave no indication of the decomposition or the melting below 320 °C has been proved not to be consistent with reality.

Carboxylethylgermanium sesquioxide (Ge–132), a new anticancer drug, is a white crystalline powder. It has the structural formula

$$\begin{array}{l} O=GeCH_2CH_2COOH \\ \quad\quad | \\ \quad\quad O \\ \quad\quad | \\ O=GeCH_2CH_2COOH \end{array}$$

Its function and structure have been studied, but research into its thermal behaviour has not gone further. Minoru Tsutsai reported that Ge–132 gave no indication of the decomposition or the melting below 320° [1].

The sample of Ge–132, a white crystalline powder, is insoluble in almost all organic solvents, but is soluble in water with a high dependency on PH. It was supplied by Pharmaceutical Institute of Guangzhou Military Area.

Asai discovered its favourable effects in the treatment of cancer, hypertension, etc. [2, 3]. Chang Ching-Te reported that its IR spectrum contained a strong absorption peak at 800–900 cm^{-1}, and its NMR spectrum gave three continuous peaks containing the same protons at 1.6 and 2.5 ppm [4]. Minoru Tsutsai observed a monoclinic form by means of X-ray diffraction [1].

In order to study its thermal behaviour, we have performed research work by using DSC, TG and FTIR.

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Experimental

DSC and TG experiments were carried out with a Perkin–Elmer DSC–2C instrument with a 3600 data station. The sample weighed ca. 10 mg. A heating rate of 10 deg/min was applied under N_2 protection. Indium was used to calibrate the temperature and enthalpy.

FTIR experiments were carried out with a Nicolet 170 SX FTIR instrument and a Perkin–Elmer heating device. The sample disk was made by the KBr disc technique. Put the sample disk in the heating device, and then put the heating device in the light path of FTIR to record. In situ IR spectra were recorded during heating at a rate of 10 deg/min. The IR spectrum was recorded at 30° intervals.

Results and discussion

1. Characteristics of endotherm A

When the original sample of Ge–132 was scanned by DSC–TG (Fig. 1), an endotherm (peak *A*) appeared between 153° and 199° in the DSC curve; the peak temperature was 181°. The enthalpy was 3.88 cal/g. The TG curve showed that the sample did not lose weight within the temperature range of peak *A*.

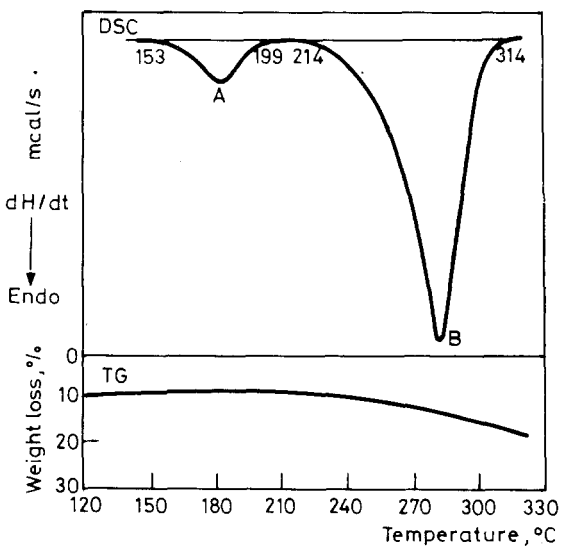

Fig. 1 DSC–TG curves of Ge–132

When the original sample was subjected to a heating scan by DSC up to 199° (the peak tail temperature of peak *A*), maintained there for 5 min (Fig. 2a), and then subjected to a cooling scan to room temperature, a cooling crystallization peak emerged (Fig. 2b); its temperature was 177° and the enthalpy was 3 cal/g. A heating scan on the cooled sample resulted in another peak, similar to peak *A*; its

