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# DICYCLOHEXYLCARBODIIMIDE ASSISTED SYNTHESIS OF ALIPHATIC POLYESTERS AT ROOM TEMPERATURE

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# DICYCLOHEXYLCARBODIIMIDE ASSISTED SYNTHESIS OF ALIPHATIC POLYESTERS AT ROOM TEMPERATURE

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## ABSTRACT

We investigated the use of dicyclohexylcarbodiimide (DCC) as an activating agent in the synthesis of aliphatic polyesters. Butylhexanoate was synthesized in order to optimize the reaction conditions. The reactions were carried out in methylene chloride at room temperature. It was shown that nearly complete conversion is achieved if 4-(dimethylamino)pyridinium 4-toluenesulfonate (DPTS) is used as the catalyst. DPTS is a complex formed from 4-(dimethylamino)pyridine (DMAP) and *p*-toluenesulfonic acid (PTSA). The polyesters based on 1,10-octanedicarboxylic acid and 1,4-butanediol, synthesized in this way, had degrees of polymerization up to 67.

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## INTRODUCTION

Low-temperature synthesis of aliphatic polyesters often requires the conversion of the condensation monomers to activated derivatives, like conversion of carboxylic acids to acid chlorides. This conversion often takes place at elevated temperatures and more vigorous conditions. Moreover, these derivatives can be easily hydrolyzed and high conversion levels are only possible under rigorously anhydrous conditions. Polyesterification via direct condensation, with the use of inactivated monomers is often rejected because the high temperatures required in that case often lead to side reactions that limit the molecular weights of the synthesized polyesters.

The use of carbodiimides as activating agents offers a low-temperature and mild alternative. Carbodiimides are used as oxidating agents for alcohols as well, but provided that aliphatic carbodiimides are used, this oxidation does not occur [1]. In that case, chain termination via alcohol coupling is not induced. Because of the fact that this direct polymerization method does not make use of activated monomers, traces of moisture can be tolerated since the activated intermediate can be regenerated if hydrolysis does occur.

The mechanism of carbodiimide condensation (see Figure 1) is believed to involve the formation of an *O*-acylisourea intermediate (1) from a carboxylic acid and a DCC molecule. Starting from this intermediate, several reactions can take place. Formation of the *N*-acylurea (2) will occur by an intramolecular transfer of an acyl group from an oxygen atom to a nitrogen atom (path A). This inactive *N*-acylurea will terminate the chain end, and thereby prevent formation of high molecular weight polyesters.

