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Note

A kinetic study of the solvolysis of 1,6-dibromo-1,6-dideoxygalactitol (Mitolactol)

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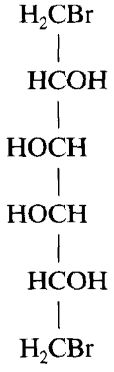
The active substance of the cytostatic agent Mitolactol, 1,6-dibromo-1,6-dideoxygalactitol (**1**), spontaneously undergoes solvolysis in solution, yielding 3,6-anhydro-1-bromo-1-deoxy-DL-galactitol (**2**) as a major product. Since **2** is biologically inactive, it is important to know the rate of this reaction in the metabolic pathway[1,2]. The solvent (protic or aprotic) appears to play no fundamental role in the ring closure of **1**: in the earlier work[1], methanol and water were used.



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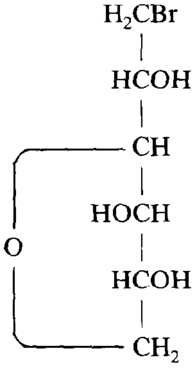

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The poor solubility of **1** in methanol and in water precluded kinetic measurements, therefore $(CD_3)_2SO$ was used. The solvolysis was monitored by ^{1}H-n.m.r. spectroscopy at 40° and 55°, and the reactions were followed to 67 and 73% conversion, respectively. The reaction co-ordinate was calculated by comparison of the integrated intensities of the n.m.r. peak for **2**, which appeared at 3.78 p.p.m., with that of the peaks at ~3.9 p.p.m. In the latter group of peaks, there was a vanishing 1-proton signal for **1** (3.92 p.p.m.) and increasing 1-proton signals for **2** (3.90 and 3.93 p.p.m.). The rate constants were obtained graphically by plotting $\log(1 - x) + 1$ *vs.* time (x is the reaction co-ordinate)[3]. The relationships were linear (correlation coefficients, $R = 0.9965$ and 0.9972, respectively), indicating that the reaction was first order (Fig. 1). The rate constants were $k_{313} = 4.56 \times 10^{-1}$ s^{-1} and $k_{328} = 1.398$ s^{-1}.

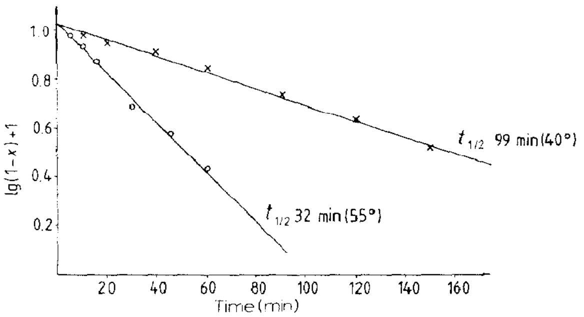

Fig. 1. Kinetic plots of the reaction **1**→**2** at 313 and 328 K.

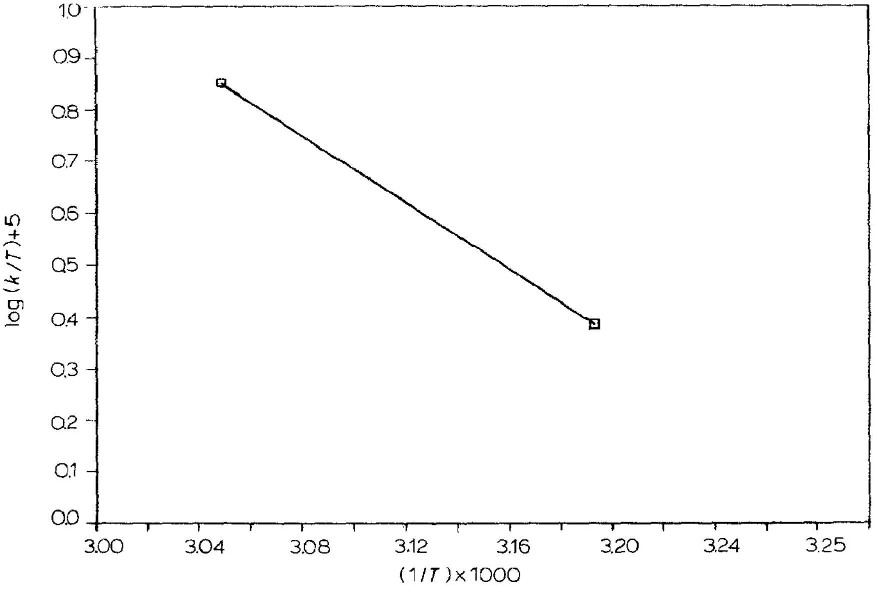

Fig. 2. Arrhenius plot of the reaction **1**→**2**.

However, this reaction could be a pseudo-first-order reaction. From the Arrhenius plot (Fig. 2), the energy of activation of the reaction[3] was obtained (E_A 63.6 kJ.mol^{-1}). The activation enthalpy ($\Delta H^{\ddagger}$ 61.1 kJ.mol^{-1}) and activation entropy ($\Delta S^{\ddagger}$ −64.9 J.deg^{-1}.mol^{-1}) were also calculated from the rate constants.

The relatively low thermodynamic activation parameters indicate that the reaction **1**→**2** can take place readily even at room temperature.

EXPERIMENTAL

The 400-MHz ^{1}H-n.m.r. spectra were recorded with a Varian XL-400 FT n.m.r. spectrometer (spectral width, 4000 Hz; pulse length, 6 μs; number of transients, 16).

REFERENCES

1 I. VIDRA, K. SIMON, L. INSTITÓRIS, I. CSÖREGH, AND M. CZUGLER, *Carbohydr. Res.*, 111 (1982) 41–57.
2 S. M. PULST, V. A. LEVIN, AND D. F. DEEN, *Pharm. Res.*, 3 (1986) 302–306.
3 K. SCHWETLICK, *Kinetische Methoden zur Untersuchung von Reaktionsmechanismen*, VEB Deutscher Verlag der Wissenschaften, Berlin, 1971.