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VISCOSITY STUDIES ON MESTRANOL

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ABSTRACT:

The viscosity of $1x10^{-4}$M to $4x\ 10^{-4}$M solution of Mestranol (synthetic oestrogenic steroidal hormone) in ethanol was measured at 32^{o}, 40° and 50°C in a viscometric bath. The viscosity rates are maximum at 30°C as compared to 40^{o} and 50°C. The disappearance rate of Mestranol at higher temperature and lower viscosity is due to triplet state of species transitions at higher thermal conditions.

INTRODUCTION

Mestranol is a synthetic steroid oestrogen. Chemically, it is 17a-ethynyl-3-methoxycstra-1,3,5 (10)-trien-17β-ol. The steroid oestrogens are the most important group of these hormones and are related biologically to the natural human oestrogens i.e., oestrone, oestradiol and oestriol. These oestrogenic hormones are characterized by their effects on various female organs (Klimestra, 1969).

Mestranol as a synthetic oestrogen is medically used along with gestrogens as oral contraceptive purposes. In consequence, a large number of pharmaceutical preparations containing mestranol are available in the market by many manufacturers for clinical use. The essential contraceptive effects are attained by the use of progestin with Mestranol.

Mestranol metabolites *in vivo* into simple oestrone and oestradiol derivatives (Mahesh, V.B., 1977). Moreover its stability is affected by physico-chemical environments.

Mestranol like oestrogens are light and heat sensitive and decompose into various degradation products which are physiologically non-effective. Many workers studied the stability of oestrogens. e.g. oestrone (Fieser and Fieser, 1967), Mestranol and other oestrogens (Aulesa et al., 1981). Prista et al. (1972) and Fuerst et al. (1984) studied thermal decomposition of steroids and identified some degradation products along with some unidentified fractions. Thus, a study on factors affecting stability of the Mestranol is carried out which would be helpful for investigation of proper formulation.

EXPERIMENTAL SECTION

In order to obtain reliable data, considerable care was taken in the selection and purification of materials and in the experimental procedures for the flow time measurements of the solution during thermal degradation.

MATERIALS

Mestranol: Mestranol (ethynyl-estradiol-3-methylether anhydrous M.W. 310.4) was obtained from Sigma Chemical Co., St. Louis, USA. It was found to be chromatographically pure, Rf 0.86 (dichloromethane: ether: methanol: water, 77:15:8:1.2, v/v organic phase/silica gel G; Clark, 1986; Rf 0.86).

Ethanol: From Merck A.R. Grade. Double distilled prior to use.

Apparatus and Techniques:

Viscometer: Cannon Fenske Viscometer of capillary No. 100 (constant 0.01585) and German thermostat bath with ± 0.01°C accuracy were employed for flow time measurement at various temperatures.

The viscosity of $1x10^{-4}$M to $4x10^{-4}$M solutions of Mestranol in ethanol was measured at 32°, 40° and 50°C at different time intervals. The kinematic viscosity (V) is calculated as described elsewhere (Shamim, 1990).

RESULT AND DISCUSSION

Attempt was made to interpret the degradation of Mestranol through experimentation by viscosity determination. It is carried out for non-photolysed solutions of Mestranol at three temperatures and four different concentrations.

For Mestranol having concentration $1x10^{4}$M to 4x 10°M at temperatures 32°C to 50°C, the rate of viscosity decreases from $6.969x10^{6}$ to $6.00x\ 10^{-6}$ as shown in the table and figure.

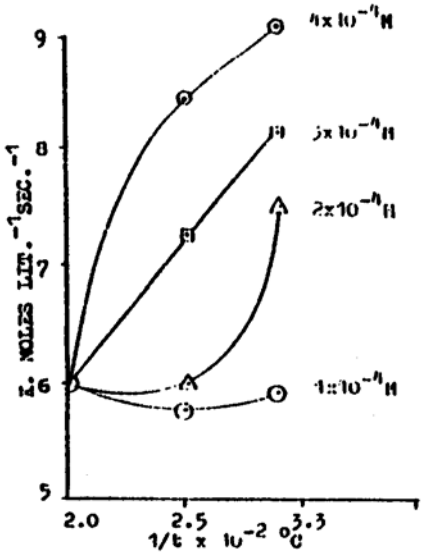

Figure 1: Thermal viscosity degradation of mestranol ethanol solution.

TABLE

Relative Viscosity Rates 1-4 x 10^{-4}M Mestranol Solutions at 32°, 40° and 50°C

Temperature °C	Concentration C x 10^{-4}M	Zero Order Rates K moles. Lit:$^{-1}$ Soc.$^{-1}$
32	1	6.969 x 10^{6}
	2	7.526 x 10^{4}
	3	8.182 x 10^{6}
	4	9.091 x 10^{6}
40	1	5.757 x 10^{6}
	2	6.061 x 10^{6}
	3	7.273 x 10^{6}
	4	8.485 x 10^{6}
50	1	6.00 x 10^{-6}
	2	6.00 x 10^{6}
	3	6.00 x 10^{6}
	4	6.00 x 10^{4}

The same behaviour is noticeable with higher concentration of Mestranol solutions in ethanol. The viscosity rates are maximum at 32°C as compared to 40°C and 50°C, when all the three concentrations of Mestranol have higher rate of viscosity at particular temperature. It could be concluded that the rate of disappearance of Mestranol is more at higher temperature because of lower viscosity rates at these temperatures.

These experiments support triplet state of species transitions at higher thermal conditions i.e., new excited species of Mestranol degradation are produced. Porter and Hochstrasser (1960) explained energy of excitation that it is either singlet or triplet may be non-radiatively transferred from one molecule to another provided that certain conditions are satisfied. These conditions as pointed out by Kan (1966) are firstly, the acceptor should have energy states lower than the excited state of the donor, otherwise the process would be endothermic and, therefore, unlikely to take place. Secondly, the donor excited state must have a life lime long enough to transfer its energy to the acceptor before that energy is dissipated by radioactive or non-radioactive processes. Thirdly, the total spin should be conserved, e.g., a donor molecule in its first triplet state may transfer en*ergy* to an acceptor one in its ground state raising it to its triplet level and quenching the donor to its ground state (Wagner spin conservative rule). This process using Ivert and Pits terms as:

$$D\ (T_1) + A\ (S\Phi) \rightarrow D\ (So) + A\ (T_1)$$

where, D = donor and A = acceptor.

These energy transfer processes are known to occur in all types of media gaseous/liquids and crystalline systems (Porter and Hochstrasser, 1960).

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