Carbohydrate Polymers 92 (2013) 997–1005

Contents lists available at SciVerse ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

Kinetics and mechanism of imidazole-catalyzed acylation of cellulose in LiCl/*N*,*N*-dimethylacetamide

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A R T I C L E I N F O

Article history:
Received 23 May 2012
Received in revised form 2 October 2012
Accepted 4 October 2012
Available online 12 October 2012

Keywords:
Kinetics
Imidazole-catalyzed homogeneous acylation
Cellulose
Anhydrides

A B S T R A C T

Cellulose acylation by anhydrides (ethanoic to hexanoic) plus tosyl chloride, TsCl, or imidazole in LiCl/*N*,*N*-dimethylacetamide solution has been studied. Contrary to a previous claim, TsCl does not catalyze acylation. For the diazole-catalyzed reaction, *N*-acylimidazole is the acylating agent. Third order rate constants (k_3; 40–70 °C) have been calculated from conductivity data and split, by using information from model compounds, into contributions from the primary- ($k_{3;\mathrm{Prim(OH)}}$) and secondary- ($k_{3;\mathrm{Sec(OH)}}$) hydroxyl groups of cellulose. Values of $k_{3,\mathrm{Prim(OH)}}/k_{3,\mathrm{Sec(OH)}}$ are >1, and increase linearly as a function of increasing the number of carbon atoms of the acyl group. Rate constants and the degree of biopolymer substitution decrease on going from ethanoic- to butanoic-, then increase for pentanoic- and hexanoic anhydride, due to enthalpy/entropy compensation. Relative to the uncatalyzed reaction, the diazole-mediated one is associated with smaller enthalpy- and larger entropy of activation, due to difference of the acylating agent.

1. Introduction

Although the acylation of cellulose in LiCl/*N*,*N*-dimethylacetamide (DMAC) and in other solvent systems, e.g., tetraalkylammonium fluoride hydrate/DMSO by carboxylic acid anhydrides and acyl chlorides is efficiently catalyzed by tertiary amines, e.g., imidazole, Imz, or 4-(*N*,*N*-dimethylamino)pyridine there is no information on the kinetics and activation parameters of these reactions. This information is important *per se*, and because it allows calculation of the reaction time under a given set of experimental conditions, an important aspect in green chemistry. Additionally, kinetic data are required in order to compare: (1) The efficiency of different catalysts for the same derivatizing agent/solvent; (2) the reactivity of distinct derivatizing agents in the same solvent; (3) the reactivity of celluloses with different structural characteristics, under fixed reaction conditions.

A principle reason for the lack of kinetic studies is that they are laborious, involving determination of the degree of the biopolymer substitution, DS, as a function of reaction time (t), e.g., by saponification and subsequent back titration of the residual base. Consequently, the calculation of the observed rate constants, k_{obs} is based on a limited number of data points, e.g., 3–12 (Kwatra, Caruthers, & Tao, 1992; Tosh & Saikia, 2000; Tosh, Saikia, & Dass, 2000). Recently, we have shown that conductivity is a convenient experimental technique for investigating the kinetics of the uncatalyzed acylation of microcrystalline cellulose, MCC, in LiCl/DMAC (Nawaz, Casarano, & El Seoud, 2012). By using cyclohexylmethanol (CHM, one primary hydroxyl; Prim(OH)) and *trans*-1,2-cyclohexanediol (CHD, two secondary hydroxyls; Sec(OH)) as models for the C6-OH, and the C2-OH plus C3-OH groups, respectively of the anhydroglucose unit, AGU, of cellulose, we were able to split the overall rate constants into contributions from the distinct hydroxyl groups. The dependence of the rate constants and DS on the number of carbon atoms of the acyl group, *N*c, has been explained based on the reaction activation parameters (Nawaz et al., 2012).

