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# Synthesis and reactivity of highly versatile VDMO-VBC copolymers

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## Summary

The synthesis of a copolymer containing two reactive functional groups is described. The reactive monomers are 2-vinyl-4,4-dimethyl-5-oxazolone (VDMO), I and vinylbenzyl chloride (VBC), III The resulting polymer is then reactive in two different ways and can produce many different kinds of polymers with specific properties.

## Introduction

Over the last several years the development of reactive polymers has become a highly active area of research. These materials are currently under exploitation for use in a variety of biotechnology related applications where there exists a desire to covalently couple proteinaceous materials to solid supports. The subsequent use of these immobilized protein systems for purification schemes, immunodiagnostics, enzyme catalysis, etc. has been adequately covered in the literature. In relationship to these applications as well as to the utilization of these polymers in instant photography, we embarked on the design of a versatile material which would possess pendant groups reactive to nucleophiles in an aqueous environment. Our two major concerns were to control the reactivity of one functionality relative to pH and to utilize a second functionality to control hydrophilic-hydrophobic balance. Controling the hydrophobic balance is key not only to surface reactivity but is also an important practical aspect for a coating application. In planning the synthesis it was obviously important to bear in mind the stability of the latent reactive group in an aqueous enviroment. In most cases this takes into account the relative reactivities of the desired nucleophile, which for protein would ordinarily be the primary amino group associated with lysine, versus the solvent water.

Having had some experience in working with the homopolymer derived from 4,4-dimethyl-2-vinyl-5-oxazolone (VDMO, I ), (1) we felt under the right set of conditions it would be possible to manage the rate of hydrolysis to N-acryloyl-2-methylalanine units,II. Precedence for amine, alcohol and mercaptan addition to the oxazolone or "azlactone" ring has been well documented in the literature. (2)

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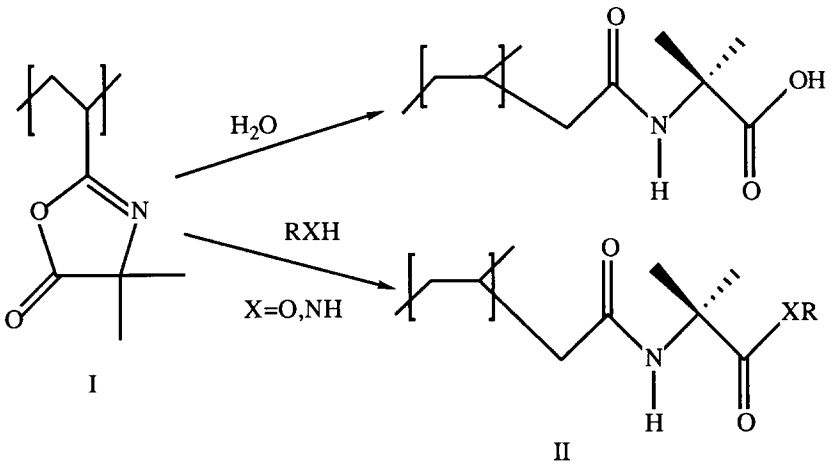
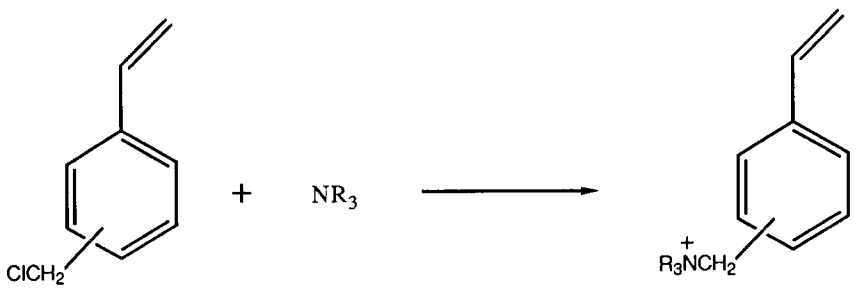


