

# Side Reactions During the Homogeneous Esterification of Starch with Unsaturated Cinnamic Acid Derivatives in Molten Imidazole

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## Abstract

The homogeneous synthesis of starch cinnamates was studied. Molten imidazole was employed as efficient reaction medium for the polysaccharide and cinnamoyl chloride as reagent. It was postulated that an activated cinnamoyl imidazolide is generated in the process, which would result in efficient esterification and high degrees of substitution (DS). It was found, however, that side reactions of the  $\alpha,\beta$ -unsaturated carboxylic acid derivative and the reaction medium occurred. By spectroscopic experiments, it was demonstrated that imidazole reacts with the double bond by Aza-Michael addition reaction. Mixed esters of starch cinnamate and starch 3-(1*H*-Imidazol-1-yl)-3-phenyl-propanoate (StIPP) are obtained.

**Keywords:** starch; imidazole; cinnamic acid derivatives; esterification; side reactions

## Introduction

In the context of current sustainability and climate change discussions, products made from renewable and biodegradable sources, in particular polysaccharides, gain increasing importance as alternatives to oil-based synthetic polymers [1,2]. The homogeneous modification of polysaccharides may lead to novel, advanced materials with tailored properties [3]. In this context, the chemical modification of starch, especially by esterification, opens a wide range of opportunities to obtain biopolymer-based materials with promising properties, e.g., for applications in the field of biodegradable plastics, adhesives, and additives for the adjustment of rheological and colloidal properties [4-7]. Dimethyl sulfoxide (DMSO) and certain aqueous media are usually employed as solvents for the esterification reactions [8-11]. Recently, a novel approach was found in which molten imidazole is used as reaction medium for the efficient homogeneous synthesis

of long chain aliphatic and complex starch esters with thermoplastic properties [4,12]. Therein, imidazole acts not only as solvent for the polysaccharide but also as base as well as activation agent for the esterification reagent. The reaction proceeds by the *in situ* formation of a carboxylic acid imidazolide, which is formed by conversion of imidazole with an acid chloride or anhydride. Variation of the type and the amount of ester moieties as well as the starch used, opens up a wide range of products, with diverse properties and a broad range the melting temperatures [4]. In order to broaden the spectrum of thermoplastic starch esters and, hence, their properties, the introduction of unsaturated ester moieties is of great interest. The double bonds can be crosslinked after melting, e.g., by UV irradiation, making the melting irreversible (“thermosetting properties”) [13-15]. Reactions of starch with the chlorides of unsaturated fatty acids

have been reported in the system *N,N*-dimethyl acetamide / LiCl in the presence of *N,N'*-carbonyldiimidazole (CDI) as activator [16]. Furthermore, studies on transesterification of starch with unsaturated fatty acid esters were carried out [17]. Cinnamates, i.e., esters of the aromatic  $\alpha,\beta$ -unsaturated cinnamic acid, are very interesting compounds that can be crosslinked easily by irradiation with UV light [18,19]. Moreover, cinnamic acid and its derivatives are of great interest in the context of valorization of lignocellulosic biomass. Thus, aim of the present work was to study the homogeneous synthesis of starch cinnamates by conversion of the polysaccharide with cinnamoyl chloride in molten imidazole.

## Experimental

### Materials

Starch, FLOJEL 60 ACS 1240 ( $M_w = 454.29$  g/mol, National Starch) was applied as starting polymer. It was dried in vacuum at 105 °C over potassium hydroxide for 24 h before use. Cinnamoyl chloride, imidazole, and isopropyl alcohol were purchased from Sigma Aldrich. Further chemicals and reagents were of analytical grade and were used as received.

### Measurements

NMR spectra were acquired at room temperature and 60 °C on a Bruker Avance 250 MHz or 400 MHz spectrometer with 16 scans for  $^1\text{H}$ -NMR spectroscopy and up to 20.000 scans for  $^{13}\text{C}$ -NMR spectroscopy and at least 50 mg sample per ml dimethyl sulfoxide ( $\text{DMSO-d}_6$ ). 2D experiments were measured with the 400 MHz spectrometer. Elemental analysis (C, H, S content) was carried out using a Vario EL III (Elementaranalysensysteme Hanau, Germany). The chlorine content was determined according to Schöniger's method [20].

### Methods

#### *Dissolution of starch in imidazole*

Starch (2.5 g, 15.4 mmol) was mixed with imidazole (22.7 g, 333.4 mmol) and the temperature was increased to 100 °C under stirring. After the melting of imidazole was completed, the mixture was stirred for 1 h at 100 °C to obtain a clear, slightly yellow solution of starch.

