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Synthesis of multifunctional coupling agents and their selective reactions with hydroxy and amino groups in the melt

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ABSTRACT

Three new coupling agents with different numbers of *N*-acyl lactam and 4*H*-3,1-benzoxazin-4-one groups were synthesized. A selective stepwise conversion of the coupling agents with 1-dodecanol and 1-dodecylamine was demonstrated by means of solvent-free model reactions in melt at 195 and 210 °C, respectively. These coupling agents are regarded as potential cores for the synthesis of novel star-like compounds and polymers with defined arms varying in type and lengths.

1. Introduction

Coupling reactions are widely used in organic chemistry. Besides immediate coupling, utilization of coupling agents has become more and more important especially in those cases where the reactivity of groups to be coupled is not high enough to achieve direct coupling. Equal functional groups can be linked relatively easily by using symmetric bifunctional coupling agents such as bisoxazolines,[1] bisoxazinones,[2] diisocyanates,[3] bislactams,[4,5] and bisepoxides.[6] Such coupling agents have very often been used in polymer chemistry as chain extenders and compatibilizers. However, they are only partly usable when linking different compounds or components in a defined manner. Here, coupling agents with different highly selective reacting groups are required. Under the above mentioned symmetric bifunctional coupling agents, only carbonylbiscaprolactam (CBC) meets this requirement. Loontjens et al.[7] figured out that the lactam groups of CBC possessed different reactivity. In bulk at 100 °C, the conversion of equimolar amounts of amino or hydroxy group terminated oligomers with CBC yielded *N*-carbamoyl caprolactam terminated oligomers. The remaining *N*-carbamoyl caprolactam group is on disposal for further reactions. At higher temperatures, this selectivity is lost. We have introduced a new bifunctional coupling agent with one oxazoline and one 4*H*-1,3-benzoxazin-4-one (hereinafter referred to as benzoxazinone) group for the simultaneous conversion of carboxylic and amino groups, respectively.[8–11] These reactions have proved to be very selective at higher temperatures up to 220 °C.

An even greater challenge is a selective linking reaction between aliphatic hydroxy and amino groups, which do not react with each other under normal conditions. As described by Milstein et al.,[12] direct coupling between both groups could be performed by a dehydrogenation reaction in the presence of a ruthenium catalyst resulting in the formation of an amide bond. Zeng and Guan[13] utilized this reaction for the preparation of polyamides. One limitation of this reaction is that it has to be performed in solvents.

Selective coupling reactions that link aliphatic hydroxy and amino groups in a defined manner in the melt are rare. Reason for this is their similar reactivity at elevated temperatures. As typical nucleophiles, both groups react with carboxylic acids, acid chlorides, acid anhydrides, epoxides, *N*-acyl lactams, isocyanates, etc. Toward benzoxazinone groups, amino groups have proved to be distinctly more reactive than hydroxy groups.[14] We utilized this behavior in developing a new selectively reacting bifunctional coupling agent for amino and hydroxy groups in melt.[14,15] Beside the benzoxazinone group, this coupling agent possesses an *N*-acyl lactam group, which serves as a potential reactant for hydroxy groups. The chemistry of benzoxazinones and *N*-acyl lactams is described in detail.[16–18]

In this article, we describe the synthesis of novel tri- and tetrafunctional coupling agents (**CA1**–**3**) containing *N*-acyl lactam and benzoxazinone groups in varying numbers. These coupling agents are designed for solvent-free coupling reactions up to 220 °C. This is especially important for polymers, which are usually processed in the melt. Their selective reactivity with amino and hydroxy groups

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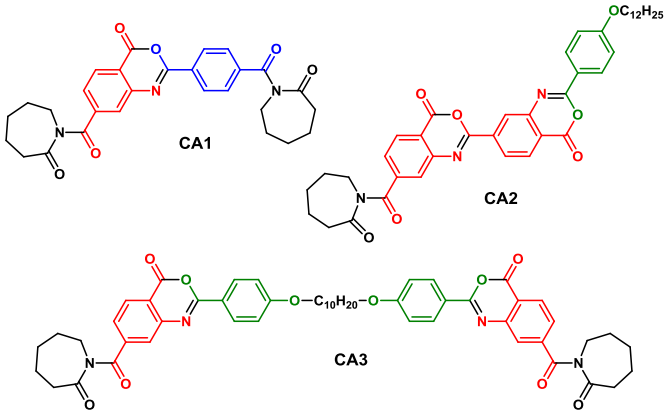
is demonstrated by means of model reactions. These coupling agents are regarded as potential cores for the synthesis of novel star-like compounds and polymers with defined arms varying in type and lengths.

2. Results and discussion

The new compounds **CA1**–**3** were synthesized following the principles described in our earlier publication.[14] The benzoxazinone and *N*-acyl lactam functional groups contained therein are derivatives of carboxylic acids. For the preparation of **CA1**–**3** three basic compounds are used, these are terephthalic acid (**TA**), 2-aminoterephthalic acid (**ATA**), and 4-hydroxybenzoic acid (**HBA**) as illustrated by means of color enhancements in Scheme 1. The synthetic approach is very similar for all three compounds. At first, the benzoxazinone group is synthesized by conversion of the amino group of **ATA** with the acid chloride of alkoxybenzoic or monomethoxylated terephthalic acid followed by cyclization in the presence of a water withdrawing agent (acetic anhydride). After cyclization, the carboxylic groups are converted into acyl chloride groups, which after reaction with ε-caprolactam (**CL**) form the *N*-acyl lactam groups. The specific synthetic routes of **CA1**, **CA2**, and **CA3** are shown in Schemes 2–4, respectively.