The amount of *N*-acylurea formed depends on the choice of solvent, $pK_a$ of the carboxylic acid and pH of the reaction mixture [1]. A bimolecular reaction between a second carboxylic acid and the *O*-acylisourea will lead to the formation of a urea (3) and the acid anhydride (4) (path B). Acylation of the acid anhydride, aided by DMAP, will provide an active *N*-acylpyridinium intermediate (5). This *N*-acylpyridinium intermediate can also be obtained by the reaction of the *O*-acylisourea intermediate with DMAP, including generation of urea (3) (path C). Finally, the *N*-acylpyridinium intermediate (5) reacts with an alcohol and regenerates the catalyst which forms the ester linkage (6). DMAP is thought to limit the formation of *N*-acylurea (2) by reacting with the *O*-acylisourea intermediate (1) before rearrangement can occur [2]. The role of PTSA is thought to prevent the formation of *N*-acylurea (2) by protonation of the *O*-acylisourea [3].
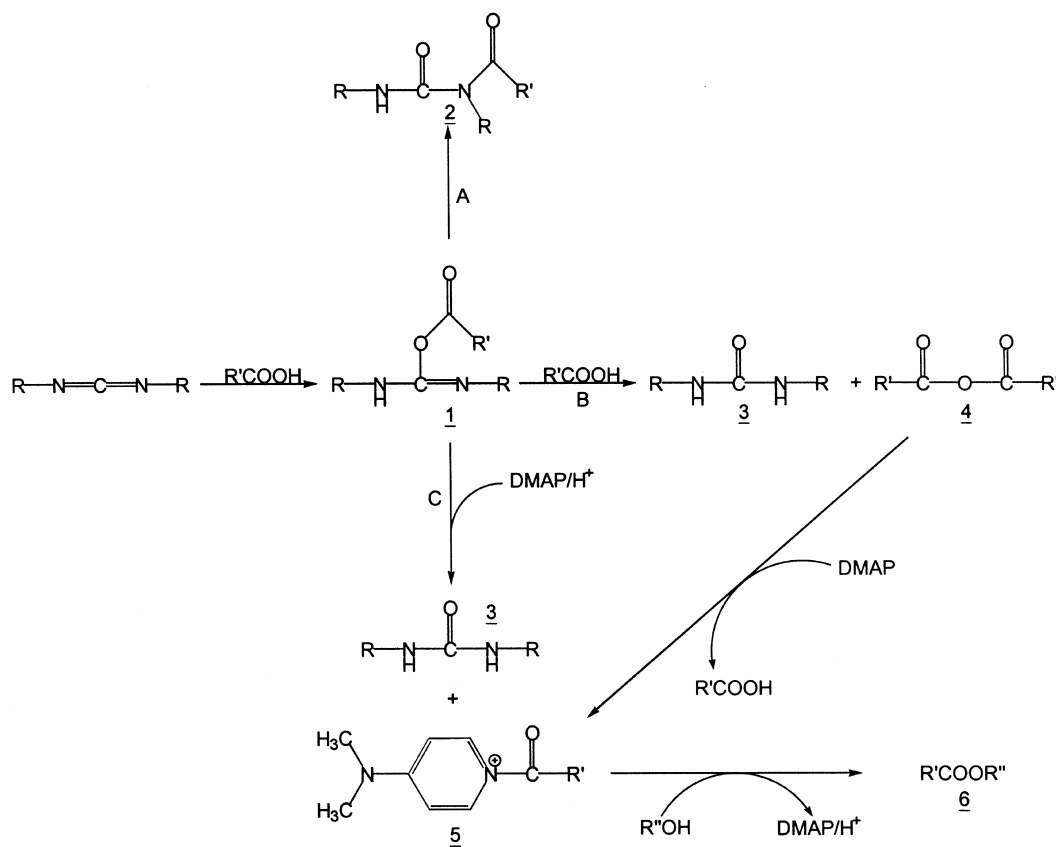
**Figure 1.** Reaction pathways in carbodiimide assisted condensation of a carboxylic acid and an alcohol.

The presence of a positive charge on the imine nitrogen in one of the tautomeric forms of the protonated *O*-acylisourea, is thought to decrease the nucleophilicity of the nitrogen atom and to suppress the rearrangement to *N*-acylurea. Another role of PTSA may be to lower the pH of the reaction medium, which results in the suppression of *N*-acylurea formation [4].

As far as we know, the combined use of DCC and DPTS for the synthesis of polyesters was limited to the condensation of aromatic alcohols with aromatic carboxylic acids [5, 6, 7, 8], and to the condensation of hydroxy acids containing aromatic alcohols and aromatic or aliphatic carboxylic acids [4] or hydroxy acids containing aliphatic alcohols and carboxylic acids [9]. This is the first time that the synthesis of fully aliphatic polyesters starting from aliphatic

dicarboxylic acids and aliphatic diols with use of DCC and DPTS has been reported, thus furnishing an elegant route for the room-temperature synthesis of fully aliphatic polyesters.

## EXPERIMENTAL

### Materials

Methylene chloride ($CH_2Cl_2$) was dried by refluxing over phosphorous pentoxide, followed by distillation and stored over 4Å molecular sieves. 1,10-Octanedicarboxylic acid and dicyclohexylcarbodiimide (DCC, Acros) were used as received. 1-Butanol, 1,4-butanediol, 1-hexanoic acid, 4-(dimethyl-amino)pyridine (DMAP) and *p*-toluenesulfonic acid (PTSA) (Aldrich) were used as received. 4-(dimethylamino)pyridinium 4-toluenesulfonate (DPTS) was obtained using the procedure described by Moore and Stupp [4].

### Synthesis of Butylhexanoate

A single-necked round-bottom flask, equipped with a magnetic stirrer, was charged with 1-butanol (3 mmol), 1-hexanoic acid (3 mmol), DPTS (1.5 mmol) and 6 ml of $CH_2Cl_2$. As soon as the mixture became homogeneous, 3.9 mmol of molten DCC was added and the mixture was stirred for about 12 hours at room temperature. After reaction, the DCU, insoluble in $CH_2Cl_2$, was removed by filtration over a paper filter. The solvent was removed by evaporation and the residue was analyzed by ^{1}H NMR without further treatment.

