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Unusual Competition of Intermolecular *vs.* Intramolecular Reactions. Kinetics of the Condensation of Decamethylpentasiloxane-1,9-diol

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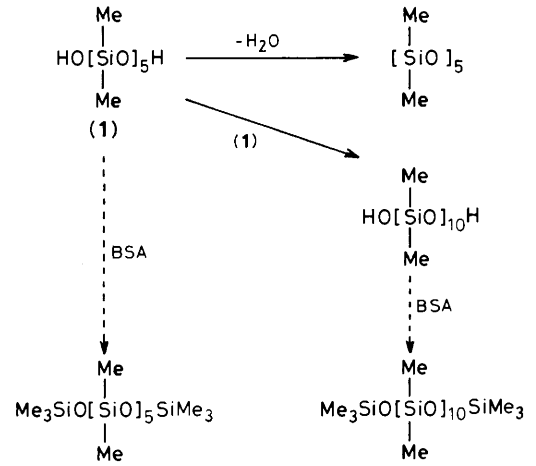
The assistance of a third functional group in the condensation of a bifunctional species may lead to the situation in which the competition of intramolecular *vs.* intermolecular reactions is not affected by the dilution of the system.

Competition between inter- and intra-molecular reactions of the same groups is very common in condensation processes of bifunctional compounds and it is often the major problem if cyclic or linear products need to be synthesized in high yield.[1—5] Considerable interest has been shown in the problem recently in connection with the synthesis of cyclic and macrocyclic natural and bioactive products, such as macrolides[1] and cyclic peptides,[2] as well as cyclic polydentate ligands like crown ethers,[3—5] cyclic amines, or cyclic sulphides.[5]

Since cyclisation is a unimolecular reaction while linear condensation is bimolecular, they should differ in order with respect to the substrate. A high dilution of the reaction system is generally thought to be the best way of directing the condensation towards cyclic products.[1—5] This method is often applied in synthetic procedures for the construction of macrocycles. It is therefore useful to demonstrate that acid–base interaction involving the substrate may strongly affect the relative rates of cyclisation and linear growth, which in some systems may become independent of the substrate concentration.

The kinetics of the condensation of decamethylpentasiloxane-1,9-diol (**1**) catalysed by strong acids ($MeSO_3H$



Scheme 1

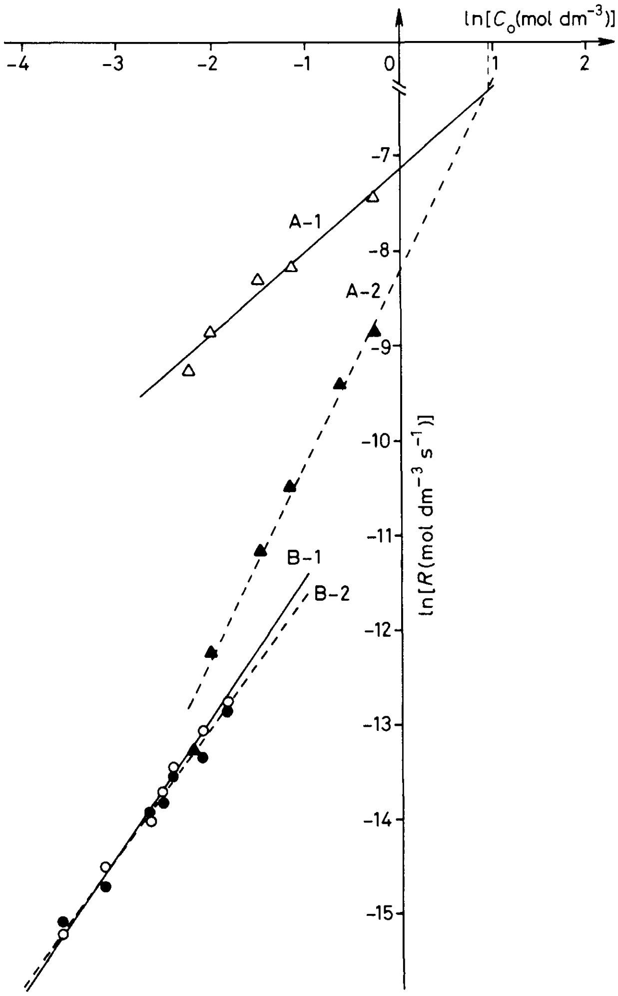


Figure 1. The dependence of the initial rate R of cyclisation (curves A-1, B-1) and linear growth (curves A-2, B-2) on the initial concentration of decamethylpentasiloxane-1,9-diol (C_0): A—dioxane, $[CF_3SO_3H]$ 5 × 10^{-4} mol dm^{-3}, 35 °C; B—methylene chloride, $[CH_3SO_3H]$ 5 × 10^{-4} mol dm^{-3}, 35 °C.

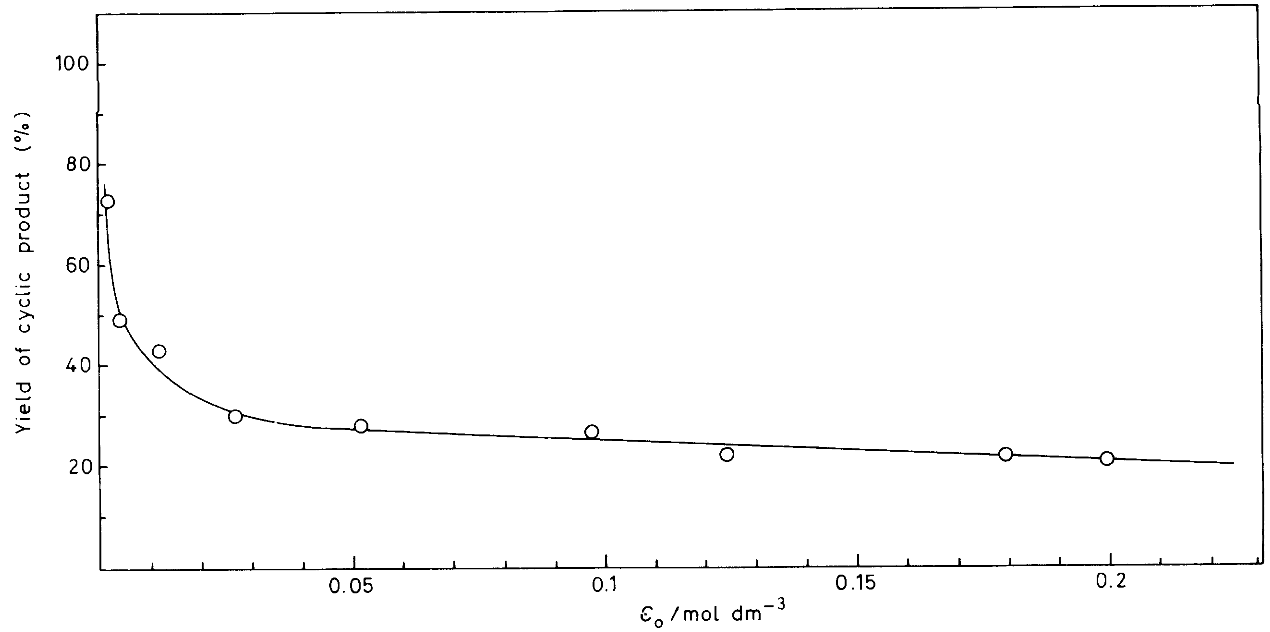
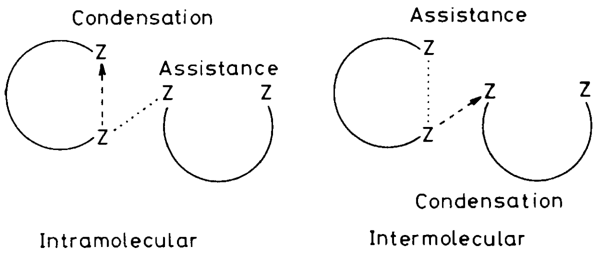


Figure 2. The dependence of the yield of the cyclic product on the initial diol concentration C_0 in the condensation of decamethylsiloxane-1,9-diol in methylene chloride in the presence of [CF_3SO_3H] 5 × 10^{-4} mol dm^{-3} at 35 °C.



