

## Optically Active Poly-N-Vinyl-3-Methyl-2-Pyrrolidones

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*Dedicated to Prof. Dragutin Fleš on the occasion of his 60th birthday*

### Summary

Optically active S-(+)- and R-(-)-N-vinyl-3-methyl-2-pyrrolidones are synthesized and radically polymerized using AIBN as the initiator. The resulting high molecular weight polymers are optically active and soluble in a wide variety of solvents including water. IR and  $^{13}\text{C}$ NMR spectra are reported and agree with a polyvinyllic enchainment of the repeating units. The ORD and CD spectra of (+)poly-N-vinyl-3-methyl-2-pyrrolidone in methanol are described.

### Introduction

Though it is still generally believed that changes in ORD and CD spectra of optically active polymers primarily reflect conformational modifications, it is now known that, in many cases, informations on the chemical behavior of these polymers can be deduced from their optical activity too (Vert 1979).

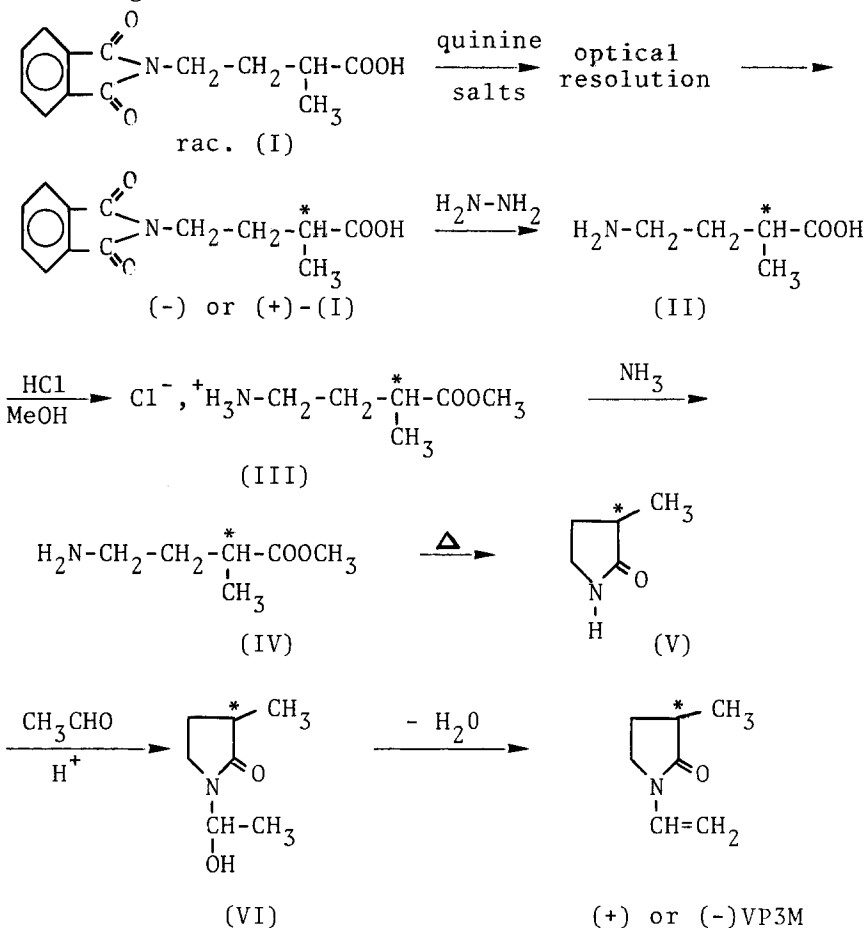
To take advantage of optical activity for investigating chemical reactions or interactions of a given type of macromolecules in solution, it is necessary to deal with optically active macromolecules of the same type, *i.e.* bearing configurationally enriched asymmetric carbon atoms.

Poly-N-vinyl-2-pyrrolidone (PVP) is a neutral amide-containing polymer well known for its outstanding and useful ability to form complexes with a wide variety of compounds (Tomalia 1974), including macromolecules (Kirsh et al 1979), in organic solvents as in water.

In this paper, we report the synthesis and the characterization of two optically active poly-N-vinyl-3-methyl-2-pyrrolidones ((+) and (-)PVP3M with opposite signs and different optical purities. In regard to PVP, these compounds are rendered optically active by the presence of a methyl group at the 3-position of the five-membered ring.

Synthesis of configurationally enriched S-(+)- and R(-)-N-vinyl-3-methyl-2-pyrrolidones ((+) and (-)VP3M).