Scheme 1. Multifunctional coupling agents with *N*-acyl lactam and benzoxazinone groups in varying numbers.

As shown in Scheme 2, synthesis of **CA1** starts from 4-(methoxycarbonyl)benzoyl chloride, the acyl chloride group of which is converted with the amino group of **ATA** under Schotten–Baumann conditions yielding compound **1**. After deprotection of the ester group of **1** by saponification with KOH and cyclization in presence of acetic anhydride compound **2** is obtained. The carboxylic groups of **2** are activated by $SOCl_2$ and reacted with **CL** yielding compound **3** (**CA1**). Alternatively, cyclization of deprotected **1** can also be performed in presence of $SOCl_2$ with simultaneous activation of the carboxylic groups. The latter route, however, is accompanied by the formation of side products, which makes purification of the final product more difficult.

Synthesis of **CA2** is depicted in Scheme 3. Here, **HBA** is reacted first with an alkyl bromide resulting in compound **4**. The carboxylic group of **4** is chlorinated with $SOCl_2$ and then reacted with the amino group of **ATA**. Cyclization of the resulting intermediate **5** proceeds as described above yielding compound **6** with one benzoxazinone group. To introduce a second benzoxazinone group, the whole procedure including chlorination, reaction with **ATA**, and cyclization is repeated. In the last step, the carboxylic group of **8** is converted into an *N*-acyl lactam group as described for **CA1**.

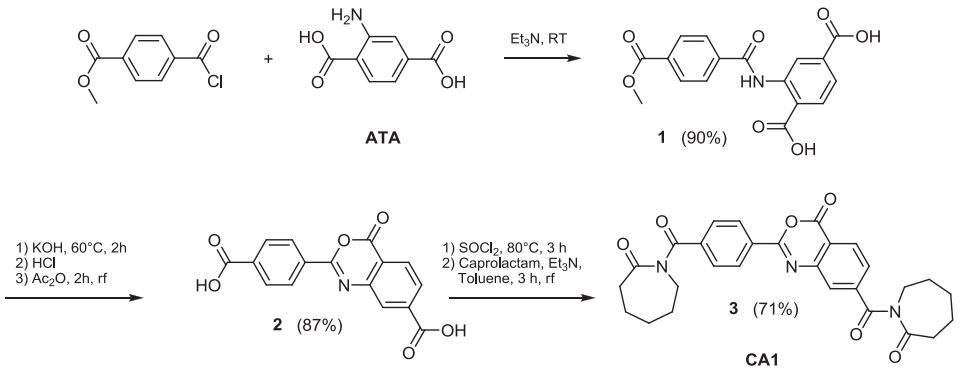
Synthesis of **CA3** follows nearly the same protocol (see Scheme 4). However, instead of an alkyl bromide, **HBA** is converted with a dibromoalkane to yield the symmetric dicarboxylic acid **10**. This is followed by a successive introduction of a benzoxazinone group and an *N*-acyl lactam group on both sides as described for **CA2**.

In the syntheses of compounds **CA1**, **CA2**, and **CA3**, we avoided laborious workup of the intermediates. The carboxylic acid intermediates are difficult to be recrystallized because of their reduced solubility in organic solvents. Therefore, only some of the acyl chloride intermediates, but all final products were recrystallized in toluene or acetone. This approach ensures acceptable overall yields at high purity of the final products.

Thermal behavior and solubility of compounds **CA2** and **CA3** can be tailored by the length of their aliphatic parts. For our purposes, melting points between 170 and 220 °C are required. With T_m=185 °C, 180 °C, and 171 °C for **CA1**, **CA2**, and **CA3**, respectively, all values meet our requirements.

The reactivity of the synthesized compounds with aliphatic hydroxy and amino groups was tested at higher temperatures in melt. For this, model reactions were performed with 1-dodecanol and 1-dodecylamine. In our earlier publications[14,15] it has been shown that the reactivity of amino groups with benzoxazinone and *N*-acyl lactam groups was not selective. Both groups react in a similar extent. Therefore, the conversions of the *N*-acyl lactam groups with 1-dodecanol were performed first at 195 °C. This is an elimination reaction in the course of which **CL** is generated. In the second step, the benzoxazinone groups of intermediates **I1**–**3** were converted in an addition reaction with 1-dodecylamine at 210 °C. The reactions are depicted in Scheme 5.

The conversion with 1-dodecanol proceeded with pronounced selectivity. However, a certain portion of the benzoxazinone groups (20, 4, and 7% for **CA1**–**3**, respectively) reacted also by ring opening as determined by ^{1}H NMR measurements. The side products could be separated by recrystallization in acetone yielding pure intermediates **I1**–**3** with unreacted benzoxazinone groups. The conditions applied (195 °C, 2 h) represent a compromise with regard to selectivity and



Scheme 2. Synthesis of coupling agent **CA1**.