THE HYDROLYSIS OF PROPYL BENZOATE IN AQUEOUS SOLUTIONS OF CETOMACROGOL

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The alkaline hydrolysis of n-propyl benzoate in aqueous cetomacrogol solutions has been investigated. The rate of hydrolysis of solubilised ester in the presence of 100 per cent excess of sodium hydroxide is a first order process in which the rate decreases with increase in cetomacrogol concentration. This indicates that incorporation of ester within the micelles protects it against hydrolysis. The rate of reaction depends on the degree of saturation of the dispersion and not on the actual concentrations of ester or cetomacrogol except in so far as these control the degree of saturation. The degree of saturation is expressed as a "Saturation Ratio" which is the ratio of the ester concentration to its solubility.

THE alkaline hydrolysis of certain esters in aqueous solutions of cetrimide, a cationic surface-active agent, has been studied previously (Mitchell, 1962). It was found that the initial hydrolysis rate of emulsions increases with cetrimide concentration while that of solutions decreases. In the later stages of the reaction, the rate of hydrolysis of both emulsions and solutions decreases with increasing cetrimide concentration. This paper reports studies on the alkaline hydrolysis of n-propyl benzoate in solutions of cetomacrogol, a non-ionic surface-active agent.

Increasing concentrations of both cetrimide and cetomacrogol reduce the hydrolysis rate of solutions indicating that solubilisation within the micellar "phase" of the dispersion protects the ester against hydrolytic attack.

The rate of hydrolysis in cetomacrogol solutions is shown to depend on the degree of saturation of the dispersion where this is expressed as a Saturation Ratio R, in which

$$R = \frac{c}{c_s} \qquad \qquad \qquad \qquad \qquad \qquad \qquad (1)$$

where c is the concentration of ester, and c_s its solubility in the solution of surface-active agent.

EXPERIMENTAL

Materials

Cetomacrogol 1000 B.P.C. m.p. $40°$, $n^{60°}$ 1.499_0, hydroxyl number (B.P.C. 1959 method) 51.6. Assuming a molecular weight of $1,300$, concentrated stock solutions were prepared, stored in the dark and diluted as required. n-Propyl benzoate fractionally distilled under reduced pressure, b.p. $231°$, $n^{22°}$ 1.499_1.

Determination of Solubility

The solubility of propyl benzoate at 35° in varying concentrations of cetomacrogol solution was determined using the method previously described (Mitchell, 1962).

Determination of Hydrolysis

The rate of hydrolysis was measured at 35° in the presence of sodium hydroxide sufficient to provide 100 per cent in excess of that needed for complete hydrolysis. The technique was similar to that described earlier except that samples withdrawn at definite intervals were added to excess hydrochloric acid and the remaining acid back-titrated with sodium hydroxide using bromothymol blue as indicator. The reaction between sodium hydroxide and propyl benzoate was stoichiometric.
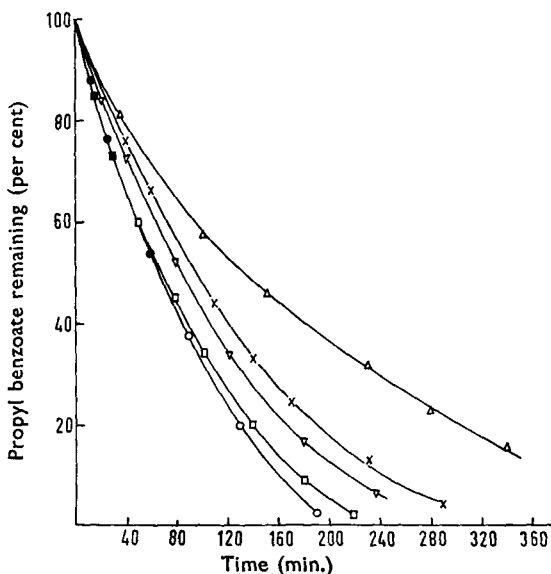

FIG. 1. Influence of cetomacrogol concentration on the alkaline hydrolysis of n-propyl benzoate (0·05 moles/litre) at 35°. Cetomacrogol concentration (moles/litre). ○ 0·01. □ 0·02. ▽ 0·06. × 0·08. △ 0·128. ● emulsion; ○ solution.

