Polyethyleneglycol-catalysed benzil–benzilic acid rearrangement: A reaction in soluble macromolecular cavities

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Abstract. Kinetics of benzil–benzilic acid rearrangement was investigated in the presence of polyethyleneglycols (PEG) at different concentrations. PEG of molecular weights 400 and 6000 were used for the studies. A set of solutions was prepared with varying PEG contents. The rearrangement was carried out in these systems and the rate constants were calculated. The rates surprisingly increased with PEG content instead of decreasing due to the reduced ionic movement in these viscous macromolecular solutions. In the presence of KOH and NaOH, PEG acts as a catalyst for the rearrangement. But in presence of LiOH, an inverse relation was observed between PEG content and the rate of reaction. These observations were explained on the basis of the cation-binding ability of polyethyleneglycols.

Keywords. Benzilic acid; cavities; macromolecules; rearrangement.

1. Introduction

The concept of 'cavity in solution' was put forward by Cramer in the 1950's during his work on inclusion compounds (Uekama *et al* 1978; Cramer 1981). Molecules of suitable size and geometry can be trapped in these organized cavities without any chemical bonding. The structure of inclusion compounds in the near vicinity of the entrapped molecules is exemplified by the structure of the solvents in the environment of an ion. A start in research of inclusion compounds was made around the 1960s and, following this, many papers relating to the synthesis and molecular transformation of diverse compounds which have excellent applications in the field of agriculture, pharmaceuticals and industry appeared in various journals (Pedersen 1967, 1970; Kopolow *et al* 1973; Takaki and Smid 1974). Crown ethers and cyclodextrins were widely used for these investigations. Polyethylene glycols were used for mimicking the typical inclusion compounds like cyclodextrins and crown polyethers (Sam and Simmons 1972; Lee and Freeman 1976; Lehmkuhl *et al* 1977; Balasubramanian *et al* 1979).

Investigations on benzil–benzilic acid rearrangements in PEG solutions of different concentrations and molecular weights are reported here. The substrates entrapped in the cavities of these macromolecular coils are less available to the ionic attacking species. This will retard the kinetics of the reaction. Thus the molecular movement can be controlled by varying the nature of the medium. This can be compared or

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contrasted to the restricted functional group availability with increasing crosslink density in crosslinked polymer systems.

2. Experimental

2.1   *Benzil–benzilic acid rearrangement in PEG-400 medium: General procedure*

Recrystallised benzil (5·25 g) was mixed with potassium hydroxide (1·4 g) or sodium hydroxide (1 g) or lithium hydroxide monohydrate (1·05 g) and absolute ethanol (30 ml). A definite volume of PEG-400 was pipetted out into the mixture and the total volume was made upto 100 ml using distilled water. The mixture was thoroughly shaken, 5 ml was withdrawn and titrated against HCl (0·1 N). The mixture was heated on a thermostat at 100°C. 5 ml of the reaction mixture was taken at different time intervals, added to crushed ice and titrated against HCl. Titrations were repeated. Rate constants were calculated according to the second-order rate equation.

2.2   *Benzil–benzilic acid rearrangement in PEG-6000 medium: General procedure*

Recrystallised benzil (5·25 g) was mixed with potassium hydroxide (1·4 g) or sodium hydroxide (1 g) or lithium hydroxide monohydrate (1·05 g) in absolute ethanol (30 ml) and PEG-6000 in the required ratio. Distilled water was added to make up the total volume to 100 ml. The mixture was thoroughly shaken to dissolve the PEG. Kinetics of the rearrangement was followed. Rate constants were calculated according to the second-order rate equation.

3. Results and discussion

Macromolecular solutions with different PEG contents were prepared in water–alcohol mixture and the viscosities of the solutions were measured using AVS-400 viscometer. Benzil was suspended in these systems and rearrangement condition was applied. All the reactions were carried out under identical conditions and the kinetics of the reactions were followed titrimetrically. Rate constants were calculated following the second-order rate equation for benzil–benzilic acid rearrangement.

Polyethyleneglycol with molecular weight 400 was selected for the preliminary investigations. 5, 10, 15 and 20% solutions of PEG-400 in water–ethanol mixture were prepared. Benzil and potassium hydroxide were added to the mixture and the progress of the reaction was followed titrimetrically. Rate constants were calculated according to the second order rate equation of benzil–benzilic acid rearrangement. The average rate constants were calculated and the results are presented in table 1.

It was expected that as the PEG concentration increased the rate of rearrangement would normally decrease, owing to the reduced freedom of movement of the ionic attacking species into the interior cavities of the macromolecular assemblies. Such a situation would create a partial inaccessibility of the rearranging system to the reagents. As the concentration of the medium increased, the freedom of movement of the anionic attacking species would decrease and consequently the inaccessibility would increase. This could be correlated to the increased rigidity with increased degree of crosslinking in heterogeneous polymeric systems with functional groups.