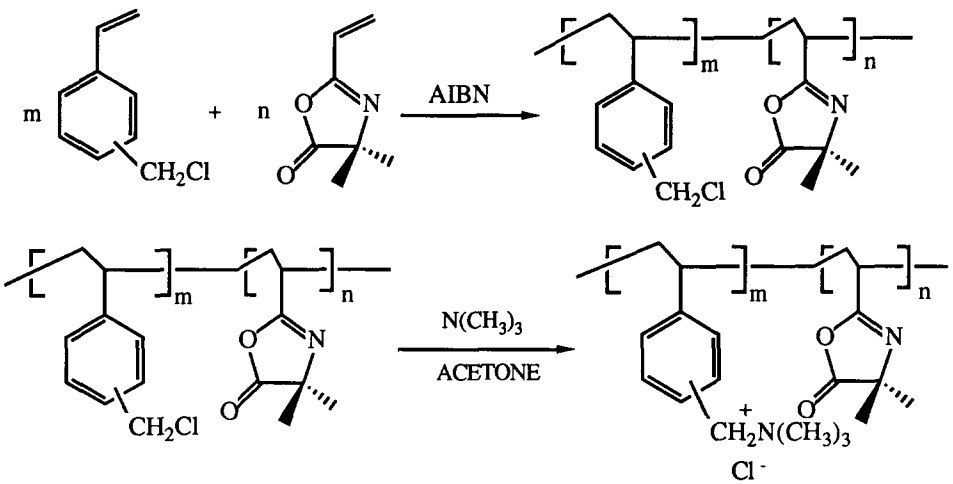

I II

Another advantage in using the azlactone moiety is the simple nature by which nucleophilic addition occurs. The mechanism involves no generation of by-products. The selection of the comonomer, vinylbenzyl chloride (VBC), III, was made in order to provide a means for controlling the hydrophilic properties of the polymer. As was the case for the vinylazlactone, precedent for this chemistry has been well documented in the patent literature. Tertiary alkyl amines are known to react with vinylbenzyl chloride to yield their respective vinylbenzyl quaternary chlorides. The nature of the "R" group provides the versatility for managing the hydrophilic/hydrophobic balance.




III

The two monomers, VDMO and VBC, complement each other nicely in that where units of III react with tertiary alkyl amines units of I do not; however it is known that addition of primary amines and alcohols to I is catalyzed by tertiary amines. This condition has the potential for providing a unique one pot synthesis of a large and diverse group of polymers.




In scheme 1 are depicted some examples , detailed in this paper.

## Experimental

### Preparation of Copoly(Vinylbenzyl chloride: 2-Vinyl-4,4-dimethyl-5-oxazolone) (2:1)

A 500 mL three neck flask equipped with a mechanical stirrer, thermometer, and nitrogen inlet was charged with 50 mL of dry acetone, vinylbenzylchloride,(3) (0.3 mol, 45.65 g) and 2-vinyl-4,4-dimethyl-5-oxazolone,(4) (0.15 mol, 20.9 g). The solution was purged with dry nitrogen through a fritted glass airation tube for 10 minutes. 2,2'-azobisisobutyronitrile (100 mg) was added under stirring. The reaction temperature was raised to 50 °C and stirred for 16 hours while a very slow stream of nitrogen was passed through the vessel. A second 100 mg aliquot of AIBN was added and the reaction stirred an additional 20 hours. The reaction volume, reduced by approximately one third, was poured into 500 mL of dry hexane forming a white precipitate. The supernatant was discarded and the precipitate redisolved in a minimal amount of dry acetone (25-30 mL) and reprecipitated in 300 mL hexane. The supernatant was again discarded and the precipitate dried under high vacuum at 50 °C for 20 hours. Yield 36.5 g , 54% . FTIR analysis, cast on AgCl plates, confirms a strong azlactone carbonyl at 1820 $cm^{-1}$. The monomeric ratio incorporated into the polymer was confirmed by high field proton and carbon-13 NMR and found to be consistent with the title compound.

**Preparation of Copoly(vinylbenzyltrimethylammonium chloride : 2-vinyl-4,4-dimethyl-5-oxazolone) (2:1)**

A 1L side-arm erlenmyer flask scroupulously dried and equipped with a magnetic stir bar and nitrogen inlet was charged with 400 mL of dry acetone and 28 g copoly(vinylbenzyl chloride : 2-vinyl-4,4-dimethyl-5-oxazolone) (2:1). After complete dissolution of the polymer the reaction temperature was reduced to 5°C with the aid of an ice bath. To the rapidly stirred solution was added 13 g of anhydrous trimethylamine. In approximately 15 minutes a white precipitate began to form. The mixture was then gradually allowed to rise to room temperature with excess volatile TMA trapped by aqueous hydrochloric acid. After a total reaction time of 3.0 hours, the reaction liquid was decanted away and the white precipitate was broken up, washed with dry acetone and dried for 24 hours at 50°C under high vacuum, yield 29 g . Care was taken to avoid any contact with moisture. FTIR (KBr pellet) confirms the strong presence of the azlactone carbonyl at 1820 $cm^{-1}$ and a minor presence of the carboxylate carbonyl resulting from the ring opened acid form of the azlactone.High field proton and carbon-13 NMR (DMSO-$d_6$ ) confirm the formation of the benzyltrimethyl ammonium chloride.