Both compounds were derived from racemic 2-methyl-4-phthalimidobutyric acid according to the following route :



A method to synthesize (+) and (-)-(V) from rac-(I) has already been reported (Adams and Fles 1959) (Fles and Ghyczy 1964) however the yields were not high enough to afford reasonable large scale preparation. The route that we have followed is basically the same. However, two modifications have significantly risen the final yields. Firstly, the optical resolution of racemic (I) to its (-) and (+) enantiomers was carried out directly by recrystallizing the quinine diastereoisomeric salts in a 30-70 V/V water-ethanol mixture. Secondly, the lactam ring was closed directly during the

distillation of methylester (IV) . The N-vinylation of enantiomers (V) was performed according to the procedure already used for optically inactive pyrrolidones (Falbe 1967) . Two samples of optically active N-vinyl-3-methyl-2-pyrrolidone ((+) and (-)VP3M) were thus obtained with optical purity  $\approx 0.93$  and  $0.60$  respectively assuming the absence of racemization during the N-vinylation. The IR spectrum of (+)VP3M is shown in figure 1 . The C=O and C=C stretching vibrations are located at  $1700$  and  $1630$   $\text{cm}^{-1}$  respectively.

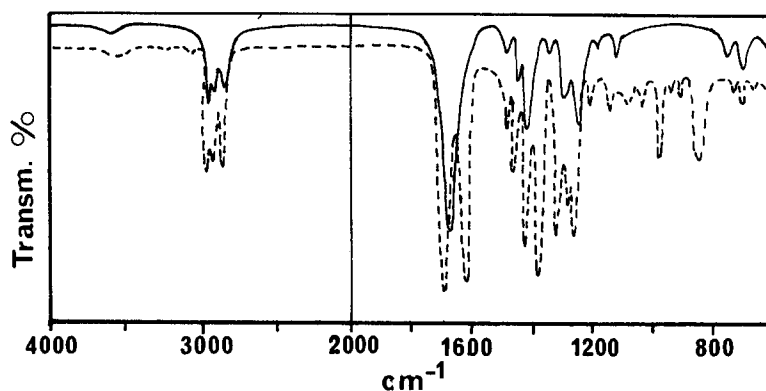


Figure 1 : IR spectra of S-(+)VP3M ----- (neat) and of the corresponding polymer (+)PVP3M \_\_\_\_\_ (film).

#### Polymerization of S-(+)- and R-(-)VP3M

Both samples of optically active N-vinyl-3-methyl-2-pyrrolidone were radically polymerized in water by using AIBN as the initiator according to the procedure described in British patent n°919,757 (1963). The experimental conditions are given in Table 1.

TABLE 1  
Polymerization Data

Sample	Monomer		Polymerization		
	a) $[\alpha]_D^{25}$	Conc. M.l <sup>-1</sup>	I/M %	time mn	yield %
S-(+)VP3M	+ 69°3	9.2	0.3	45	70
R-(-)VP3M	- 42°5	7.2	0.3	45	65

a) C = 2 g.100  $\text{cm}^{-3}$  in benzene

For both samples, high molecular weight optically active polymers were obtained whose characteristics are given in Table 2 .

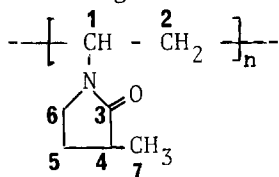
TABLE 2  
Characteristics of the PVP3M polymers

Polymer	a) $[\alpha]_D^{25}$	b) $[\eta]$ $100\text{cm}^3 \cdot \text{g}^{-1}$	c) $\bar{M}_w$	d) $\bar{M}_{\text{GPC}}$
(+)PVP3M	+ 28°	0.80	$7 \times 10^5$	$2.7 \times 10^5$
(-)PVP3M	- 18°	0.32	$1.3 \times 10^5$	$5.6 \times 10^5$

- a)  $C = 0.5 \text{ g} \cdot 100 \text{ cm}^{-3}$  in methanol  
 b) in methanol  
 c) as determined by laser light scattering in methanol ( $dn/dc = 0.16$ )  
 d) in regard to polystyrene standards in chloroform

The two polymers are very hygroscopic materials. Their intrinsic viscosities are similar to those of commercially available poly-N-vinyl-2-pyrrolidones. They are soluble in most of the usual solvents but  $\text{CCl}_4$  and both the saturated and the aromatic hydrocarbons.<sup>4</sup> The IR spectrum of (+)PVP3M is shown in figure 1. The  $\text{C}=\text{O}$  stretching band comes out at  $1680 \text{ cm}^{-1}$  and the bands in the  $2960\text{-}2870$  and the  $1580\text{-}1450 \text{ cm}^{-1}$  ranges correspond to the stretching and the deformation modes respectively of  $\text{CH}_2$  and  $\text{CH}$  bonds of the lactam ring.

