ADHESION 10

Edited by

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ADHESION 10

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Preface

Each year as Easter approaches and with it the Annual Conference on Adhesion and Adhesives, I am impressed by the continuing growth in interest and understanding of all those phenomena which are encompassed by the titles. People come from an enormous variety of backgrounds and countries to talk together about them. It is this enthusiastic interest and participation which makes this conference so satisfactory year after year and provides the material from which this series of books is produced.

May I express my gratitude for this and for all those who continue to make this conference and the publication so successful.

K. W. ALLEN

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Chapter 1

SYNTHETIC ADHESIVES FOR SURGERY

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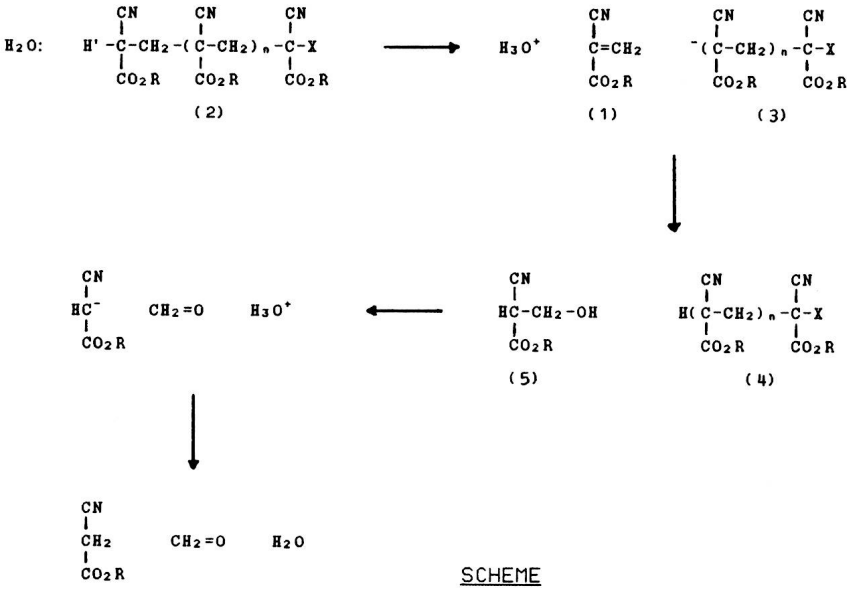
1 INTRODUCTION

The scope for surgical adhesives has recently been reviewed by Hastings[1] and the need for new adhesives was highlighted. Recent research effort has centred mainly on searches for suitably modified natural polymers. Following the discovery of the potential of the alpha-cyanoacrylates,[2] a variety of analogues were prepared and their adhesive properties studied. However, when more fundamental changes were made to the functional groups the monomers lost either their reactivity or the required physical properties. No new alternate synthetic organic monomers have been found for application in this field. This is due largely to the stringent chemical and physical requirements that the adhesives must satisfy. Part of the problem lies in the nature of the tissue environment. The wide range of tissues, the constant state of change and the moist nature of tissue surfaces make them quite unsuitable as substrates for most synthetic adhesives. Also, the adhesive and its degradation products must be biocompatible. This requirement removes the possibility of using most organic solvents and the catalysts usually employed to polymerise organic monomers. It confronts the synthetic chemist with the challenge of producing a monomer that is sufficiently reactive to polymerise rapidly, either, by the action of substances already present in living tissue, or, by new initiators which will not cause biocompatibility problems. The monomer and polymer must have appropiate physical properties and it is also desirable to be able to vary

the duration of adhesion by structural modifications which will alter the rate of biodegradation.

2 SYNTHETIC MONOMERS

The alpha-cyanoacrylates (1)[3] wet and spread on aqueous surfaces to give a continuous film with high initial tack and they set rapidly under the influence of weak base catalysts, such as water and phosphate.[4] There is also strong bonding to the tissue which may be in part due to initiation by anionic and basic groups of the tissue itself. Although the modulus of the polymer is far from ideal, the main disadvantage lies in its unfortunate property of slowly degrading in aqueous media to formalin which causes inflamation and eventual scarring of the tissue. The Scheme shows some of the steps which are probably involved in the degradative processes.