Scheme 2

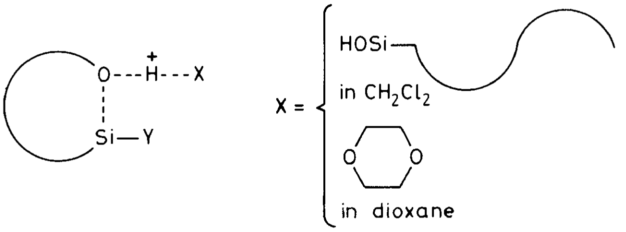


Figure 3. Y = OH_2^+ or OSO_2R (ref. 8).

and CF_3SO_3H) was compared in two non-hydroxylic non-polar solvents, dioxane and methylene chloride, in homogenous systems. The substrates, products, and catalysts dissolved rapidly and completely in both solvents under the experimental conditions. The formation of both products, cyclic decamethylcyclopentasiloxane and linear permethyldecasiloxane-1,19-diol, and the disappearance of the substrate were followed by g.l.c. Since the siloxanediols may undergo condensation during the g.l.c. analysis, the reaction system was quenched with bis(trimethylsilyl)acetamide (BSA) to convert quantitatively the hydroxy groups into trimethylsilyl ether groups (Scheme 1).

The kinetics were complicated by the presence of the water formed during the course of the reaction, thus the initial rates only were taken into consideration.

In dioxane the reaction shows classical cyclisation *vs.* linear growth competition exhibiting first order in the substrate for formation of the cyclic product and second order in the substrate for linear growth (Figure 1).

The effective concentration at which the rates of the competing reactions are equal was found to be 2.65 mol dm^{-3}. Thus, the system shows a considerable tendency towards cyclisation, which would be expected from the known thermodynamics of the polymerization of cyclic polydimethylsiloxanes.[6]

A different situation is encountered when the kinetics are studied in methylene chloride where the relative rates of formation of linear and cyclic products are virtually independent of the initial concentration of the substrate (Figure 1). Even at a diol concentration as low as 10^{-2} mol dm^{-3} a considerable amount of the linear product is formed [about 50% on a molar basis (Figure 2)] although under these conditions in dioxane the reaction results almost exclusively in ring formation.

Since the 10 membered siloxane ring formed is virtually free from strain[6] and since the distance between the end groups in the substrate is enough to exclude any possible through bond electronic effect, no difference between the mechanisms of cyclic and linear product formation would be expected.

The rate of linear condensation of (**1**) in CH_2Cl_2 was found to be almost 10^2 faster than the rate of condensation under the same conditions of its analogue with the same siloxane chain length and only one silanol group $Me_3Si[OSiMe_2]_4OH$. In dioxane the rates were approximately equal.

This behaviour may be explained by the assistance of a third functional group (Z) in the condensation in methylene chloride according to Scheme 2.

The assistance has general acid–base character. The condensation requires the withdrawal of the proton from the OH group attacking silicon. In dioxane this may be achieved by a solvent molecule, however methylene chloride is not able to enter an acid–base equilibrium and the proton can be stabilized only by the substrate itself. The silanol group is more basic than the siloxane chain[7] and consequently much more efficient in giving this assistance (Figure 3).

A sharp increase in the yield of the cyclic product is observed with increasing dilution below the initial diol concentration of 10^{-2} mol dm^{-3}. Evidently the intramolecular condensation, unassisted by other substrate molecules, is dominant in this region.

Therefore, improved conditions for cyclisation in acid–base catalysed condensation processes of bifunctional substrates may be achieved in solvents able to enter into acid–base equilibria.

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