**Hydrolysis of Copoly(vinylbenzyltrimethylammonium chloride : 2-vinyl-4,4dimethyl-5-oxazolone) (2:1)**

Into a 25 mL round bottom flask, equipped with a magnetic stiring bar, was added 250 mg of the title copolymer, followed by 20 ml of distilled water at pH 6.5 . The rate of ring opening of the azlactone functionality was studied by FTIR with complete hydrolysis occuring in approximately five hours. The IR spectrum of the exhaustively hydrolyzed material displayed a complete loss of the ring carbonyl at 1820 $cm^{-1}$and the appearance of the carboxylic acid carbonyl at 1730 $cm^{-1}$ .

**Preparation of the methyl ester derived from Copoly(vinylbenzyl-trimethylammonium chloride : 2-vinyl-4,4-dimethyl-5-oxazolone) (2:1)**

A one liter dry Erlenmeyer flask, equipped with a magnetic stir bar and nitrogen inlet, was charged with 68 g copoly(vinylbenzyltrimethyl ammonium chloride : 2-vinyl-4,4-dimethyl-5-oxazolone) (7:3) and 500 ml of dry methanol. The solution was stirred under nitrogen at room temperature for 24 hours. A 100 ml aliquot of this solution was dried and used for characterization, yield 72 g. Quantitative conversion to the methyl ester was determined by FTIR ( loss of the characteristic azlactone carbonyl at 1820 $cm^{-1}$ ) and high field NMR ($D_2O$ , methyl of the methyl ester was assigned to $\partial$ 3.5) .

In a variation of the above procedure, butanol was used in place of methanol . The rate of reaction, followed by FTIR, was much slower for butanol than methanol. Complete conversion to the butyl ester required 48 hours at 50°C .

**Reaction of Histamine with Copoly(vinylbenzyltrimethylammonium chloride: 2-vinyl-4,4-dimethyl-5-oxazolone) (2:1)**

A solution containing histamine ( 111.0 mg, 1.0 mmol) and 10 mL distilled water was added to a 50 mL round bottom flask. To the rapidly stirred solution copolymer xxxxx ( 0.5 g, 0.9 mmol in azlactone functionality) was added and allowed to mix for 8 hours. The reaction was quenched with 20 mL 1.0 N acetic acid and dialyzed in water at 30°C for 24 hours. GPC analysis indicated less than 0.004% free histamine. FTIR displayed a minimal presence of carboxylic acid carbonyl at 1730 $cm^{-1}$ as compared with the authentically derived hydrolysis product described above. The two amide carbonyls were present at 1600 and 1650 $cm^{-1}$. Proton NMR ($D_2O$) also supported the presence of the attached histamine group. Similiar examples of the above reaction, involving the addition of water-soluble primary amines, have been demonstrated with L- alanine and 3-aminopropionitrile fumarate.

**Antibody Immobilization on surfaces coated with Copoly(vinylbenzyl-trimethylammonium chloride: 2-vinyl-4,4-dimethyl-5-oxazolone) (2:1)**