### Synthesis of Polyesters

The amounts of activating agent (DCC) and catalyst (DPTS) were varied as shown in Table 1.

A single-necked round-bottom flask, equipped with a magnetic stirrer, was charged with 1,10-octanedicarboxylic acid (6 mmol), 1,4-butanediol (6 mmol), DPTS (6 mmol) and 40 ml $CH_2Cl_2$. The 1,10-octanedicarboxylic acid is poorly soluble in $CH_2Cl_2$, but this does not affect the further reaction. Molten DCC (3.9 mmol) was added and the mixture was stirred for about 12 hours at room temperature. After reaction, DCU, insoluble in $CH_2Cl_2$, was removed by filtration over a paper filter. The solvent was removed by evaporation and 30 ml

TABLE 1. Results of Polymerization of 1,10-octanedicarboxylic Acid and 1,4-Butanediol, using DPTS or DMAP as the Catalyst and DCC as the Activating Agent. $\overline{X}n$ and $\overline{X}w$ are Number Average and Weight Average Degrees of Polymerization Respectively

| Entry | DCC[a] | DMAP[a] | DPTS[a] | $\overline{Mn}$ (g/mole) | $\overline{Xn}$ [b] | $\overline{Mw}$ (g/mole) | $\overline{Xw}$ [b] |
|-------|--------|---------|---------|--------------------------|---------------------|--------------------------|---------------------|
| 1 | 1.3 | 0.50 | - | 3900 | 30 | 4630 | 36 |
| 2 | 1.1 | - | 0.50 | 4020 | 31 | 6930 | 54 |
| 3 | 1.2 | - | 0.50 | 4220 | 33 | 6540 | 51 |
| 4 | 1.3 | - | 0.50 | 7660 | 60 | 18900 | 147 |
| 5 | 1.4 | - | 0.50 | 7810 | 61 | 13900 | 108 |
| 6 | 1.3 | - | 0.10 | 8570 | 67 | 13600 | 106 |
| 7 | 1.3 | - | 0.25 | 7790 | 61 | 14300 | 112 |
| 4 | 1.3 | - | 0.50 | 7660 | 60 | 18900 | 147 |
| 8 | 1.3 | - | 0.75 | 4390 | 34 | 7070 | 55 |
| 9 | 1.3 | - | 1.00 | 5550 | 43 | 9410 | 73 |

[a] Given values are mole equivalent to the carboxylic acid groups.

[b] The mass of end groups has been neglected.

methanol was added to the remaining solid. All products and starting materials are soluble in methanol, except for the polyester. The polyester was collected by suction filtration and dried *in vacuo* at 70°C. The yield of all polyesters was around 90%.

**Analytical Techniques**

^{1}H NMR spectra were recorded on a Bruker AC250 Spectrometer. All spectra were recorded in CDCl$_3$ with 0.03% v/v TMS as an internal reference. Size exclusion chromatography (SEC) data were obtained using a Waters 2690 Alliance system equipped with two Styragel HR 5E columns, using THF as the eluent. The system was also provided with a Waters 410 differential refractometer. A Viscotek T50a differential viscometer detector measured the intrinsic viscosities 'on line'. The absolute molecular weights were calculated using a universal calibration method using polystyrene standards.

## RESULTS AND DISCUSSION

Our first step in optimizing the esterification method based on the use of DCC was the coupling of an aliphatic monofunctional carboxylic acid and an aliphatic monofunctional alcohol. For this model reaction, 1-hexanoic acid and 1-butanol were chosen. The degree of conversion of this reaction was determined by ^{1}H NMR. The intensity of absorption of the methylene group protons adjacent to the alcohol function in 1-butanol was compared with the resonance of the corresponding methylene group protons adjacent to the oxygen of the formed ester-bond. Using this method, we concluded that applying 0.5 mole equivalent of 4-(dimethylamino)pyridine (DMAP) as the catalyst and 1.3 mole equivalent of dicyclohexylcarbodiimide (DCC) results in a hydroxyl conversion of 0.98 . This conversion is too low, because according to Carothers [10], for stoichiometric amounts of OH and COOH groups, it would lead to a number average degree of polymerization, $\overline{X}n$, of only 50 (=1/(1-0.98)). Using 0.5 mole equivalent of 4-(dimethylamino)pyridinium 4-toluenesulfonate (DPTS) as a catalyst instead of DMAP, ^{1}H NMR spectra pointed to a complete conversion of 1-butanol to butyl-hexanoaat (see Figure 2a and Figure 2b). Although the error in the conversion, calculated on the basis of integrated ^{1}H NMR spectra, can be quite significant (± 3%), it can be concluded that DPTS is clearly a better catalyst than DMAP, as was already concluded by Moore and Stupp [4]. Varying the amount of DPTS (0.10 eq., 0.25 eq., 0.50 eq., 0.75 eq., 1.00 eq.) with the constant use of 1.3 eq. of DCC showed no change in the degree of conversion.