The primary structure of optically active PVP3M polymers was further checked by  $^{13}\text{C}\{^1\text{H}\}$  NMR. Table 3 gives the position of the various lines observed in different solvents with increasing dielectric constant. The different lines were identified by gate decoupling and are assigned according to the following:



Data in Table 3 bear out the primary structure of PVP3M as no additional peak was observed in regard to the expected polyvinyl structure. It is of value to notice that the more polar the medium the larger the chemical shift of the carbonyl carbon atom. None of the peaks showed clear fine structure due to stereosensitivity to tacticity or chirality.

TABLE 3

Chemical shifts and assignment of the peaks observed in  $^{13}\text{C}$ NMR spectra of (+)PVP3M in various solvents (as referred to internal TMS)

carbon atom solvent	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C <sub>4</sub>	C <sub>5</sub>	C <sub>6</sub>	C <sub>7</sub>
CDCl <sub>3</sub>	44.9	35.0	178.1	37.4	27.7	40.6	15.9
CH <sub>3</sub> OH	45.6	34.8	179.6	37.9	27.6	40.8	14.9
CF <sub>3</sub> CH <sub>2</sub> OH	46.8	36.5	182.2	39.4	28.7	42.5	16.3
D <sub>2</sub> O	47.0	35.8	182.5	38.7	28.1	42.7	16.3

Figure 2 shows ORD and CD spectra of (+)PVP3M in methanol.

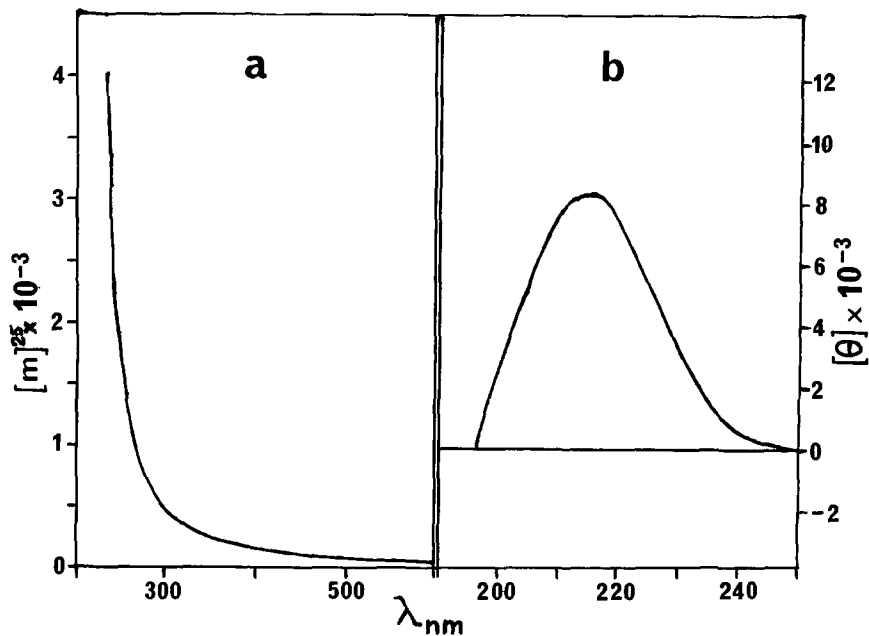


Figure 2 : a) ORD spectrum of (+)PVP3M in methanol ( $c = 0.5 \text{ g} \cdot 100 \text{ cm}^{-3}$ ), ( $[m]$  = monomolar rotatory power);  
 b) CD spectrum of (+)PVP3M in methanol ( $c = 0.15 \text{ g} \cdot 100 \text{ cm}^{-3}$ )

The ORD curve (Fig.2a) is positive and complex i.e. it does not obey the one-term Drude equation  $[\alpha] = A/(\lambda^2 - \lambda_0^2)$ . Therefore, at least two cotton effects of opposite signs contribute to the optical activity of PVP3M polymers (Vert and Selegny 1973). The CD spectrum (Fig.2b) shows one CD band only above 190 nm whose maximum is located at 212 nm. On the basis of the CD spectra of other monosubstituted 2-pyrrolidones, one can tentatively assigned that CD band to the  $n-\pi^*$  electronic transition of the amide chromophore (Geiger and Wagnière 1975).

In conclusion, the method reported in this article provides a simple way to make optically active polymers of the poly-N-vinyl-2-pyrrolidone-type. Optically active PVP3M are to be used for investigating the protonation behavior of amide-containing macromolecules in strong acid media however their optical activity has to be studied in more detail before.