#### *Homogeneous esterification of starch with cinnamoyl chloride (starch ester 1, typical example)*

Directly before the synthesis, cinnamoyl chloride, which forms solids blocks in the storage bottle in which it is supplied, was heated to 60 °C. An appropriate amount

of the liquid was removed, quenched, grinded into a powder, and weighted to obtain the amount of reagent required for each individual reaction. Cinnamoyl chloride (2.6 g, 15.4 mmol) was added to the above described solution of starch (2.5 g, 15.4 mmol) in imidazole (22.7 g, 333.4 mmol) at 100 °C. The reaction mixture was allowed to react for 1 h at 100 °C under mechanical stirring. The reaction was stopped by adding isopropyl alcohol (50 ml) and the reaction mixture was poured into an excess of isopropyl alcohol (200 ml). The precipitating product was removed by filtration, washed with isopropyl alcohol (four times with 200 ml each), and dried at room temperature under vacuum.

Mass yield: 4.8 g.

Elemental analysis: 47.3% C, 5.1% H, 4.1% N, 0.0% Cl.

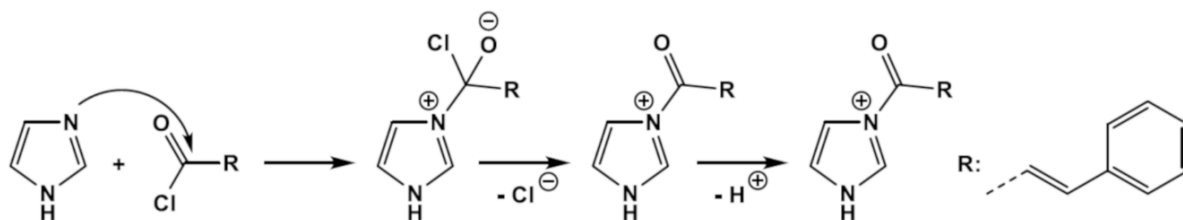
$^{13}\text{C}$ -NMR spectroscopy ( $\text{DMSO-d}_6$ , ppm): 170.2 (C-7), 166.1-167.0 (C-16), 145.4 (C-9), 140.3 (C-19), 137.2 (C-25), 134.0 (C-10), 130.5 (C-13, C-22), 128.7 (C-12, C-14, C-21, C-23), 127.3 (C-11, C-15, C-20, C-24), 122.0 (C-26, C-27), 118.4 (C-8), 100.9 (C-1), 106.2 (C-1'), 82.2-77.0 (C-2, C-3, C-4, C-5), 64.1 (C-6), 60.7 ( $\text{C}_{\text{substituted}}$ ), 57.3 (C-18), 40.0 (C-17).

FTIR spectroscopy (KBr,  $\text{cm}^{-1}$ ): 3400  $\nu$  OH, 3010  $\nu_{\text{as}}$   $\text{CH}_{\text{aromatic}}$ , 1750  $\nu$  C=O, 1665  $\nu$  C=N, 3010  $\nu_{\text{as}}$   $\text{CH}_{\text{aromatic}}$ , 1500  $\delta$   $\text{CH}_{\text{aromatic}}$ , 1320  $\nu$  C-N,  $\nu_{\text{as}}$  C-C(=O)-O-, 1022  $\nu$  C-O- $\text{C}_{\text{AGU}}$ , 740  $\gamma$  C=C.

## Results and Discussion

It was found that molten imidazole can efficiently dissolve starch and that it can be employed as reaction medium for the homogeneous chemical derivatization of the polysaccharide [4]. It likewise acts as solvent for starch and the reactants as well as base and activating agent (mediator) for esterification reactions. In the present work, starch was dissolved in imidazole at 100 °C and converted with different amounts of cinnamoyl chloride for 1 to 24 h. As has been described previously, the acid chloride first reacts with imidazole to form the corresponding activated carboxylic acid imidazolide (Figure 1) [4].

The reaction of the cinnamic acid imidazolide with starch dissolved in imidazole was carried out at different molar ratio of cinnamoyl chloride per anhydroglucose unit (AGU) from 1 / 1 to 5 / 1 (Table 1). The products obtained at lower molar ratios (up to 2 / 1) were soluble



**Figure 1:** Reaction scheme for the synthesis of carboxylic acid imidazolides by conversion of an acid chloride with imidazole.

in chloroform, which was expectable considering the hydrophobicity of the aromatic ester moiety that was introduced. Interestingly, products obtained at higher molar ratios (3 / 1 and higher), i.e., derivatives with supposedly higher degrees of substitution (DS), did not dissolve in chloroform but in more polar solvents like dimethyl sulfoxide (DMSO). Despite rigorous washing and reprecipitation, the products showed a

considerable amount of nitrogen (about 4 to 6%). This was unexpected based on previous studies using molten imidazole as medium for the synthesis of a broad variety of starch esters in which imidazole traces could be removed with low efforts to obtain pure products. Thus, it was speculated that side reactions with the reaction medium might occur in the present case.