Our next step was the condensation of an aliphatic bifunctional carboxylic acid and an aliphatic bifunctional alcohol. We used 1,10-octanedicarboxylic acid and 1,4-butanediol. A ^{1}H NMR spectrum of synthesized polyester is
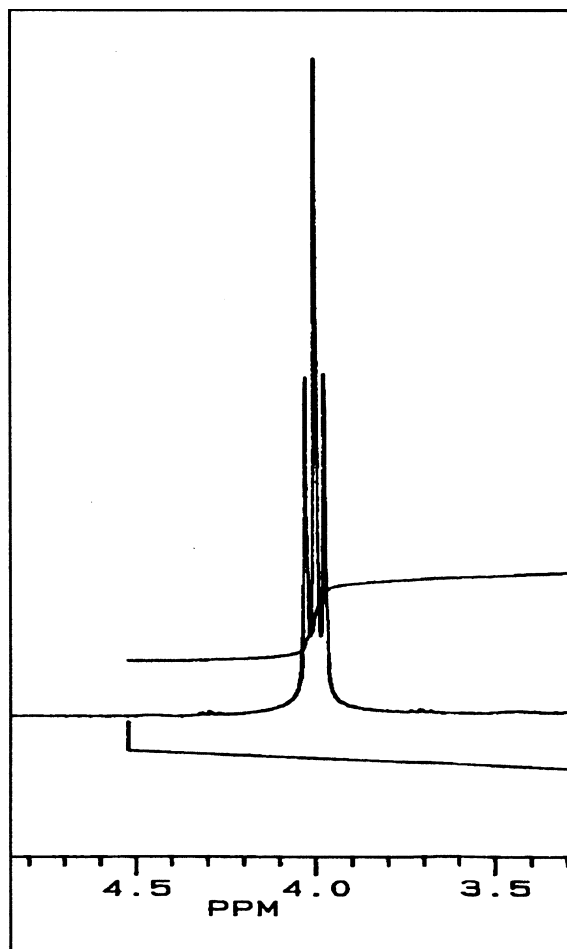
**Figure 2a.** ^{1}H NMR (250-MHz) spectrum of butylhexanoate, more specific the adsorption of the protons of the methylene group adjacent to the oxygen of the ester-bond of the protons of the methylene group adjacent to the alcohol function.

shown in Figure 3. The applied amounts of the activating agent and the catalyst, as well as the obtained molecular weights are summarized in Table 1.

The results obtained show that DMAP is an inferior catalyst compared to DPTS (see entries 1 vs 4). Upon optimizing the amount of DCC, no increase in molecular weight was obtained beyond 1.3 eq. DCC (see entries 2 to 5). Optimizing the amount of DPTS showed that the highest molecular weights are obtained using the lowest amount of DPTS (see entry 4 and entries 6 to 9). A possible explanation for this may be that the DPTS, which is a salt, contains
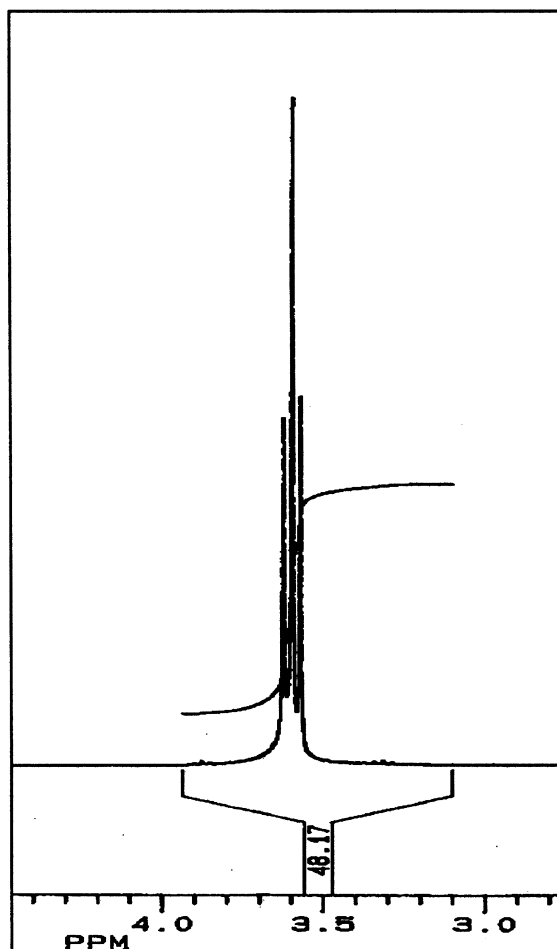
**Figure 2b.**   ^{1}H NMR (250-MHz) spectrum of 1-butanol, more specific the adsorption.