Table 1. Benzil–benzilic acid rearrangement in PEG-400 medium using KOH.

PEG concentration (%)	Average time of flow (s)	Viscosity of the medium $(\text{kg m}^{-1}\text{s}^{-1})$	Mean k $(\times 10^{-4}\,\text{mol/l})^{-1}$ (min^{-1})
0	18·55	1·86	1·79
5	21·14	2·12	2·59
10	23·92	2·39	3·27
15	27·17	2·72	4·23
20	30·18	3·02	4·67

Table 2. Benzil–benzilic acid rearrangement in PEG-6000 medium using KOH.

PEG concentration (%)	Average time of flow (s)	Viscosity of the medium $(\text{kg m}^{-1}\text{s}^{-1})$	Mean k $(\times 10^{-4}\,\text{mol/l})^{-1}$ (min^{-1})
0	18·55	1·86	1·78
5	33·39	3·34	2·82
10	58·75	5·89	3·72
15	90·33	9·06	4·89
20	130·28	13·00	5·63

In contrast to the expectation, however, the observed results show that the rate of rearrangement increases with increased concentration of the PEG medium. The rate constant of the control experiment was $1\cdot79 \times 10^{-4}(\text{mol/1})^{-1}\text{min}^{-1}$. A regular increase in rate constant was observed with increase in the PEG content and the mean k value for 20% PEG medium was $4\cdot07 \times 10^{-4}(\text{mol/1})^{-1}\text{min}^{-1}$.

The rearrangement was carried out in PEG-6000 solutions with varying PEG contents. Here also, the observed rate constants were directly related to the PEG concentration. The mean k value of the reaction for the 5% PEG solution was $2\cdot82 \times 10^{-4}(\text{mol/1})^{-1}\text{min}^{-1}$. For the 20% PEG-6000 medium, the mean k value was observed as $5\cdot63 \times 10^{-4}(\text{mol/1})^{-1}\text{min}^{-1}$ (table 2).

The cation-binding property of polyethylene glycol appears to be responsible for this unexpected result (Chan *et al* 1970; Pedersen and Frensdorff 1972; Sam and Simmons 1974). Due to the complexation of K^+ ions and hence the accumulation of anionic attacking species in the near vicinity of the migration origin, the rearrangement process is accelerated in the presence of PEG.

The cation-binding ability of polyethyleneglycols was further tested with Na^+ and Li^+ ions. The benzil-benzilic acid rearrangement was carried out in the presence of sodium hydroxide and lithium hydroxide in PEG-400 and PEG-6000 solutions with varying PEG concentrations. When sodium hydroxide is used as the reagent, a direct relation is obtained between the PEG concentration and speed of the reaction (table 3). Here also, the macromolecular system catalyses the rearrangement of α-diketone into α-hydroxy acid by the selective binding of the Na^+ ions and hence the accumulation of hydroxide ions around the reaction site. The attack of the hydroxide ion on the carbonyl carbon of the diketo group is thus facilitated. In contrast to the

Table 3. Benzil–benzilic acid rearrangement in PEG medium using NaOH.

PEG 400		PEG 6000	
PEG concentration (%)	Mean k $(\times 10^{-4} \text{mol/l})^{-1}$ (min^{-1})	PEG concentration (%)	Mean k $(\times 10^{-4} \text{mol/l})^{-1}$ (min^{-1})
0	1·7	0	1·7
5	1·9	5	2·0
10	2·4	10	2·8
15	3·1	15	3·5
20	4·0	20	4·9

Table 4. Benzil–benzilic acid rearrangement in PEG medium using LiOH.

PEG 400		PEG 6000	
PEG concentration (%)	Mean k $(\times 10^{-4} \text{mol/l})^{-1}$ (min^{-1})	PEG concentration (%)	Mean k $(\times 10^{-4} \text{mol/l})^{-1}$ (min^{-1})
0	1·7	0	1·8
5	1·5	5	1·8
10	1·4	10	1·5
15	1·1	15	1·3
20	1·1	20	1·0

above observations, PEG is not an efficient catalyst for the rearrangement of α-diketone into α-hydroxy acid when lithium hydroxide is used as the reagent. In this case, an inverse relation is observed between the PEG concentration and speed of the reaction (table 4). A small but notable decrease in rate constant is obtained with increased PEG content.

The size of the cavity of the macromolecular coils of polyethyleneglycols may be suitable for accommodating cations like K^+ and Na^+. Thus, complexation is equally efficient with these cations and thereby these catalyse the reaction in presence of KOH and NaOH. The Li^+ ion is comparatively small, and is not effectively entrapped in the cavities of PEG. Here the movement of hydroxide ion is hindered by viscous macromolecular medium and the speed of the reaction decreases.