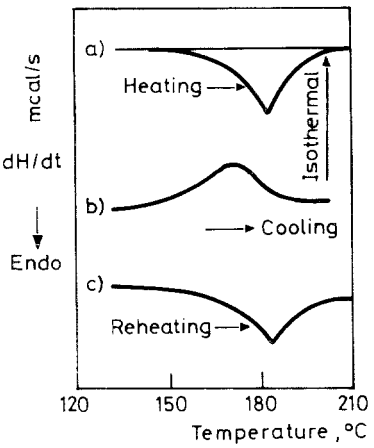

Fig. 2 Preliminary judgement on nature of endotherm *A*

temperature was 180.5°, and the enthalpy was 3.22 cal/g. This phenomenon indicates that peak *A* originated from either the melting or the crystal transition in the original sample. The original sample was observed under a melting point microscope up to 200° but it gave no sign of melting. This indicates that peak *A* is not a melting characteristic of the original sample.

The use of X-ray diffraction proved that Ge–132 has a monoclinic structure at room temperature.

The band characterizing the same structure was found in the IR spectrum. The IR spectrum of the original sample exhibited a moderately strong absorption peak at 733 cm^{-1} (Fig. 3a). The band related to swing and vibration of the CH_2 groups. On thermal treatment of the original sample with in situ recording of the IR spectrum, the strength of the 733 cm^{-1} band became progressively weaker with temperature rise (Fig. 3b–f). When the temperature rose to 210°, the 733 cm^{-1} band disappeared completely (Fig. 3g). This can be regarded as due to the gradual transformation of Ge–132 from monoclinic to amorphous glass in the course of the temperature rise. Consequently, the 733 cm^{-1} band appears to be characteristic of monoclinic Ge–132. When the solid-state hydrocarbon is heated, a 732 cm^{-1} band is observed. It is interesting that the 733 cm^{-1} band became stronger and the former situation was restored when the original sample was gradually cooled from 210° to

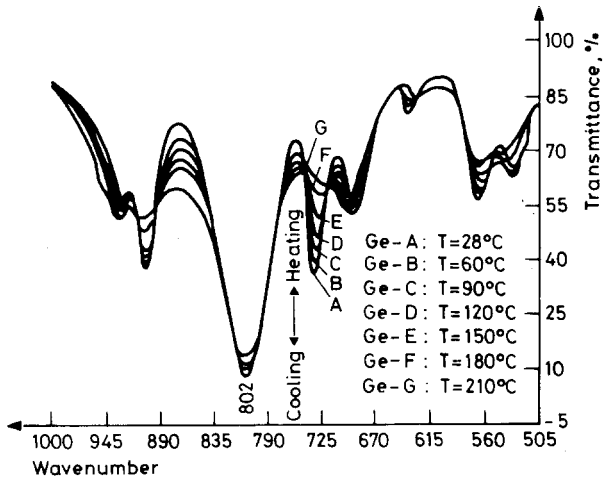

Fig. 3 Effect of thermal treatment on 733 cm^{-1} band

room temperature. This proved that the structure of Ge–132 was transformed from amorphous glass to monoclinic. The conclusion can therefore be drawn that endotherm *A* in the DSC curve is a crystalline-amorphous transition peak.

2. Characteristics of endotherm B

As shown in Fig. 1, endotherm *B* appeared between 214° and 314° in the DSC curve; the peak temperature was 275°. The enthalpy was 54.7 cal/g. The TG curve showed that the sample lost about 7% in weight within the temperature range of peak *B*.

In order to probe into the reason for the weight loss, the original sample was heated again to 314° by DSC, kept there for 5 min (Fig. 4a), then cooled to room temperature: no crystallization peak appeared (Fig. 4b); when the cooled sample was reheated, peaks *A* and *B* both disappeared (Fig. 4c). Thus, peak *B* can be preliminarily assumed to characterize the decomposition of the original sample.

In order to examine further the characteristics of peak *B*, two IR spectra of Ge–132 were recorded, one at 314°, and the other after keeping at 314° for 1 hr, then cooling to room temperature (Fig. 5b, c). The results indicated that the latter IR spectrum was completely different from that of the original Ge–132 sample (Fig. 5a). The structure of Ge–132 changed greatly when the original sample was heated to 314°: it decomposed into other substances. The FTIR experimental results led to the same conclusion as drawn from DSC. Accordingly, the findings by Minoru Tsutsai on the thermal properties of Ge–132 have been refuted.

