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Hydrolytic processes and condensation reactions in the cellulose solvent system *N*,*N*-dimethylacetamide/lithium chloride. Part 2: degradation of cellulose☆

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Abstract

Certain cellulose samples, especially those of higher molecular weight, are initially insoluble in *N*,*N*-dimethylacetamide (DMAc, **1**)/lithium chloride, which is a very common solvent system for cellulosic materials. According to a common protocol, heating or refluxing these samples in DMAc, or in DMAc containing dissolved LiCl, represents one of several so-called 'activation' procedures, which are aimed at facilitating subsequent dissolution. In the present work, it is shown that the improved solubility achieved by this method is not only caused by a better activation or improved accessibility of the pulp, but also by a progressing degradation of the cellulosic material (DP loss).

The degradation of cellulose in DMAc or DMAc/LiCl is due to two separate chemical processes. The first one, involving *N*,*N*-dimethylacetoacetamide (**2**) which is the primary condensation product of DMAc, causes a slow degradation by thermal endwise peeling. The glucose units peeled off the reducing end are released as furan structures (**3**). The mechanism appears to be a thermal cleavage of the glycosidic bond, which becomes quite selective towards the proximal anhydroglucose unit by a neighbor group-assisted effect according to quantum-chemical calculations. Due to its stepwise and thus slow mechanism, this pathway contributes only insignificantly to the overall cellulose degradation.

The second degradation mechanism causes random chain cleavage and thus pronounced and rather fast changes in the molecular weight distribution. It involves *N*,*N*-dimethylketeniminium ions (**5**), whose presence in DMAc/LiCl at temperatures above 80 °C—the coalescence temperature of DMAc as determined by dynamic NMR—was unambiguously demonstrated by specific trapping in a thermal [2 + 2]-cycloaddition with lipophilic olefins. The keteniminium ion is an extremely reactive electrophile, which is able to directly cleave glycosidic bonds. The detrimental effect of this intermediate on the integrity of cellulosic pulps was confirmed by addition of an external degrading agent of the keteniminium type. Also the precursor compound, a ketene aminal, was confirmed to be present in heated DMAc or DMAc/LiCl by trapping with allyl alcohol in a spontaneous *Claisen*-type rearrangement.

Keywords: Cellulose; Cellulose solvents; *N*,*N*-Dimethylacetamide

1. Introduction

N,*N*-dimethylacetamide (DMAc, **1**) containing lithium chloride is a solvent system that is capable of dissolving cellulose within certain concentration ranges of LiCl and pulp. It has thus been used very frequently in polysaccharide chemistry [1,2], especially in synthesis for derivatization under homogeneous conditions [3,4]. Moreover, it has meanwhile become a standard solvent for gel permeation chromatography (GPC) measurements of cellulosics [5–8].

As paper pulps and some higher-molecular weight dissolving pulps are insoluble in DMAc/LiCl, several 'activation' procedures have been proposed, which aim at accelerating the dissolution in the case of soluble pulps, and at making dissolution at all possible in the case of initially insoluble pulps. Among those activation procedures are the treatment with liquid ammonia [9,10], swelling in water

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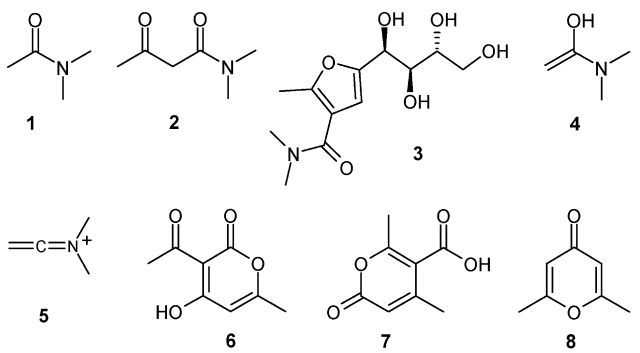
followed by solvent exchange to DMAc [5,11], freeze-drying [12], or swelling in 0.1 M LiCl followed by a number of extraction steps [13]. A very common protocol is also heating or refluxing the cellulose samples in DMAc, or in DMAc containing low concentrations of LiCl [14,15]. All activation treatments are thought to cause intra- and inter-crystallite swelling, breaking of hydrogen bonds and increased accessibility. A yellowing of the mixture upon heating in DMAc or DMAc/LiCl has been noticed, sometimes accompanied by a yellowish discoloration also of the activated pulp sample. In previous work, we have shown this discoloration to be caused by chromophores formed in LiCl-catalyzed condensation reactions from DMAc, such as dehydroacetic acid (**6**), isodehydroacetic acid (**7**), and 2,6-dimethyl-γ-pyrone (**8**). The discoloration of the pulp was demonstrated to originate also from furan-type structures (**3**) which are formed by condensation of *N*,*N*-dimethylacetoacetamide (**2**) with reducing end groups.