## Experimental

### Chemicals

Rac-2-methyl-4-phthalimido butyric acid (I)

This compound was prepared from butyrolactone and potassium phthalimide according to the procedure reported by Adams and Fles (1959). (Mp=114-115°C).

Optical resolution of rac-2-methyl-4-phthalimido butyric acid

Anhydrous quinine (215 g, 0.65 moles) was added to a well stirred solution of (I) (163 g, 0.65 moles) in 2,260 g of a 30-70 V/V water-ethanol solvent system. The mixture was then warmed up to dissolve the precipitated diastereoisomeric salts. The solution was allowed to stand for 36 h at room temperature. White crystals formed mostly composed of the (-)-(I)-quinine salt. These crystals were recrystallized once only in the same solvent system (6 cm<sup>3</sup>/ 1 g of precipitated salt) that yielded 101 g of the less soluble diastereoisomeric quinine salt (Mp= 150°C). By adding concentrated HCl to a water solution of these crystals, 40 g of (-)-(I) were recovered within 2 h in a 25 % yield in regard to the racemic material. (Mp= 102-104°C;  $[\alpha]_D^{25} = -19.9^\circ \pm 0.6$  (c= 2.1 g.100 cm<sup>-3</sup> in benzene); optical purity  $\approx 0.93$  based on  $[\alpha]_D^{24} = -21.5^\circ \pm 0.4$  (c= 1.75 g.100 cm<sup>-3</sup> in benzene) for pure (-)-(I) (Adams and Fles 1959). (+)-(I) was recovered from the different filtrates without further separation ( $[\alpha]_D^{25} = + 13.0^\circ \pm 0.5$  (c= 2.13 g.100 cm<sup>-3</sup> in benzene); optical purity  $\approx 0.60$ ).

### S-(+) and R-(-)-3-methyl-2-pyrrolidones

The (-) and the (+) isomers of (I), respectively, were treated in the same way. The phthalimide protective group was cleaved by using hydrazine (Adams and Fleš 1959). The aminoacid thus obtained was dissolved in methanol saturated with dry HCl and the mixture was refluxed for 1 h to yield the hydrochloride derivative (III) after evaporation of the excess methanol. (III) was then dissolved in chloroform and dry NH<sub>3</sub> was allowed to bubble through the solution for 10 mn. NH<sub>4</sub>Cl which precipitated was filtrated and washed twice with pure chloroform. Aminoester (IV) was recovered as a residue by evaporation of the solvent from the filtrate and the washings. That residue decomposed during vacuum distillation to yield directly the substituted pyrrolidone. S-(+)-(V) (Mp= 45°C,  $[\alpha]_D^{25} = + 57.9 \pm 0.4$  (c= 2.07 g.100 cm<sup>-3</sup> in benzene)).

### N-vinyl-3-methyl-2-pyrrolidones

(V) (10g) was placed in a three-necked flask equipped with a condenser and efficient stirring. Acetaldehyde (50 cm<sup>3</sup>) was then added dropwise so that the temperature remained below 10°C. Concentrated HCl (0.3 cm<sup>3</sup>) was slowly introduced into the mixture, keeping the temperature below 20°C. After 25 mn, the medium was neutralized with 2,4,6-trimethyl pyridine (4.5g) and the excess acetaldehyde was removed by evaporation. The residue was then distilled in the presence of hydroquinone. VP3M (8 g, Bp= 51°C 1-2 mm Hg) was thus recovered. (+)-VP3M ( $[\alpha]_D^{25} = + 69.3 \pm 0.5$ , (c= 2.02 g.100cm<sup>-3</sup> in benzene)).

### Poly-N-vinyl-3-methyl-2-pyrrolidones

A mixture of VP3M (6.3g) and AIBN (25 mg) was added dropwise to a solution of 25 mg sodium hydrogenocarbonate in 7 cm<sup>3</sup> of pure water at 95°C under nitrogen atmosphere. The flask was allowed to stand at 95°C for 45 mn. The content was then cooled and poured into a 50-50 V/V water-methanol mixture. The resulting solution was dialyzed against water for two days and finally freeze-dried to yield powdered PVP3M

### Measurements

IR spectra were performed using a 251 Perkin Elmer spectrophotometer  
 ORD spectra were carried out using a Spectropol I FICA spectropolarimeter  
 CD spectra were obtained by using a JASCO J 40 B dichrometer at room temperature  
<sup>13</sup>CNMR spectra were performed on a BRUCKER WP 80 apparatus operated by the University of Rouen.  
 GPC's were obtained using a WATERS apparatus

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