**Table 1:** Conditions for and results of the esterification of starch with cinnamoyl chloride in molten imidazole at 100°C.

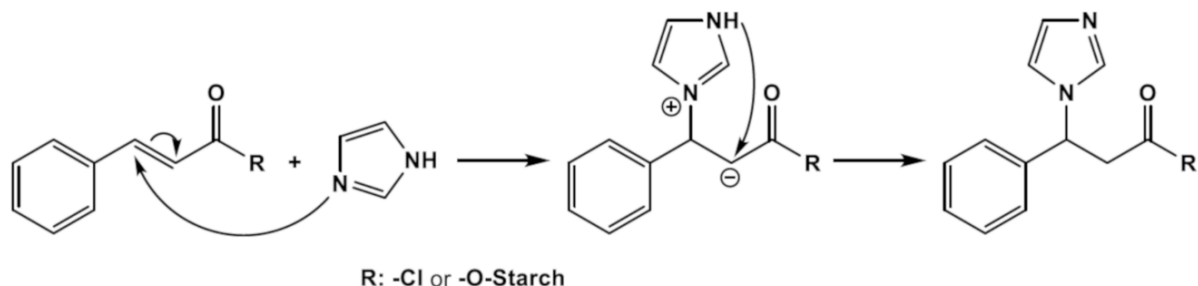
Reaction conditions		Product					
Reaction time, h	Molar ratio CCl/AGU <sup>a</sup>	#	Elemental composition			Solubility <sup>b</sup>	
			C	H	N	DMSO	CHCl <sub>3</sub>
1	1 / 1	1	47.3	5.1	4.1	+	+
1	2 / 1	2	59.0	5.0	4.1	+	+
1	3 / 1	3	63.0	5.4	5.0	+	-
1	4 / 1	4	69.6	5.1	4.5	+	-
24	5 / 1	5	66.8	5.3	5.6	+	-

<sup>a</sup> Mol cinnamoyl chloride (CCl) per mol anhydroglucose unit (AGU).

<sup>b</sup> DMSO: dimethylsulfoxide, CHCl<sub>3</sub>: chloroform, + = soluble, - = insoluble.

The analysis of the reaction products by FTIR spectroscopy revealed typical absorption bands for the polymer backbone ( $\nu_{\text{as}}$  C-C(=O)-O-) around 1020  $\text{cm}^{-1}$  and the ester moieties ( $\nu$  C=O) around 1750  $\text{cm}^{-1}$ . This clearly indicates the successful esterification of starch. However, additional absorption bands were observed in the FTIR spectra at 1320  $\text{cm}^{-1}$  ( $\nu$  C-N) and 1665  $\text{cm}^{-1}$  ( $\nu$  C=N) that are characteristic for the presence of aromatic tertiary amine moieties and imines, respectively. Thus, it is speculated that side reactions of the unsaturated carboxylic acid derivative and imidazole occurred that resulted in a covalent binding of the aromatic amine to the polysaccharide. It has been reported that the conversion of aliphatic  $\alpha,\beta$ -unsaturated carboxylic acids such acrylic- and methacrylic acid with  $N,N'$ -carbonyldiimidazole (CDI) in DMSO can result in an addition of imidazole to the