Herein, we wish to report the results of recent studies which revealed that cellulose undergoes progressive degradation when heated or refluxed in DMAc/LiCl [16].[1] The reactive species responsible for the degradation, such as keteniminium ion **5** and its precursor **4**, have been identified by specific trapping reactions, and the mechanisms underlying these degradation processes have been investigated in more detail.



2. Experimental

Chemicals were obtained from commercial sources. TLC was recorded on Merck pre-coated silica gel 60 plates. Computational results reported throughout this paper were performed with the Spartan '02 program package (Wavefunction Inc., Irvine, USA). Carbonyl groups have been determined according to the CCOA method [12].

NMR spectroscopy. ^{1}H NMR spectra were recorded on a Bruker Avance Instrument at 300 MHz for ^{1}H and 75.47 MHz for ^{13}C, with a probe head heatable up to 120 °C with an accuracy of ±0.1 °C. ^{13}C peaks were assigned by means of DEPT as well as HMQC and HMBC spectra. Resonances are given in ppm referenced to the solvent peak. The abbreviation 'd.i.' denotes peaks originating from two magnetically equivalent carbons.

Capillary electrophoresis. As running electrolyte a solution of 0.001% (w/v) 1,5-dimethyl-1,5-diaza-undecamethylene polymethobromide (hexadimethrine bromide, HDB), 550 mM boric acid, 5% methanol and 5% 1-propanol in purified water was used. The pH was adjusted to 10.7 with 3 M KOH. For CE measurements, a HPCE-3D instrument (Agilent Technology) equipped with a capillary column ($L = 64$ cm; $l = 56$ cm × 50 μm) and DAD-UV detector was used. The capillary was kept at 15 °C. The run current was set to −100 μA. Conditioning of the column was performed by flushing with 1.0 M aqueous NaOH for 10 min. Between the runs, the capillary was preconditioned by flushing with running electrolyte for 8 min. Absorption of the furan derivative was determined at 200 nm with the detector being placed 8 cm from the anodic end of the column. Hydrostatic injection was performed by applying 50 mbar for 8 s. To achieve optimum reproducibility, an internal standard was used for the quantification of the furan derivative **3**. Benzoic acid proved to be advantageous as its peak was clearly separated from the analyte signal. A benzoic acid stock solution was prepared by dissolving 50 mg of benzoic acid in 10 ml of water, and 15 μl of this solution were added to each analyte sample.

Gel permeation chromatography. For GPC measurements, the system as described by Schelosky et al. [7] was modified. DMAc/LiCl (0.9%, w/v), filtered through 0.02 μm filter, was used as the eluant. The sample was injected automatically, chromatographed on four serial GPC columns and monitored by fluorescence, MALLS, and refractive index (RI) detection. Molecular weight distribution and related polymer-relevant parameters were calculated by software programs, based on a RI increment of 0.140 ml/g for cellulose in DMAc/LiCl (0.9% w/v). Following parameters were used in the GPC measurements: flow: 1.00 ml/min; columns: four, PL gel, mixed A, ALS, 20 μm, 7.5 mm × 300 mm; injection volume: 100 μl; run time: 45 min.

Thermal treatment of pulps in DMAc/LiCl. Pulp samples (400 mg, o.d.) have been activated by solvent exchange (water–DMAc) and dissolved in 32 ml DMAc/LiCl (9%, w/v) over night. The pulp solution was heated to the desired temperature and samples were taken, cooled to r.t., diluted with DMAc, and analyzed by GPC. For carbonyl group determination, the samples were precipitated in 50 ml of deionized water, washed, labeled according to Ref. [12] and analyzed by GPC.

Thermal treatment of DMAc/LiCl—trapping of intermediate **4** *by allyl alcohol*. A solution of 0.5 wt% LiCl in DMAc (100 ml, 1.075 mol) was heated to 130 °C under magnetic stirring in a two-neck, 250 ml flask equipped with

[1] This study was undertaken to demonstrate the disadvantages of the heating procedure. The authors use solvent exchange (water to ethanol to DMAc) or freeze-drying as activation procedure prior to dissolution of the cellulose in DMAc, which is carried out at r.t. or preferably at 4 °C, see for instance [8,12].

a dropping inlet and an efficient reflux condenser. Allyl alcohol (10 ml) was added through the funnel after the bath temperature was reached. After 3 h, the reaction was quickly stopped by cooling the reaction vessel in a water bath. Water (200 ml) was added to the reaction mixture, which was subsequently extracted three times by ethyl acetate (50 ml). The combined organic extracts were washed with water (10 ml), dried over Na_2SO_4 and evaporated to a volume of 2 ml. Microdistillation of the residue provided 4-pentenoic acid dimethylamide (**15**) as a colorless oil.

