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ON THE MEMORY OF SYNTHESIZED VINYL POLYMERS FOR THEIR ORIGINS

Julien Damen and Douglas C. Neckers*
Department of Chemistry
Bowling Green State University
Bowling Green, Ohio 43403

As a continuation of a program designed to take advantage of the properties of polymers in organic processes,[1,2] we have been investigating the synthesis of polymeric materials which maintain a recognizable macrostructure throughout subsequent photochemical processes.[3,4] In this communication we describe model studies toward this end and report a simple example of what may well be an important general phenomenon in polymer synthesis - the selective memory of a synthesized polymer for its origins.

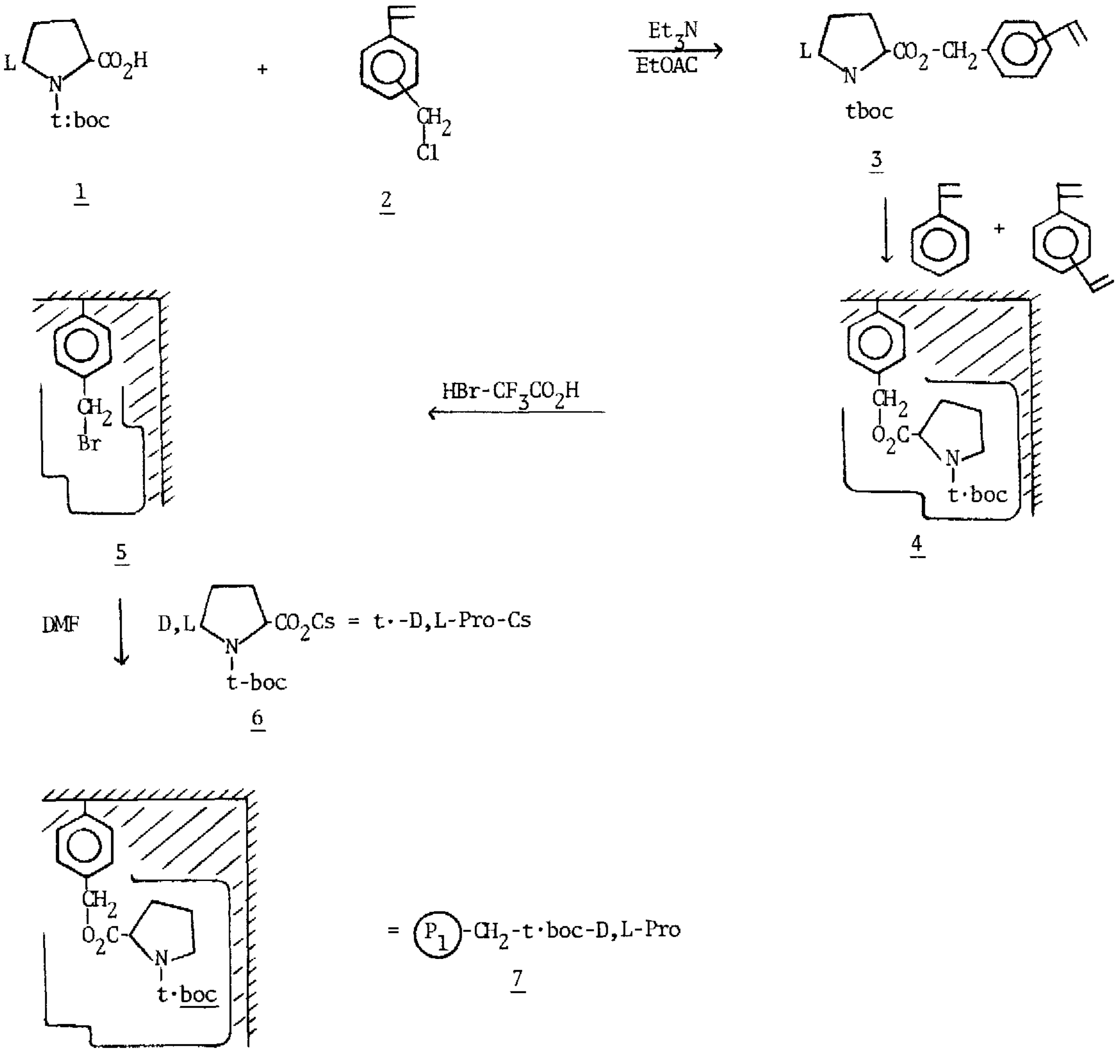
In principle the work is based on that of Dickey[5] who demonstrated that silica gel, prepared from sodium silicate and acetic acid in the presence of methyl orange, had a specific affinity for methyl orange in the presence of the ethyl, n-propyl and n-butyl isomers. More recent work, first by Wulff[6,7] and later by Shea[8] has shown that a vinyl polymer may also develop molecular pattern recognitions during its construction based on the monomers from which it was constructed - even though the specific molecules of construction no longer remain.