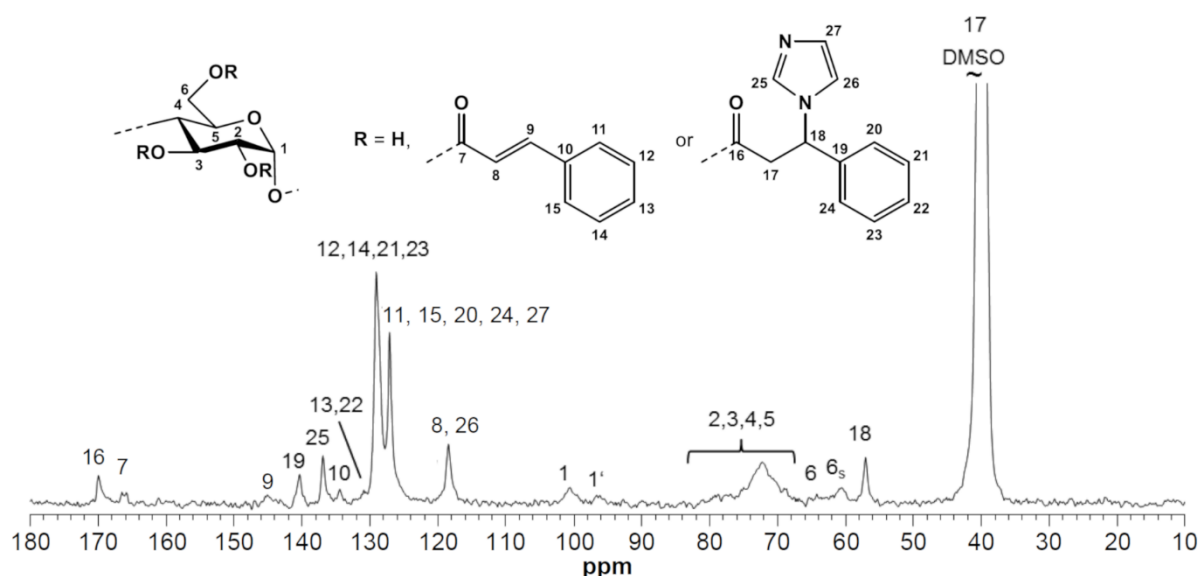
double bond [21, 22]. Aryl substituted, i.e., conjugated,  $\alpha,\beta$ -unsaturated carboxylic acid like cinnamic acid did not show this side reaction and CDI activated esterification of starch in DMSO was feasible [21]. However, the present study indicates that this might be the case for conversion in molten imidazole. Based on the spectroscopic results, it is hypothesized that cinnamoyl chloride reacts with imidazole by a nucleophilic attack of the nitrogen atom of imidazole at the double bond according to Aza-Michael addition reaction (Figure 2). 3-(1*H*-Imidazol-1-yl)-3-phenyl-propanoyl chloride is formed, which can react with the hydroxy groups of starch to form starch 3-(1*H*-Imidazol-1-yl)-3-phenyl-propanoate (StIPP) esters. Comparable reactions have been described for low molecular weight organic compounds in the literature [23].



**Figure 2:** Proposed reaction scheme for addition of imidazole to the double bond of cinnamic acid derivatives.

The starch derivatives obtained were well soluble in DMSO or chloroform. Thus, solution state NMR spectroscopy could be performed to elucidate the molecular structure of the derivatives. The  $^{13}\text{C}$ -NMR spectrum of sample 1 is shown in Figure 3. It features the characteristic peaks of the carbon atoms C-1 to C-6 of the AGU between about 60 ppm and 106 ppm. The peak at 106.2 ppm can be attributed to the anomeric C-1 atom adjacent to C-2 with an unmodified hydroxy group. In addition, a less intensive peak at 100.9 ppm was observed that can be attributed to a C-1 atom in vicinity to an esterified C-2 position. Thus, it can be concluded that the position C-2 is partially converted to an ester moiety. Moreover, minor peaks corresponding to an esterified position C-6 were observed (60.7 ppm). In addition to peaks that could be attributed to the starch backbone, characteristic peaks for cinnamic ester moieties were identified between around 118 ppm and 170 ppm. Two separate peaks were observed in the “carbonyl region” at 170.2 ppm (attributed to StIPP that was introduced by a side reaction) and at