We have now extended this study to MCC-catalyzed acylation in the same solvent system by carboxylic acid anhydrides; ethanoic-, propanoic-, butanoic-, pentanoic-, and hexanoic anhydride (all *normal-chain* compounds). It has been claimed that this reaction is catalyzed by tosyl chloride, TsCl (Tosh and Saikia, 2000; Tosh et al., 2000). The latter reaction however, was not faster than that its uncatalyzed counterpart! By using ^{1}H NMR, we have shown that the acetylation reaction is not subject to catalysis due to the (claimed) formation of a reactive intermediate (mixed carboxylic-sulfonic anhydride, vide infra) which (presumably) reacts with cellulose (Tosh and Saikia, 2000; Tosh et al., 2000). We have then studied the imidazole (Imz)-catalyzed acylation. Use of ^{1}H NMR and FTIR has confirmed the intermediate formation of *N*-acylimidazole; a combination of kinetic data and theoretical calculations has shown that this is the actual acylating agent, in agreement with previous opinions (El Seoud,

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http://dx.doi.org/10.1016/j.carbpol.2012.10.009

Menegheli, Pires, & Kiyan, 1994; Hussain, Liebert, & Heinze, 2004).

Rate constants and activation parameters have been calculated from the dependence of solution conductivity (λ) on reaction time (t) at different temperatures (T). By using information from the hydroxyl groups of CHM and CHD, we were able to split the overall third-order rate constants (k_3) into contributions from both types of hydroxyl groups. Values of $k_{3;\mathrm{Prim(OH)}}/k_{3;\mathrm{Sec(OH)}}$ were >1, and increase linearly as a function of increasing Nc. *All parameters* of this reaction, rate constants, activation parameters, DS, show a nonlinear dependence on Nc, namely: a change from ethanoic- to butanoic anhydride in one direction, followed an opposite change for pentanoic-, and hexanoic anhydride, vide infra. This is attributed to subtle and compensating changes of the reaction enthalpy, $\Delta H^{\neq}$, and entropy, $\Delta S^{\neq}$, to the free energy of activation, $\Delta G^{\neq}$. Relative to the uncatalyzed reaction, the rate enhancement is due to a decrease in $\Delta H^{\neq}$, with concomitant increase in $\Delta S^{\neq}$.

2. Experimental

2.1. Solvents and reagents

All solvents and reagents were purchased from Alfa Aeser, Merck, or Mensalão Cachoeirense Química and were purified as recommended elsewhere (Armagero & Chai, 2003). TsCl was purified by dissolving 10 g in 25 ml of dry chloroform. The solution was filtered, 125 mL of dry hexane was added, the solution filtered, and the solvent evaporated to give a white solid, m.p. 67–68 °C; literature m.p. 67–69 °C (Hacon et al., 2007). DMAC was purified by distillation from CaH_2. Its purity was established by measuring its density at 25 °C, 0.9372 (DMA 4500D digital densimeter, Anton Paar, Graz) (Lide, 2004). The pH of 20% solution DMAC in water was equal to that of water. The expanded-scale pH paper employed is able to detect 1.4×10^{-4} mol L^{-1} of diethylamine. MCC (Avicel PH 101) was obtained from FMC, Philadelphia (degree of polymerization by viscosity, DPv = 150); (ASTM 2001) index of crystallinity, Ic, by X-ray diffraction = 0.82 (Buschle-diller & Zeronian, 1992).

2.2. Preparation of solution of cellulose in LiCl/DMAC

LiCl was dried at 300 °C for 2 h, and then cooled to room temperature under reduced pressure. The electrolyte was quickly weighed (6.0 g; 0.141 mol) in 100 mL volumetric flask; 80 mL of dry DMAC were added, the flask was closed with a drying tube and sonicated (Laborrette 17, Fritsch, Berlin) until a clear solution was obtained, *ca.* 3.5 h. The solution volume was completed to the mark with fresh solvent.