Our particular goal was to develop a vinyl polymer wherein was contained a molecule of specific chirality, from the appropriate vinyl monomers, to then remove the chiral center, and to replace the residue in the polymer from a mixture of the appropriate racemates in a chemical process. As a model reaction we chose the simplest possible available chiral starting material - a commercial L-amino acid - treated it with an appropriate group to form a polymerizable substrate, converted the derived monomer to a highly cross-linked polymer, hydrolyzed the L-amino acid from the polymer and treated the resulting polymer with a D,L mixture of a reactive functional derivative of the starting amino acid, Scheme I. A rather substantial preference of the produced polymer for the L-amino acid derivative rather than the D was observed. This, we believe, is a first example of a singly attached chiral isomer directing polymer synthesis to produce a recognizable macrostructure.

Specifically, t-boc-L-proline 1, was treated with an equimolecular amount of vinyl benzylchloride 2 in the presence of triethylamine. The resulting vinylbenzyl-t-boc-L-proline 3 was then copolyemrized with styrene and divinylbenzene via suspension polymerization[9] (molar composition 10-35-55). The IR spectrum of the polymer shows the superposition of the carboxyl group ($\bar{\nu}$ = 1730 cm^{-1}) over the spectrum of a styrene-divinylbenzene copolymer

The cleavage of the attached L-proline residue from the resin is the most critical step in the preservation of the stereospecific properties of the polymer. Reaction with hydrobromic acid in trifluoroacetic acid[2] at room temperature gave us the mild hydrolysis conditions by

Scheme I

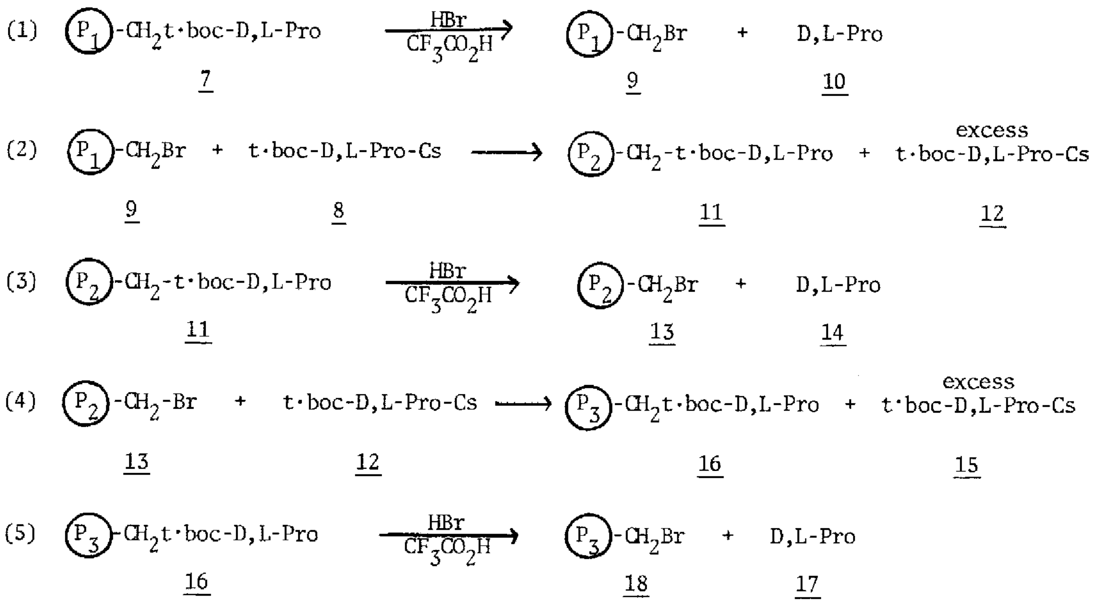


which we might conserve as much as possible the shape of the macromolecular hole and it produced a good leaving group (bromide) on the polymer for the rebinding of the amino acid 5. Using HBr 22% of the proline could be liberated from the copolymer. In a second hydrolysis no additional L-Proline was released.