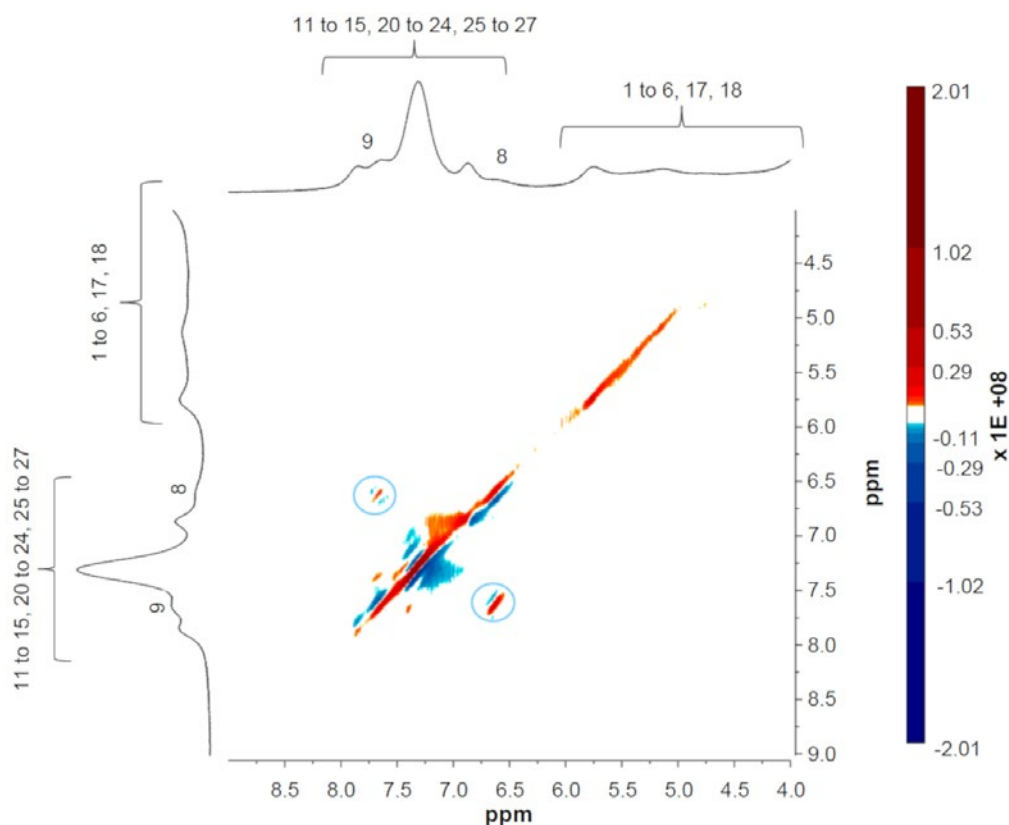
about 167 ppm (attributed to starch cinnamate), which demonstrates that two different types of ester moieties are present. The downfield shift of the carbonyl related peak in StIPP can be explained by the loss of the electron donating +M-effect of the conjugated double bond that occurred upon addition of imidazole. Peaks attributed to the aromatic ring of the cinnamic acid substituent were observed in the range of about 140 ppm to 130 ppm. At 137.2 ppm, 140.3 ppm, and 57.3 ppm, additional signals were recorded that can be assigned to C-25 (bound imidazole moiety) as well as C-19 (aromatic carbon atom adjacent to C-18) and C-18 (former  $\text{sp}^2$ -carbon atom with a covalently bound imidazole group) of the StIPP substituent. The peak belonging to the  $\alpha$ -carbon atom (C-17) of the StIPP is located around 40 ppm and covered by the DMSO solvent peak. The signals of carbons of the original double bond are located at 145.4 ppm (C-9) and 118.4 ppm (C-8), demonstrating the existence of the mixed ester of starch cinnamate and StIPP. The latter peak also includes the aromatic C-26 of the imidazole moiety.



**Figure 3:**  $^{13}\text{C}$ -NMR spectrum of the mixed starch ester derivative 1, recorded in  $\text{DMSO-d}_6$  at 25 °C.

The  $^1\text{H}$ - $^1\text{H}$ -COSY-NMR spectrum of sample **1** shows different cross peak patterns due to presence of a double bond that can potentially be in cis or trans configuration (Figure 4). The vicinal coupling constant describes two functional groups bound to two adjacent carbon atoms and it largely depends on the dihedral angle. Compared to cis isomers ( $\sim 7$  Hz),

trans isomers exhibit significantly higher values of vicinal coupling constants ( $\sim 16$  Hz). The cross peaks of the two trans isomeric protons of the double bond were recorded at 7.6 ppm and 6.6 ppm, thus, demonstrating that a certain content of the original double bonds remained in the starch ester products.



**Figure 4:**  $^1\text{H}$ - $^1\text{H}$ -COSY-NMR spectrum of the mixed starch ester derivative **1**, recorded in  $\text{DMSO}-d_6$  at  $25^\circ\text{C}$ .

## Conclusions

In this work, it was found that the esterification of starch with cinnamoyl chloride, an unsaturated aromatic acid derivative, in molten imidazole leads to side reactions. The conversion results in the desired formation of the activated carboxylic acid imidazolide. Thus, esterification of starch occurred. However, imidazole also reacts with the double bond of the  $\alpha,\beta$ -unsaturated carboxylic acid by Aza Michael addition reaction. It was demonstrated that the corresponding 3-(1*H*-imidazole-1-yl)-3-phenyl-propanoate moiety formed is also esterified to the polymer backbone. Based on these findings it can be concluded that other activation agents (e.g., tosyl chloride, oxalyl chloride / *N,N*-dimethylformamide) and / or reaction media should be employed for the synthesis of starch esters with  $\alpha,\beta$ -unsaturated carboxylic acids.

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