*4-Pentenoic acid N,N-dimethylamide (**15**):*

colorless, viscous liquid; $M = 127.19$ g/mol; 2.530 g (1.85% rel. to DMAc). ^{1}H NMR ($CDCl_3$): δ 2.36 (m, 4H, CH_2–CH_2), 2.95 (s, 3H, N–CH_3), 3.01 (s, 3H, N–CH_3), 4.99 (dd, 1H, CH=CH_2, $^3J = 10.0$ Hz, $^3J = 1.5$ Hz), 5.06 (dd, 1H, CH=CH_2, $^3J = 17.5$ Hz, $^2J = 1.5$ Hz), 5.88 (m, 1H, $CH = CH_2$). ^{13}C NMR ($CDCl_3$): δ 29.1 ($^3CH_2$), 32.5 ($^2CH_2$), 35.3 (N–CH_3), 37.1 (N–CH_3), 115.0 ($=^5CH_2$), 137.6 ($^4CH=$), 172.2 (^1CO). The two N–CH_3 group are not magnetically equivalent due to the hindered rotation around the C–N amide bond.

*Thermal treatment of DMAc/LiCl—trapping of intermediate **5** by methanol*. A solution of 0.5 wt% LiCl in DMAc (100 ml, 1.075 mol) was heated to 130 °C under magnetic stirring in a two-neck, 250 ml flask equipped with a dropping inlet and an efficient reflux condenser. Methanol (15 ml) was added through the funnel after the bath temperature was reached. After 3 h, the reaction was quickly stopped by cooling the reaction vessel in a water bath. The reflux condenser was thoroughly rinsed with DMAc and replaced by a distillation bridge. The combined DMAc phases were heated at a bath temperature of 140 °C, whereupon excess methanol and the trapping product 1-dimethylamino-ethane-1,1-diol (**16**) distilled off. Redistillation provided pure **16**. The product is highly labile and hygroscopic. It will immediately react with water or atmospheric moisture to give DMAc and two equivalents of methanol, and should be kept under inert gas in the dark to avoid decomposition or yellow discoloration. For kinetic measurements, the reaction was carried out at pre-set bath temperatures (70, 90, 100, 115 and 130, 145 and 160 °C). The amount of **16** formed in relation to non-reacted methanol was determined from the integrals in the ^{1}H NMR spectrum of the crude distillate.

*1-Dimethylamino-ethane-1,1-diol (**16**):*

colorless, viscous liquid; $M = 133.19$ g/mol; 1.848 g (1.29% rel. to DMAc). ^{1}H NMR ($CDCl_3$): δ 1.13 (s, 3H, CH_3–C), 2.21 (s, 6H, N–CH_3), 3.14 (s, 6H, O–CH_3). ^{13}C NMR ($CDCl_3$): δ 12.1 (CH_3–C), 38.1 (N–CH_3), 48.3 (O–CH_3), 109.3 (CH_3–C).

*Thermal treatment of DMAc/LiCl—trapping of intermediate **5** by lipophilic olefins*. The trapping reagent—1-decen (**11**, 1.41 g, 10 mmol) or vitamin E derivative **13** (4.74 g, 10 mmol)—was added to a solution of 0.5 wt% LiCl in DMAc (100 ml, 1.075 mol) or to a suspension of pulp (5–10 wt%) in a similar solution. The mixture was heated for 3 h to 70, 90, 100, 130, and 160 °C, respectively, under magnetic stirring and cooled to room temperature. Water (200 ml) was added, the pulp was filtered off, and the mixture was extracted three times with *n*-hexane (20 ml). The combined organic extracts were washed with water and dried over Na_2SO_4. The oily, brown residue was dissolved in ethanol (5 ml) and a concentrated solution of 2,4-dinitrophenylhydrazine in 2 M sulfuric acid was added. After 1 h, water (5 ml) was added. After another hour, the yellow precipitate of the 2,4-dinitrophenylhydrazone was removed by filtration, washed with water, dried in vacuo and analyzed. The precipitation of the trapping products as 2,4-diphenylphenylhydrazone was preferred in all cases where the amount of trapping products was expected to be rather low, as for instance upon trapping in the presence of pulp or at lower reaction temperatures.