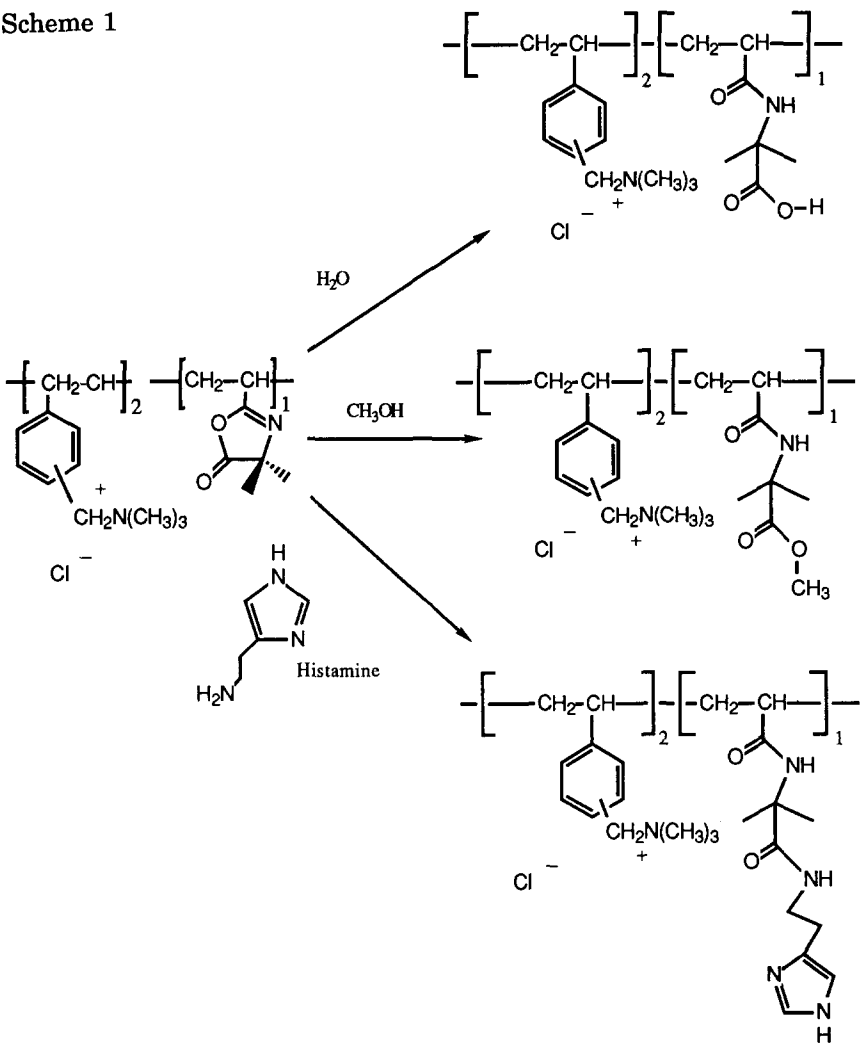
A commercially available polyester film was coated with a solution of copoly(vinylbenzylchloride: 2-vinyl-4,4-dimethyl-5-oxazolone) (2:1) in methylethyl ketone to a coverage of approximately 200 mg / $m^2$. A 3x3 cm section of this film was incubated in a 10 mL solution of anti digoxin monoclonal antibody (10 uL/ mL) in $KPO_4$ buffer at pH 7.5, overnight, room temperature at 10 rpms. The film section was then rinsed for 2 min. in 50 mm tris / 50 mm citrate / 0.01% Tween pH 7.4 followed by a second 2 min. rinse in 50 mm tris / 50 mm citrate / 0.1 % BSA pH 7.4.

After air drying, ten 5x5 mm punchouts were each placed in 2.5 ml polypropylene test tubes where a 1/500 titer solution (0.2 mL) of $I^{125}$ labeled digoxin was added. The solution was incubated for two hours at room temperature at 170 rpms. Unbound tracer was removed by washing in triplicate with a standard ELISA wash buffer. This same procedure was followed for a sample of untreated polyester base in order to provide a control. The average total radioactivity exhibited for the control was found to be 2100 cpms where the copolymer- treated sample had an average total counts of 24,000 cpms.

## Results and Discussion

VBC-VDMO copolymers have been prepared in a variety of monomeric ratios with and without solvent, using AIBN as the initiator. Reaction of the copolymer with tertiary amine was accomplished in a solvent such as acetone. Reaction of the quaternary-azlactone copolymer readily occurs with compounds having amino or hydroxyl groups, including proteins.

Scheme 1




## References

1. L. D. Taylor, H. S. Kolesinski, A. C. Mehta, L. Locatell and P. S. Larson, *Makromol. Chem. Rapid Commun.*, 3, 779 (1982).

2. J. K. Rasmussen, S. Heilmann and L. Krepski, Polyazlactones", in *Encycl. Polym. Sci. Eng.* Second Edition, H. F. Mark, N. Bikales, C. Overberger and G. Menges, Editors, Wiley, New York, N. Y. 1988, Vol. 11, pp 558-571.

3. Vinylbenzyl chloride is a product of the Dow Chemical Company. A complete technical bulletin is available; Specialty Monomers, P. O. Box 1206, Midland, MI, 48641, USA.

4. VDMO is a product of SNPE, Inc. A technical bulletin is available; 103 Carnegie Center, Road 1, Princeton, NJ 08540, USA.

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