Two simple model reactions were conducted to illustrate further the relation between molecular mobility and the rate of reaction. The hydrolysis and saponification of ethyl acetate were studied in presence of PEG-6000 solutions. A set of solutions was prepared with varying concentrations of PEG. The reactions were carried out in these systems and the rate constants were calculated. The kinetics of the hydrolysis of ethyl acetate was found to be inversely related to the concentration of PEG (figure 1). For the control experiment the observed rate constant was $6·06 \times 10^{-4} (\text{mol/l})^{-1}$ min^{-1} whereas the reaction in 20% PEG solution showed a k value $3·18 \times 10^{-4}$ $(\text{mol/l})^{-1} \text{min}^{-1}$. The increased concentration of PEG causes a decreased mobility of the substrate molecules which appears to be responsible for this phenomenon.
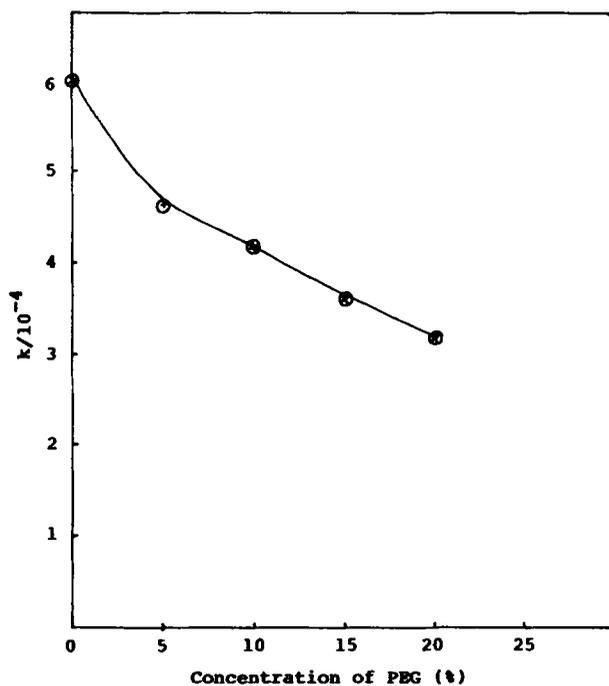
Figure 1. Effect of PEG concentration on the hydrolysis of ethyl acetate.
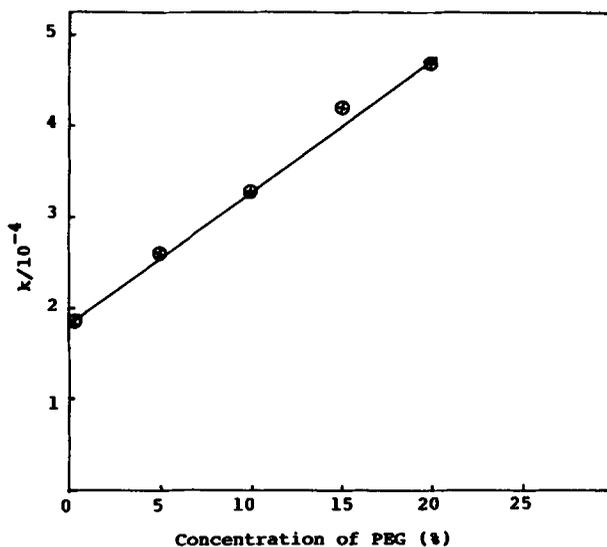

Figure 2. Effect of PEG concentration on the saponification of ethyl acetate.

A linear relationship is observed between the rate constant of the reaction and concentration of the medium in the case of the saponification of ethyl acetate in presence of PEG. For the control experiment the rate constant was 5.60×10^{-2} $(mol/1)^{-1} min^{-1}$ whereas the k value of the reaction in 20% PEG solution was

$11 \cdot 56 \times 10^{-2} (\text{mol}/1)^{-1} \text{min}^{-1}$ (figure 2). Here the sodium ions are complexed by PEG and hence the rate of the reaction gradually increases with PEG concentration.

4. Conclusions

Polyethyleneglycols are known to complex metal ions. This property brings the possibility of increased salt solubility and increased anion reactivity in organic solvents. PEG with molecular weights 400 and 6000 can complex with potassium ions and sodium ions, and thus facilitate the release of hydroxide ions. The selective cation-binding property of the polyethyleneglycols thus increases the mobility and reactivity of the anions. The benzil–benzilic acid rearrangement is usually effected by employing potassium hydroxide as the reagent. In presence of PEG, potassium ions are selectively complexed and more reactive, exposed anions are liberated. Due to the increased reactivity of the anions, the rate of the rearrangement increases. Polyethyleneglycols also act as catalysts for the benzilic acid rearrangement effected by NaOH. The cation-binding property and hence the increased reactivity of the reagent takes predominance over the constraints imposed by the viscous medium on the mobility of the anions. But PEG does not catalyse the reaction when lithium hydroxide is used as the reagent. This indicates that PEG can complex K^+ and Na^+ ions in an equally efficient way but cannot complex Li^+ ions effectively.

Acknowledgement

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