Alternatively, the combined *n*-hexane phases obtained according to the above procedure were washed with water, dried over Na_2SO_4, concentrated to a volume of about 3 ml, and chromatographed on neutral aluminum oxide (*n*-hexane/ethyl acetate, v/v = 9:1 for **12** and *n*-hexane for **14**) to provide the cyclobutanones as colorless oils.

*3-Octylcyclobutanone (**12**):*

colorless oil; $M = 182.31$ g/mol; 0.171 g (0.94 mmol, 0.09% rel. to DMAc, 9.4% rel. to **11**). ^{1}H NMR ($CDCl_3$): δ 0.91 (t, 3H, $^{8\prime}CH_3$–), 1.28 (m, 10H, $^{2\prime}CH_2$, $^{3\prime}CH_2$, $^{4\prime}CH_2$, $^{5\prime}CH_2$, $^{6\prime}CH_2$,), 1.52 (m, 4H, $^{1\prime}CH_2$, $^{7\prime}CH_2$,), 1.92 (m, 1H, ^{3}CH), 2.69 (m, 2H, $^2CH^A$, $^4CH^A$), 3.22 (m, 2H, $^2CH^B$, $^4CH^B$). ^{13}C NMR ($CDCl_3$): δ 14.1 ($^{8\prime}CH_3$), 22.6 ($^{7\prime}CH_2$); 25.9 (^{3}CH), 27.4 ($^{2\prime}CH_2$); 29.3; 29.5; 29.6 ($^{3\prime}CH_2$, $^{4\prime}CH_2$, $^{5\prime}CH_2$); 31.8 ($^{6\prime}CH_2$), 35.9 ($^{1\prime}CH_2$), 42.6 (d.i., $^2CH_2$, $^4CH_2$), 205.8 (^{1}CO).

3-Octylcyclobutanone-2,4-dinitrophenylhydrazone:

yellow crystals; m.p. = 144–146 °C; $M = 362.43$ g/mol; 0.305 g (0.84 mmol, 0.078% rel. to DMAc, 8.4% rel. to **11**). ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3H, $^{8\prime}CH_3$–), 1.28 (m, 10H, $^{2\prime}CH_2$, $^{3\prime}CH_2$, $^{4\prime}CH_2$, $^{5\prime}CH_2$, $^{6\prime}CH_2$,), 1.54 (m, 4H, $^{1\prime}CH_2$, $^{7\prime}CH_2$,), 2.56 (m, 1H, ^{3}CH), 2.65 (m, 2H, $^2CH^A$, $^4CH^A$), 3.14 (m, 2H, $^2CH^B$, $^4CH^B$), 7.86 (d, 1H, $^{6\prime\prime}$CH), 8.28 (dd, 1H, $^{5\prime\prime}$CH), 9.11 (s, 1H, $^{3\prime\prime}$CH), 10.72 (s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 14.1 ($^{8\prime}CH_3$), 22.6 ($^{7\prime}CH_2$); 27.4 ($^{2\prime}CH_2$); 28.0 (^{3}CH); 29.2; 29.4; 29.5 ($^{3\prime}CH_2$, $^{4\prime}CH_2$, $^{5\prime}CH_2$); 31.8; ($^{6\prime}CH_2$), 36.2 ($^{1\prime}CH_2$), 37.1 ($^2CH_2$), 39.5 ($^4CH_2$), 116.0 ($^{6\prime\prime}CH_2$); 123.5 ($^{3\prime\prime}CH_2$); 128.7 ($^{4\prime\prime}CH_2$); 129.9 ($^{5\prime\prime}CH_2$); 137.5 ($^{2\prime\prime}CH_2$); 144.8 ($^{1\prime\prime}CH_2$); 160.0 (^{1}CO). As *cis*/*trans* isomers occur at the C=N double bond of the hydrazone, C-2 (*cis*)

and C-4 (*trans*) of the cyclobutane moiety lose their magnetic equivalence.