RESULTS

The solubility curve of propyl benzoate in cetomacrogol solutions at 35° is linear; the solubilities of propyl benzoate being respectively 0·195, 0·0514, 0·102, 0·136, 0·169 and 0·237 moles/litre for cetomacrogol solutions of 0·01, 0·03, 0·06, 0·08, 0·10 and 0·14 moles/litre. The influence of cetomacrogol concentration on the hydrolysis of propyl benzoate is shown in Fig. 1. The initial rate of reaction of suspensions and emulsions of ester was the same while that of solutions decreased with increase in cetomacrogol concentration. In the later stages the rate decreased

progressively with increase in cetomacrogol concentration. Figs. 2 and 3 show the dependence of the reaction on the Saturation Ratio. From Figs. 2 and 3 it is evident that the hydrolysis of solutions of propyl benzoate in cetomacrogol in the presence of 100 per cent excess of sodium hydroxide is a first order reaction, whereas the hydrolysis of emulsions cannot be represented by a first order rate plot. The initial rates of reaction, first order rate constants k, and half lives $t\frac{1}{2}$, for various Saturation Ratios are given in Table I.
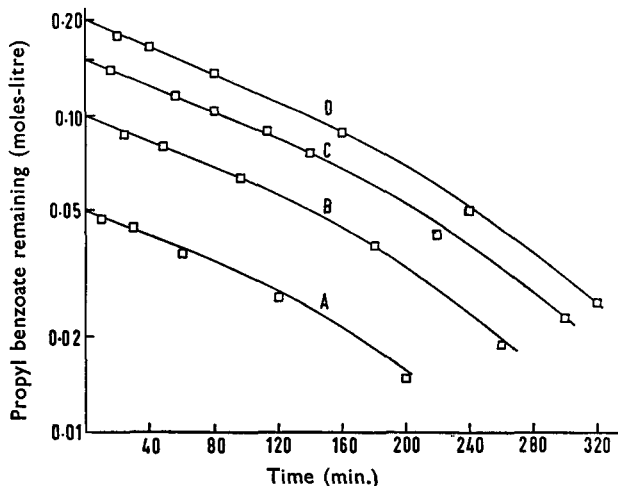

FIG. 2. Alkaline hydrolysis of n-propyl benzoate in cetomacrogol solutions at 35° plotted as a first order reaction. Saturation Ratio = 2·0. Cetamacrogol (moles/litre). A 0·0140; B 0·0285; C 0·0440; D 0·0585.

DISCUSSION

The rate of oxidation of some aliphatic aldehydes in aqueous solutions of cetomacrogol has been shown to depend on the degree of saturation of the dispersion where this is expressed as the Saturation Ratio, R (Carless and Mitchell, 1962). For a saturated solution R = 1, while for an emulsion R > 1 and for a solution R < 1. For any given value of R the rate of oxidation was found to be independent of both aldehyde and cetomacrogol concentrations except in so far as these control the Saturation Ratio. The results presented in Figs. 2 and 3 and Table I show that the hydrolysis of n-propyl benzoate in cetomacrogol also depends on the Saturation Ratio. At each value of R for solutions the first order rate constants k, and the half lives $t\frac{1}{2}$, are in close agreement. Moreover the initial rate of hydrolysis divided by the ester concentration is a constant K, Table I.

$$\text{i.e.} \quad \text{initial rate} = Kc \quad \text{..} \quad \text{..} \quad \text{..} \quad \text{..} \quad \text{..} \quad (2)$$

Where from

$$\text{Equation 1, c} = Rc_s \quad \text{..} \quad \text{..} \quad \text{..} \quad \text{..} \quad (3)$$

TABLE I

DEPENDENCE OF ALKALINE HYDROLYSIS OF PROPYL BENZOATE IN CETOMACROGOL SOLUTIONS ON THE SATURATION RATIO

Saturation Ratio R	Propyl benzoate moles/litre		Cetomacrogol moles/litre	Initial rate moles/litre/ min × 10⁴	$\dfrac{K}{\min^{-1} \times 10^3}$ $\left(\dfrac{\text{Initial rate}}{c}\right)$	k min⁻¹ × 10³ Ist order rate constant	t½ min.	t¾ min.
	c_s	c_s						
0·25	0·01250	0·050	0·0285	0·78	6·3	5·6	126	280
	0·01875	0·075	0·0440	1·20	6·4	5·1	130	282
	0·0250	0·10	0·0585	1·56	6·3	5·1	131	275
	0·050	0·20	0·1280	3·16	6·3	5·4	130	273
0·5	0·0125	0·025	0·0140	1·02	8·2	8·4	83	160
	0·0250	0·050	0·0285	2·05	8·2	8·4	83	168
	0·0375	0·075	0·0440	2·85	7·6	8·5	82	158
	0·050	0·10	0·0585	3·91	7·8	8·8	78	159
	0·10	0·20	0·1280	8·30	8·3	8·7	81	164
1·0	0·025	0·025	0·0140	2·55	10·2	9·8	71	140
	0·050	0·050	0·0285	4·80	9·6	9·7	72	138
	0·075	0·075	0·0440	7·06	9·4	10·3	69	129
	0·10	0·10	0·0585	10·0	10·0	10·4	67	129
2·0	0·05	0·025	0·0140	4·51	9·0		65	114
	0·10	0·050	0·0285	8·02	8·0		69	118
	0·15	0·075	0·0440	12·1	8·1		71	121
	0·20	0·100	0·0585	18·0	9·0		69	120

$$R = c/c_s$$

where c = ester concentration

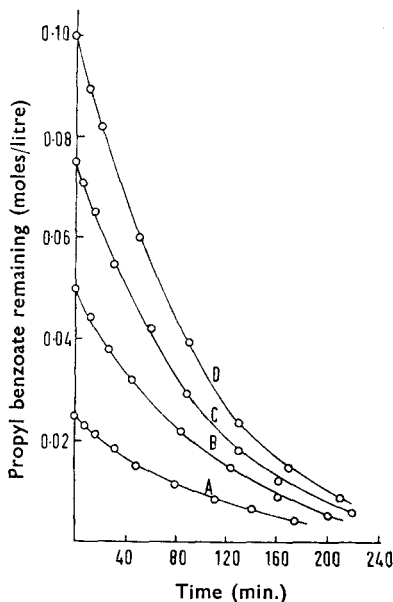c_s = solubility of ester in cetomacrogol

FIG. 3. Alkaline hydrolysis of n-propyl benzoate in cetomacrogol solutions at 35° plotted as a first order reaction. Saturation Ratio = 2·0. Cetomacrogol (moles/litre). A 0·0140; B 0·0285; C 0·0440; D 0·0585.

For emulsions e.g. $R = 2.0$, it is not possible to calculate a first order rate constant, but values for $t\frac{1}{2}$, $t\frac{3}{4}$ and K are in good agreement.

From a consideration of the effect of cetomacrogol on the hydrolysis of n-propyl benzoate it is possible to consider the part played by emulsion droplets and micelles in the reaction. By keeping the amount of ester constant and increasing the amount of cetomacrogol, dispersions are produced ranging from emulsions at low concentrations of cetomacrogol to solutions at higher concentrations. The transfer of ester from the emulsified to the solubilised state with increase in cetomacrogol concentration leads to an enormous enlargement of the interfacial area. The initial rate constant of emulsions is independent of cetomacrogol concentration however, and is the same as that for saturated solutions of ester in cetomacrogol. This indicates that the reaction is not controlled by the interfacial area of dispersed ester.

In the solubilised state the rate decreases progressively with increase in cetomacrogol concentration. Solubilisation of water-insoluble compounds in aqueous solutions of surface-active agents is associated with the presence of micelles. The dissolved material is distributed between the true aqueous "phase" and the colloidal micellar "phase" of the dispersion.

Hydrolysis will occur most rapidly in the aqueous "phase" where the ester molecules are accessible to hydroxyl ion attack. Increasing the concentration of cetomacrogol and thereby the number of micelles, increases the distribution of ester in favour of the micellar pseudo-phase and the rate of hydrolysis decreases.

REFERENCES

Carless, J. E. and Mitchell, A. G. (1962). *J. Pharm. Pharmacol.*, **14**, 46–55.
Mitchell, A. G. (1962). *Ibid.*, **14**, 172–176.