The hydrolyzed polymer 5 (0.16 mequiv. Br/g) was then treated with a large excess of the Cs-salt of t-boc-D,L-Pro 6. The IR spectrum of the polymer showed an increase in the intensity of the carboxyl group-band. All the active sites had been replaced by some mixture of t-boc-D,L-Pro. When this polymer was again subjected to hydrolysis with HBr/CF_3CO_2H the proline liberated was richer in L-form than D-form (L/D = 1.025). This corresponded to a 1.2% enantiomeric excess (50.6% L-form and 49.4% D-form).

The esterification and hydrolysis steps were subsequently carried out with the same polymer twice more, each time using the excess t-boc-D,L-Pro-Cs from the former esterification reaction, Scheme II. One would predict the excess Cs salt in the reaction should become richer each time in D-form and hence the proline from the hydrolysis steps (reactions 1,3 and 5) is expected to show a smaller enantiomeric excess after each step.

Scheme II



(1) $\underset{\underline{7}}{(P_1)\text{-}CH_2\text{t·boc-D,L-Pro}} \xrightarrow[CF_3CO_2H]{HBr} \underset{\underline{9}}{(P_1)\text{-}CH_2Br} + \underset{\underline{10}}{\text{D,L-Pro}}$

(2) $\underset{\underline{9}}{(P_1)\text{-}CH_2Br} + \underset{\underline{8}}{\text{t·boc-D,L-Pro-Cs}} \longrightarrow \underset{\underline{11}}{(P_2)\text{-}CH_2\text{-t·boc-D,L-Pro}} + \underset{\underline{12}}{\overset{\text{excess}}{\text{t·boc-D,L-Pro-Cs}}}$

(3) $\underset{\underline{11}}{(P_2)\text{-}CH_2\text{-t·boc-D,L-Pro}} \xrightarrow[CF_3CO_2H]{HBr} \underset{\underline{13}}{(P_2)\text{-}CH_2Br} + \underset{\underline{14}}{\text{D,L-Pro}}$

(4) $\underset{\underline{13}}{(P_2)\text{-}CH_2\text{-Br}} + \underset{\underline{12}}{\text{t·boc-D,L-Pro-Cs}} \longrightarrow \underset{\underline{16}}{(P_3)\text{-}CH_2\text{t·boc-D,L-Pro}} + \underset{\underline{15}}{\overset{\text{excess}}{\text{t·boc-D,L-Pro-Cs}}}$

(5) $\underset{\underline{16}}{(P_3)\text{-}CH_2\text{t·boc-D,L-Pro}} \xrightarrow[CF_3CO_2H]{HBr} \underset{\underline{18}}{(P_3)\text{-}CH_2Br} + \underset{\underline{17}}{\text{D,L-Pro}}$

This is exactly what we observe. The D,L-Pro from the hydrolysis 14 and 17 showed respectively an enantiomeric excess L/D = 1.015 and 1.005. The excess t-boc-D,L-Pro-Cs 15 showed an enrichment on D: D/L = 1.038.

A specific adsorption of the L-form over the D-form through complex formation with the resin can be excluded because the proline can only be liberated by a second hydrolysis, which means that the template is covalently bound to the polymer and not through a complex.

Our results suggest a likely new and useful component of polymer synthesis. We are now investigating this feature of memory effect polymer synthesis and in particular are looking at the ability of stereoisomeric cavities in synthesized polymers to direct other processes.

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9. The reaction mixture composition was: 50 ml deaereted water, 10 mg lauryl sulfate, 150 mg sodium polyacrylate, 500 mg sodium sulfate, 150 mg stearic acid, 70 mg benzoyl peroxide, 100 mg gelatin, 4.12 g vinylbenzyl-t·boc-proline, 8.92 g divinylbenzene and 4.55 g styrene. It was heated at 60° under N$_2$ with stirring for 5 hrs. The obtained polymer was filtered and washed in a Soxhlet extractor overnight with MeOH.

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