small quantities of water, which can limit the degree of polymerization. Nevertheless, Moore and Stupp describe the DPTS as being not hygroscopic [4]. The amount of DPTS had no effect on the degree of conversion in the synthesis of butylhexanoate. This can be explained by the fact that the characterization was performed by ^{1}H NMR and the differences in degree of conversion are to small to be quantified by ^{1}H NMR. Closer study of the molecular weight distributions revealed that the polyesters with higher $\overline{M}$w's exhibit a bimodal molecular weight distribution, with a low molecular weight fraction around 1500-2500
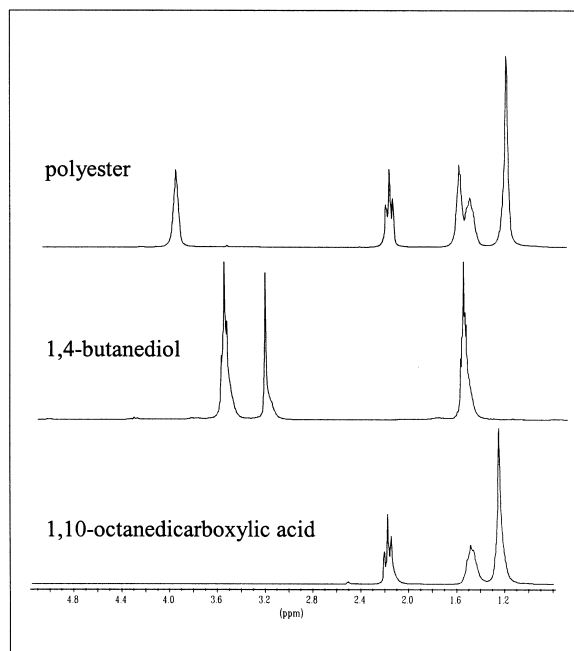
**Figure 3.** ^{1}H NMR (250-MHz) spectra of the monomers and of polyester synthesized from 1,4-butanediol and 1,10-octanedicarboxylic acid.

g/mole. This low molecular weight fraction is also present in the polyesters with lower $\overline{M}w$ values, but merely as a low molecular weight shoulder. This might explain the higher polydispersity of the polyesters with higher $\overline{M}w$'s, since the influence of a low molecular weight fraction on $\overline{M}n$ is larger for polymers having a high molecular weight compared to polymers having a low molecular weight.

For the condensation of hydroxyacids with use of DCC and DPTS, Linert and Wagener obtained number average degrees of polymerization of about 30 [2]. Moore and Stupp were able to obtain polyesters from hydroxyacids with a number average degree of polymerization higher than 50 using the same method [4]. So compared to these results, we were able to synthesize fully aliphatic polyesters, starting from diols and dicarboxylic acids with a comparable or higher number average degree of polymerization. Our results are especially encouraging in view of the fact that equivalence of reactive groups is guar-

anteed when hydroxyacids are used [4, 9], whereas in our case the degree of polymerization can be limited by small weighing errors.

## CONCLUSION

It was already shown that the use of DCC as activating agent and DPTS as catalyst offers a low-temperature and mild method for the synthesis of poly-esters, starting from partially or fully aromatic hydroxyacids [4, 9]. This paper shows that this method can also be used for the condensation of aliphatic diols and aliphatic dicarboxylic, with high degrees of polymerization as a result. The polymers can be prepared at room temperature in methylene chloride, using 1.3 mole equivalents of DCC and merely 0.10 mole equivalent of DPTS to the car-boxylic acid groups.

## ACKNOWLEDGEMENT

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