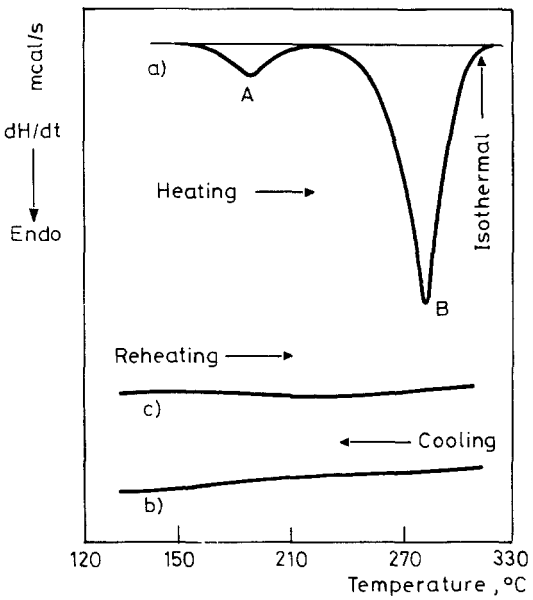

Fig. 4 Preliminary judgement about nature endotherm *B*

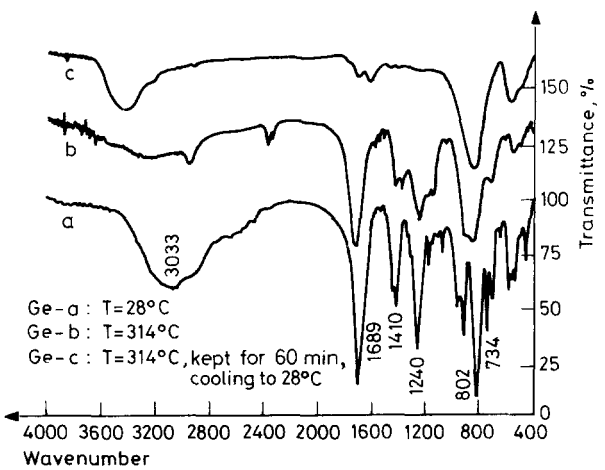

Fig. 5

Conclusion

The experimental results indicated that endotherm *A* in the DSC curve and the 733 cm^{-1} band in the FTIR spectrum characterize a crystalline-amorphous transition, while endotherm *B* characterizes sample decomposition. The initial decomposition temperature is 214°. Thus, the conclusions of Minoru Tsutsai concerning the thermal properties of Ge–132 have been refuted.

References

1 U. S. Patent 3, 689, 51b, K. Asai, Sept. 5 (1972).
2 U. S. Patent 3, 793, 455, K. Asai et al. Feb. 19 (1974).
3 E. P. Patent 0, 086, 569, Chang, Ching-Te, April. 22 (1983).
4 Minoru Tsutsai et al. J. Am. Chem. Soc., 98 (1976) 8, 8287.

Zusammenfassung — Mittels DSC, TG und FTIR wurde das thermische Verhalten von Karboxylethylgermaniumsesquioxid (Ge–32) untersucht. Unterhalb von 320 °C konnte ein Kristallphasenübergangs- und ein Zersetzungspeak beobachtet werden. Der Schluß von Minoru Tsutsai, namentlich daß Ge–132 unterhalb 320 °C keine Anzeichen von Zersetzung oder Schmelzen zeigt, wurde somit widerlegt.

Резюме — Методом ТГ, ДСК и инфракрасной фурье-спектроскопии изучено термическое поведение карбоксилэтилполуторной окиси германия (Ge–132). Ниже 320° на кривых наблюдается пик кристаллического перехода и пик разложения. Это противоречит заключению Минору Цуцаи о том, что Ge–132 ниже 320° не показывает пиков разложения и плавления.