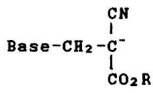


SCHEME

The evidence available indicates that the main degradative pathway involves a reversal of the polymerisation process due to the ready removal of an acidic terminal proton (H') of the polymer (2) with cleavage of the carbon-carbon

bonds, as shown, to regenerate the monomer (1) and a stabilised carbanion (3). The presence of the protic medium will ensure rapid protonation of the carbanion, probably even before it is fully formed, to give the shortened polymer (4). The monomer (1) is then hydrated to the alcohol (5) which undergoes elimination to regenerate the synthetic starting materials - formaldehyde and cyanoacetate. It is apparent that the electron-accepting properties of the cyano and carbonyl groups play a key role in the first and third steps of the degradation. Furthermore both groups are resistant to hydrolysis and therefore remain intact in the polymer and able to initiate de-polymerisation for a sustained period. It should be noted that the hydroxymethylene end-groups or similar groups, which arise from the initiation step and are therefore present in the initially formed polymer (2, X=CH_2OH), will be eliminated directly as formaldehyde and the polymer (2, X=H'), which has identical end-groups, is obtained.

An important role of the cyano group in the cyanoacrylates (1) is its ability to activate the monomer towards weak base catalysed polymerisation. In this capacity it is supported by the presence of the alkoxycarbonyl group (which has less powerful but still moderate electron-accepting properties) bound to the same carbon atom. The combined powerful electron-accepting properties of these groups polarise the monomer making the beta-carbon of the methylene group electron-deficient and lowering the activation energy for nucleophilic attack at this centre. Whilst the resultant carbanion (6) is stabilised by delocalisation of the charge onto the cyano and ester carbonyl groups, it must remain sufficiently nucleophilic to propagate the polymerisation process. On the other hand, the basic properties of the carbanion should be minimal since protonation would terminate the polymerisation process. Note that if water acts as the initiator a strongly acidic group is formed in the intermediate (7) and intramolecular protonation could occur. At the first stage of polymerisation this would give the alcohol (5). This does not occur to any appreciable extent which indicates that the polar group (the possible proton source) remains isolated near the polar tissue surface, away from the reacting centre, so that the polymerisation occurs within the hydrophobic bulk of the monomer.



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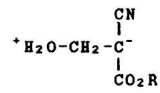


(7)

Thus any group which is used in place of the cyano or carboxylic group must have similar electronic properties and impart a corresponding reactivity on the monomer and the carbanionic intermediate. It would seem that the organic chemist is placed in a dilemma since the groups needed to initiate polymerisation also initiate depolymerisation. However the problem might be overcome if a new group could be produced which was more vulnerable to degradation under in vivo conditions than the cyano or carboxylic ester groups. In this way the activating influence could be removed before the onset of the depolymerisation and subsequent retro-condensation.

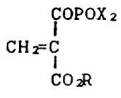
3 ORGANOPHOSPHORUS MONOMERS

One possible candidate functional group that might achieve the above aim is the ketophosphonate group ($COPOX_2$). The phosphoryl group would be expected to increase the electron-accepting properties of the carbonyl group to which it is bound. Most importantly, the ketophosphonate group is known to hydrolyse slowly at pH 7 in aqueous media[5] to give a carboxylate group which has poor electron-accepting properties. Furthermore it should be possible to control the electronic and hydrolytic properties of the phosphonate group by suitable modifications of the phosphorus substituents (X).

The electronic properties of functional groups can be conveniently compared using Hammett sigma substituent constants determined by a study of the ^{19}F and ^{13}C NMR spectra of the fluorophenyl and phenyl derivatives, respectively.[6] We have shown that the ketophosphonate groups have Hammett substituent constants of 0.67 and greater, compared to 0.66 for the cyano group. The relative resonance and inductive contributions are different with the ketophosphonate groups having a larger resonance contribution than the cyano group. The effects of these electronic differences on the rates of polymerisation are not known. However, a large resonance contribution would be expected to increase the sp^2 character of the alpha-carbon ensuring a planar group of atoms at the carbanionic centre offsetting the increase in steric crowding caused by replacing the linear cyano group by the phosphorus grouping. It is also important to avoid any substituents on the methylene carbon which would sterically hinder the approach of the nucleophilic intermediate (6).

