5,6-dihydrouracil-6-sulphonate (III) by the covalent addition of bisulphite ion (HSO^{3-}). We observed that II and III were both formed rapidly from I and that the relative amount of III increased as the concentration of general acids in the solution was increased. For example, the ratio of initial yields of III and II ([III]/[II]) when I reacted in a 4×10^{-2} M solution of sodium bisulphite at pH 7·0 was 1·58 when no sodium dihydrogen phosphate was present but was 4·78 when the concentration of the latter species was $3{\cdot}8 \times 10^{-1}$ M). A much slower subsequent reaction did result in the conversion of II to III.

The rates of disappearance of I and of formation of II and III were identical and were a complex function of pH and of the initial sodium bisulphite concentrations, S_T. At constant pH values the following identity related the observed pseudo-first order rate constants, k_{obsd} values, to S_T values: $k_{obsd} = C_1S_T^2/(1 + C_2S_T)$. In this identity C_1 and C_2 are constants whose values vary with the pH of the reaction solution. Typical values of C_1 and of the ratio C_1/C_2 were 0·29 M^{-2} s^{-1} and 0·07 M^{-1} s^{-1} at pH 6·5 and 0·11 M^{-1} s^{-1} and 0·025 M^{-1} s^{-1} at pH 7·5.

The results can be rationalized in terms of a reaction sequence which includes the following steps: (a) Covalent addition of HSO_3^- to I to yield 5-bromo-5,6-dihydrouracil-6-sulphonate (IV). This is a two step reaction which is acid catalysed when small concentrations of acid are present but whose rate is independent of acid concentrations when the latter are large. (b) A displacement reaction by $SO_3^=$ on the bromine atom of IV to yield an unstable enolate ion. (c) Either protonation of the enolate ion by acids to yield III or elimination of $SO_3^=$ in both spontaneous and acid catalysed reactions to yield II. The results suggest that the formation of IV from I is the rate determining process under the experimental conditions.

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Degradation of paracetamol by a *Penicillium* species

A. HART AND D. L. J. ORR

School of Pharmacy, Liverpool Polytechnic, Byrom Street, Liverpool L3 3AF, U.K.

A mould was isolated from an acidic solution of paracetamol which had been stored in the laboratory. Analysis of the paracetamol solution by polarography showed a decrease in paracetamol concentration (Porter, personal communication). The mould was subsequently identified as a *Penicillium* species.

The *Penicillium* isolate was grown at 25° in a liquid mineral salts medium containing acetamide 1% (w/v) as the carbon source. After incubation a triple washed suspension was prepared in quarter-strength Ringer solution and used to inoculate mineral salts medium (100 ml) containing paracetamol as sole carbon source at concentrations of 0·01, 0·05 and 0·1% (all w/v). The absence of paracetamol toxicity at these concentration was determined by simultaneously inoculating mineral salts media containing both paracetamol and acetamide 1% (w/v). Uninoculated controls were similarly prepared. All media were incubated at 25° on an orbital shaker. The presence or absence of growth was estimated visually and possible degradation of paracetamol measured by ultraviolet spectroscopy.

Results showed that the *Penicillium* isolate was able to utilize paracetamol at the concentrations tested. A decrease in concentration of paracetamol occurred and a shift in ultraviolet spectrum was obtained. The previously colourless paracetamol solution darkened appreciably over 14–21 days incubation and the degree of darkening was related to the initial paracetamol concentration. The metabolic products of the degradation proved to be toxic to the mould over 14–21 days incubation. Control solutions showed no change in paracetamol concentration or any visible darkening during the same period.

The *Penicillium* isolate was grown in the presence of acetamide 1% (w/v) and paracetamol 0·1% (w/v) + acetamide 1% (w/v) for 7 days at 25°. After harvesting and washing the cells, oxygen uptakes in the presence of paracetamol were determined by conventional manometric techniques.

Table 1.

Substrate	Total oxygen uptake (μ mol/μ mol substrate) Acetamide grown cells	Paracetamol-acetamide grown cells
Paracetamol	1·2	0·8
Acetate	1·1	1·2

Table 1 shows that oxygen uptakes for paracetamol were similar to those obtained for acetate metabolism. The slightly lower figure obtained for paracetamol adapted cells is possibly due to a decreased respiration of the cells exerted by toxic metabolites which accumulated during growth. Ultraviolet spectroscopy of the supernatent after oxygen uptake had ceased showed a decrease in paracetamol concentration and a characteristic shift in the paracetamol spectrum to one which was indicative of 4-aminophenol.

Grant & Wilson (1973) reported the degradation of paracetamol by *Corynebacterium pseudodiphtheriticum* to acetate, which was subsequently metabolized, and the corresponding amine. It is proposed that a similar degradation of paracetamol occurs with the *Penicillium* species isolated.

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Kinetics of microagglomeration in liquid suspension

Y. KAWASHIMA AND C. E. CAPES

National Research Council, Ottawa, Canada, K1A OR9

A novel method of agglomeration from liquid suspension in which a small amount of a second immiscible bridging liquid preferentially wets the solids has been developed (Sirianni Capes & Puddington, 1969). When microagglomerated powders produced by this so-called "Spherical Agglomeration Process" are separated from suspension and dried, a dustless free-flowing powder of high bulk density is produced. This technique has application in the pharmaceutical field as an alternative to spray drying and other size enlargement operations.

In a recent investigation, the authors (Kawashima & Capes, 1974) found that the kinetics of the microagglomeration of 1 to 4 vol. % suspensions of >70 μM sand in turbine-agitated vessels were first order. This "restricted-in-space" behaviour apparently resulted from agglomerate interaction and the relatively high solids concentrations which were used. The present work was undertaken to study the kinetics of the agglomeration of particle systems of much finer sizes and lower suspension concentrations.

Experiments were done with $CaCO_3$ particles (3·8 μM), ground glass (17·4, 23·7, 44·2 μM) or Ottawa sand (75·8 μM) suspended in 4 litres of carbon tetrachloride in a turbine-agitated polyethylene vessel. A 20% calcium chloride solution was used as the bridging liquid. The solid concentration in suspension, C_S, was 0·046 to 3·7 v/v% and the amount of bridging liquid, R_F, corresponded to 6 to 122% saturation of voids when the particles were in a close-packed, dry condition. The agitator speed was 700 to 1000 rev min^{-1}. Size and size distribution of the agglomerates were determined by a photographic counting method using a Zeiss TGZ3 particle size analyser.

In all the experiments the agglomeration kinetics could be represented as a first order process given by eqn (1), in spite of the fact that "free-in-space", second order agglomeration might have been expected to prevail with the most dilute solids concentrations: