Notes

Diels–Alder Reactions in Polymer Chemistry: Synthesis of Pyridoxine on a Polymeric Backbone

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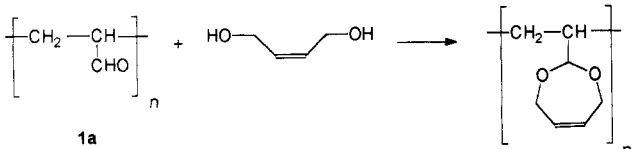
Introduction

The classical Diels–Alder (DA) reaction is still one of the most useful reactions in modern organic chemistry.[1] In macromolecular chemistry, it has been successfully applied for the construction of different kinds of polyadducts.[2-5] In this connection, for example, we recently described the use of telechelics that contain furan end groups and furan-modified substrates from renewable resources to cross-link unsaturated polyesters via DA reactions.[6-9] We also investigated the kinetics of DA modification of comblike polymers containing furan groups at the end of the side chains.[10]

The synthesis of naturally occurring products on a polymer support via DA cycloaddition has not been described extensively. As a commercially interesting example, pyridoxine (Vitamin B_6)[11-13] can be synthesized from a 2-butene-1,4-diol ketal that undergoes DA addition with an oxazole derivative. Up to now, the synthetic route is performed only with low molecular weight compounds. The advantages of solid phase synthesis have not been exploited. The covalent attachment of a dienophile to a polymeric backbone opens, for example, the possibility to use a great excess of the diene to improve the yield of the adduct. The unreacted diene component should be easily removed from the mixture by washing with a suitable solvent. Thus, it was intended in the present investigation to perform polymer-analogous DA addition to demonstrate in principle a suitable route of a pyridoxine synthesis on a polymeric support.

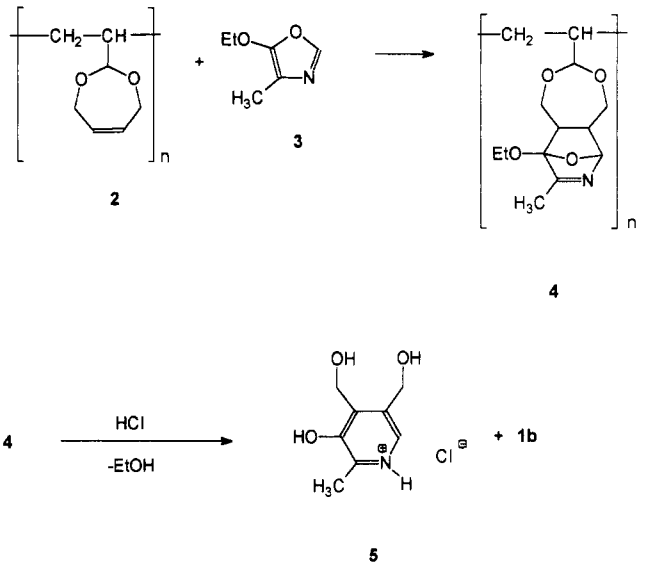
Results and Discussion

Poly(vinyl formal) (**1a**) was prepared by radical polymerization of acrolein according to the literature.[14] **1a** was converted into the cyclic acetal **2** by a condensation reaction with *cis*-2-butene-1,4-diol. From IR data it was



1a **2**

observed that the carbonyl adsorption of the aldehyde group at 1710 cm^{-1} disappeared presumably by the cyclization. The Diels–Alder addition of the diene component 5-ethoxy-4-methyloxazole (**3**) at the polymeric dienophile **2** gave the intermediate **4** which was converted under acidic conditions into pyridoxine (**5**). The oxazole



2 **3** **4**

5

3 was prepared from racemic *N*-formylalanine ethyl ester by condensation with P_4O_{10}.[15] According to TLC, UV, and IR spectroscopy, the structure of **5** was shown to be identical with that of commercially available material.

Although the remaining polymer **1b** appeared to be slightly more colored in comparison with the starting polymer **1a**, it yielded an equal IR spectrum. This indicates that the polymer **1b** can be reused in the same manner.

Therefore, this contribution also illustrates, as an example, the great potential of DA reactions to modify unsaturated polymers.

Experimental Part

Poly(2-vinyl-4,7-dihydro[1,3]dioxepine) (2). A total of 5.00 g of unsoluble poly(vinyl formal) (**1**) was suspended in 120 mL of *cis*-2-butene-1,4-diol. After addition of 0.5 g of *dl*-10-camphorsulfonic acid, the reaction mixture was heated to 70 °C for 30 min. The resulting brown solution was poured into 500 mL of water. Reprecipitation into water from acetone (twice) and drying over P_4O_{10} in vacuum yielded 5.20 g (46%) of a light yellow polymer which became unsoluble after drying.

Poly(3-methyl-7-vinyl-5,9-dihydro-6,8-dioxa-2-azabenzocyclohepten-4-ol) (4). A suspension of 1.50 g of **2** and 3.00 g of 5-ethoxy-4-methyloxazole (**3**) was heated for 5 h at 130 °C in a sealed tube. The dark brown residue was digested with 100 mL of dry ether and separated by filtration. Drying in vacuum over P_4O_{10} yielded 1.75 g of a brown polymer which was unsoluble in common organic solvents.

IR (KBr): ν 3700–3100 (OH), 3060 (sh), 2980, 2940, 2870 (sh, CH), 1730 (C=O, may be caused by partial re-formation of aldehyde), 1670, 1530 (heteroaromatics), 1290, 1205 (phenol) cm^{-1}.

Pyridoxine Hydrochloride (5). A total of 1.00 g of **5** was refluxed for 1 h in a mixture of 10 mL of water and 10 mL of 1 N aqueous HCl. The cooled mixture was reduced to dryness, and **6** was digested with warm water. The filtrate was reduced to dryness. Recrystallization from ethanol (twice) yielded 75 mg

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of pyridoxine (5). Identification was made by comparison of its UV and IR spectra with those of an authentic sample. From TLC analysis a high purity of 5 has been established.

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