We have synthesised a number of alpha-ketophosphonates and found them to be very susceptibly to nucleophilic attack.[7] The reactivity of the

unsaturated alpha-ketophosphonates towards nucleophiles rose rapidly when the beta-substituents were removed and thus the normal methods of synthesis could not be used. As a consequence the vinyl group had to be protected. A synthetic process has now been developed for the incorporation of the ketophosphonate group into the acrylic monomer (8) in place of the cyano group. A small quantity of the dimethyl phosphonate ester (8; R=Et, X=OMe) has been isolated and characterised. It has been polymerised under the action of a weak base and converted into thin films for biocompatibility and hydrolysis studies.



(8)

The common occurrence of phosphoryl compounds in metabolic processes suggests that the ketophosphonate group will impart improved biocompatibility to the monomer and polymer. The attractive forces between the polymer chains may also be improved. Hydrolysis of ketophosphonates give carboxylic acids and phosphonates. The generation of these polar functionalities should considerably enhance the biodegredation of the adhesive which is a current problem with the cyanoacrylate adhesives. It is anticipated that the carboxylate group will not only have the desired effect of inhibiting depolymerisation and the regeneration of formaldehyde but will also promote biodegredation by a different pathway. The biocompatibility of the hydrolysis products will also need to be studied. Whilst phosphonates which have powerful alkylating abilities have well established anti-cholinesterase effects, these groups would not be present in the monomers.

The relative rates of formation of formalin from the cyanoacrylate and ketophosphonylacrylate polymers in hot water, are currently being investigated.

ACKNOWLEDGEMENTS

The study is being carried out with the support of an S.E.R.C. Collaborative Grant to which Ethicon Ltd has given financial and advisory support. We also thank Dr G.W.Hastings for bringing our attention to the need for new synthetic work in this area and for helpful discussions.

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Chapter 2

ADHESION TO SKIN

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1 INTRODUCTION

Peel testing is a convenient method of assessing adhesive strength when one or both of the adherends are flexible. There is a further advantage that the peeling force converts simply to the adhesive failure energy per unit area, θ, by the formula[1]

$$\theta = P(1 - \cos \gamma)/b \qquad (1)$$

where b is the width of the peeling strip and γ is the peel angle. Equation (1) assumes of course that energy storage and dissipation in the peeled portion of the specimen is negligible and this assumption is not always justified [2]. There is an extensive literature on peel testing which will not be reviewed here because it is widely known. Some useful sources of information are given, however, in references[3-6].

The work described in this paper concerns the adhesion of polymeric adhesives to human skin and has as its ultimate objective the improvement of adhesive wound-dressings and related products. The adhesives studied were commercial products based upon uncrosslinked elastomeric polymers.

Uncrosslinked materials are capable of flow and their adhesive behaviour is considerably more complex than that of crosslinked elastomers. Crosslinked adhesives have been studied extensively[7-12] and their peeling energy can be separated into two components according to the equation [7,13]

$$\theta = \theta_o \Phi(\dot{\epsilon}, T, \epsilon_o) \qquad (2)$$

where θ_o is the interfacial bond energy (equal to the thermodynamic work of adhesion if there is no primary interfacial bonding) and Φ is a loss function

depending on velocity $\dot{c}$, temperature T and strain ε_o. Equation (2) was first derived mathematically by Andrews and Kinloch[7], but the separability of interfacial and bulk contributions to adhesive strength was originally predicted by Gent and Schultz[8] on the basis of experiments in which peeling tests were carried out under various liquids.