MCC (2.0 g; 12.3 mmol) and LiCl (6.0 g) were weighed into a 250 mL three-neck round-bottom flask. The latter was equipped with a stopcock, 100 mL graduated addition funnel (no equilibration side arm) and a magnetic stirring bar. The flask was immersed into an oil bath, and then connected to a vacuum pump. The pressure was reduced to 2 mmHg, the system was heated to 110 °C in ca. 35 min, and then kept under these conditions for (additional) 30 min. The vacuum pump was turned off, the stopcock closed, the heating bath removed, and 60 mL of pure DMAC were added dropwise. The system was then brought to atmospheric pressure with dry, oxygen-free nitrogen. The addition funnel was substituted by a condenser with a drying tube, and the flask was quickly equipped with an efficient mechanical stirrer. The temperature was raised to 150 °C in *ca.* 35 min, and the cellulose slurry was vigorously stirred for 90 min (IKA Labortechnik, model RW 20, 500 rpm) at this (bath) temperature. The latter was decreased to 50 ± 5 °C in 2 h, and the slurry was left under these conditions with magnetic stirring overnight; a clear cellulose solution was obtained. The cellulose solution was transferred to 100 mL volumetric flask, whose volume was completed by adding DMAC that has been employed in washing the walls of the round-bottom flask.

Table 1
Experimental details for the imidazole-catalyzed acylation of hydroxyl-carrying compounds (ROH).[a,b]

ROH	[ROH]; listed as mol L^{-1} (OH)	Anhydride concentration; mol L^{-1}	Imidazole concentration; mol L^{-1}
CHM	0.0288	0.288	0.576
CHD	0.0576	0.576	1.152
MCC	0.0864	0.864	1.728

[a] The experiment was carried out by adding 10 mL of ROH in 6% LiCl/DMAC to 5 mL of a solution of acid anhydride plus imidazole in pure DMAC. The final LiCl concentration was 4%, or 0.943 mol L^{-1}.

[b] CHM, CHD, and the AGU of MCC carry one, two, and three (OH) groups per molecule, respectively. Therefore the ROH concentrations are listed as moles of (OH)/liter. As shown in the second and third columns, the molar ratios [reagent]/[OH] are 10 and 20 for acid anhydride, and imidazole, respectively.

2.3. Kinetics of acylation of the model compounds and cellulose

The progress of the acylation reaction was monitored by following the increase in solution conductivity (λ) as a function of (t), at a constant (T). We have employed Fisher Accumet AR-50 ion meter, equipped with Metrohm 6.0910.120 conductivity electrode, inserted in a home-built double-walled conductivity cell through which water is circulated from a thermostat, as shown in previous work (Nawaz et al., 2012). Data acquisition and the solution temperature were controlled with a PC. Temperature control was achieved by using a glass-covered PT-100 sensor inserted into the reaction solution, and attached to the computer via RS-232 serial port.

The experiments were carried out as follows: 5 mL of pure DMAC containing the appropriate anhydride were introduced into the conductivity cell followed by the addition of required amount of solid Imz. After thermal equilibration, the solution of the compound studied (CHM, CHD, or MCC) in 10 mL of 6% LiCl/DMAC was introduced into the conductivity cell. The increase in (λ) was recorded as a function of (t), until its value was practically constant. Table 1 shows the reagent concentrations employed, where the acronym (ROH) is employed to denote any hydroxyl group-carrying compound (CHM; CHD; MCC).

A home-developed non-linear regression analysis program, based on Marquardt–Levenberg algorithm (Press, Teukolsky, Vetterling, & Flannergy, 2007) has been employed for calculating the values of the observed rate constants (k_{obs}). It relies on minimizing the sum of the squares of the residuals. The agreement between calculated and experimental "infinity" conductivity (λ_∞) was routinely checked. The relative standard deviation in k_{obs} was ≤0.5%, that between k_{obs} of triplicate runs was <3%. The values of (k_3) were obtained by dividing the corresponding k_{obs}/[anhydride][imidazole]. The activation parameters were obtained from the dependence of k_3 on T, by using standard equations (Anslyn & Dougherty, 2006).

2.4. Synthesis and analysis of the acetylation products under the conditions of the kinetic experiment

The kinetic experiments were repeated on a larger scale (three fold), as follows: in order to simplify the separation of the acetates of CHM and CHD we used LiCl suspension in acetonitrile as solvent, instead of DMAC. The solvent, 25 mL was introduced into 100 mL three-necked round bottom flask, equipped with a condenser and a drying tube. The bath temperature was adjusted to 60 °C, and 8 mL (84 mmol) of ethanoic anhydride was added, followed by addition of, 1 g LiCl and 11.76 g (0.172 mol) of Imz;