Some authors have pointed out that peel tests on crosslinked elastomers do not necessarily give simple separability of the bulk and interfacial components [14,15] but it is important to realise that equation (2) does not predict simple factorisation of θ unless Φ is independent of the applied strain ε_o. In many cases this independence is found and curves of log θ versus log $\dot{c}$ are parallel for different θ_o. At high peeling loads, low peeling angles or at temperatures close to T_g of the adhesive, however, Φ frequently becomes strain (or stress) dependent and curves for different θ_o are no longer parallel.

Since Φ is a property of the bulk phase it also controls the cohesive failure of the elastomer, thus:-

$$J = J_o\Phi(\dot{c}, T, \varepsilon_o) \qquad (3)$$

where J is the bulk fracture energy and J_o the cohesive energy per unit area of the solid. Dividing equation (2) by equation (3) we obtain

$$\theta = \theta_o(J/J_o) \qquad (4)$$

provided the dependence of Φ upon strain can be ignored. Thus a knowledge of J_o (which can be calculated[16,17] or measured by limiting fatigue testing[18]) enables θ_o to be deduced from the measured values of θ and J[7].

When we turn to uncrosslinked elastomers (and other pressure sensitive adhesives) the situation is more complex. Experimental work on such systems has been published by several authors[19-22] and a general pattern of behaviour has emerged. Some authors have demonstrated that time-temperature superposition is possible in plots of log θ versus log $\dot{c}$[20,21]. The master curves obtained by superposition exhibit the following general regions[21].

a) Cohesive failure at low $\dot{c}$, θ rising with $\dot{c}$.

b) Cohesive → adhesive transition. θ may fall sharply.

c) Adhesive failure, θ increasing with $\dot{c}$. Failure is fibrillar.

d) Adhesive failure, θ falling with $\dot{c}$. Failure is 'glassy'.

The transition (c) → (d) can be viewed as a glass transition phenomenon.

In spite of this overall phenomenological pattern, it is clear that the peel behaviour of uncrosslinked elastomers is not fully defined. We have found, for example, that a natural rubber-based adhesive exhibits no drop in peeling energy at the cohesive-adhesive transition, whereas acrylic adhesives show a

large drop in θ. A further problem commonly found in conventional peel testing is the unsteady magnitude of the peeling force, revealing time-dependent phenomena in the system which are not fully resolved by the test.

The novel test method described in this paper was adopted initially in an attempt to suppress the load oscillations which occur at higher peeling rates. It was thought that a more definitive value of peeling force might be obtained in this way. This suppression was indeed achieved but a number of new phenomena were also observed with the 'soft machine' test which are not obtained in conventional peel testing. These new effects provide fresh insights into the peel behaviour of uncrosslinked elastomers, the more so because they are fully quantitative. An added bonus is that a single test using the new technique provides the same information as a plurality of conventional peel experiments.

2 TESTING PROCEDURES

All the work reported here used a peeling angle γ of 90^{o}. The maintain this angle in machine tests, the specimen was mounted on a free-running trolley as shown in Figure 1. The effect of the trolley is, of course, to keep the point of peel detachment directly underneath the point of load application.

Normal 90^{o} peel testing (hard-machine testing) was carried out by attaching the peeling strip directly to the cross-head of a Table Model Instron machine. The new peel test method (soft-machine testing) was achieved by interposing a coil spring between the end of the peeling strip and the machine cross-head (Fig. 1).

In hard-machine tests the average rate of peeling is imposed by the cross-head which is driven at a constant rate $\dot{X}$. The peel strip responds by exerting a force P upon the load cell. Since, however, the peel strip does not necessarily 'accept' the imposed steady rate of peeling, it may peel at variable rate and force in such a way as to match the average peeling rate imposed. Since the system is stiff, rapid oscillations may occur in the peel force P (see Fig. 2).

With a soft machine, the peel strip is not compelled to follow the cross-head but may peel at a rate (including zero rate) determined only by its adhesive properties and the instantaneous load.

The rate of peel, $\dot{c}$, is easily obtained from the force-time diagram since it is the difference between the cross-head speed $\dot{X}$ and the relative rate of displacement of the two ends of the spring. This assumes that the peeled portion of the specimen is inextensible, a condition that can always be ensured by using a high modulus backing material. Then if L is the spring length,