*Acetic acid 3,5,6,8-tetramethyl-1-oxo-3-(4,8,12-trimethyltridecyl)-1,2a,3,8b-tetrahydro-2H-4-oxa-cyclobuta[a]naphthalen-7-yl ester (**14**):*

colorless oil; $M = 512.78$ g/mol; 0.574 g (1.12 mmol, 0.10% rel. to DMAc, 11.2% rel. to **13**). ^{1}H NMR ($CDCl_3$): δ 1.54 (s, 3H, ^{2a}C), 2.08 (s, 3H, $^{7a}CH_3$), 2.11 (s, 3H, $^{8b}CH_3$), 2.12 (s, 3H, $^{5a}CH_3$), 2.31 (s, 3H, CH_3CO), 2.86 (m, 1H, ^{4}CH), 3.05 (dd, 1H, $^4CH-CH_2^A-CO$), 3.24 (dd, 1H, $^4CH-CH_2^B-CO$), 3.85 (d, 1H, ^{3}CH). ^{13}C NMR: δ 12.0; 13.2; 13.4 ($^{5a}CH_3$, $^{7a}CH_3$, $^{8b}CH_3$), 19.2 (^{4}CH), 20.4 (CH_3CO), 22.5 ($^{2a}CH_3$), 43.1 ($^4CH-CH_2$), 65.9 (^{3}CH), 77.1 (^{2}C), 121.4 (^{4a}C), 122.3 (^{5}C), 126.1 (^{7}C), 130.2 (^{8}C), 147.5 (^{8a}C), 149.0 (^{6}C), 169.3 (COO), 210.5 (CO). Resonances of the isoprenoid side chain are not given.

Acetic acid 3,5,6,8-tetramethyl-1-(2,4-dinitrophenylhydrazono)-3-(4,8,12-trimethyltridecyl)-1,2a,3,8b-tetrahydro-2H-4-oxa-cyclobuta[a]naphthalen-7-yl ester:

yellow crystals; m.p. = 77–78 °C; $M = 692.90$ g/mol. ^{1}H NMR ($CDCl_3$): δ 1.54 (s, 3H, $^{2a\prime}$C), 2.05 (s, 3H, $^{7a}CH_3$), 2.08 (s, 3H, $^{8b}CH_3$), 2.11 (s, 3H, $^{5a}CH_3$), 2.30 (s, 3H, CH_3CO), 2.85 (m, 1H, ^{4}CH), 2.92 (dd, 1H, $^4CH-CH_2^A-CO$), 3.11 (dd, 1H, $^4CH-CH_2^B-CO$), 3.55 (d, 1H, ^{3}CH), 7.82 (d, 1H, $^{6\prime\prime}$CH), 8.32 (dd, 1H, $^{5\prime\prime}$CH), 9.04 (s, 1H, $^{3\prime\prime}$CH), 11.03 (s, 1H, NH). Resonances of the isoprenoid side chain are not given. Authentic samples of cyclobutanones **12** and **14** and their 2,4-dinitrophenylhydrazones were prepared according to literature procedures, and were identical to those described above.

Thermal treatment of model compounds in DMAc/LiCl. A solution of the carbohydrate model compound (5 wt%) in DMAc (10 ml) containing 0.5 wt% LiCl was heated for defined times at pre-set bath temperatures (80, 100, 115, 130, 145 and 160 °C). In regular time intervals of 10 min, a TLC of the reaction mixture was recorded. A sample of the final reaction mixtures was analyzed by CE. To isolate the furan **3** formed, the reaction mixture was added to 20 g of silica gel suspended in 50 ml of CH_2Cl_2. The mixture was transferred into a column filled with 150 g of a mixture of basic aluminum oxide and anhydrous potassium carbonate (w/w = 9/1). Excess DMAc was removed with ethyl acetate, product **3** was eluted with ethyl acetate/methanol (v/v = 2/1).

In an NMR tube, cellotetraose was heated in DMAc-d_9 containing 0.5% LiCl for 48 h. At regular intervals ^{1}H and H,H-COSY spectra were recorded to monitor the course of the reaction. The progressing formation of **3** was measured by means of the resonance at 5.90 ppm, corresponding to the aromatic proton at the furan moiety of **3**.

3. Results and discussion

3.1. Cellulose degradation in heated DMAc/LiCl

GPC measurements demonstrated unambiguously that cellulosic material suffered a loss in average degree of polymerization (DP) upon heating in DMAc/LiCl, cf. Figs. 1 and 2. Already at temperatures as low as 85 °C there was a noticeable decrease in molecular weight. The DP loss got more pronounced as temperature and LiCl content increased. At temperatures near the boiling point of DMAc (164 °C) the molecular weight degradation became rather severe. Pulp degradation in the absence of LiCl is less pronounced than in its presence. Degradation was observed for all pulps, but the degradation rate differed for pulps of different provenience, as exemplarily shown in Fig. 1 for a Beech sulfite pulp and a Eucalyptus prehydrolysis kraft pulp.

It is well-known that heating initially insoluble pulps in DMAc/LiCl causes a faster dissolution of the material in DMAc/LiCl. However, the observed improved solubility is evidently accompanied by a progressing DP loss of the pulp. Thus, the solubility gain is not only due to improved activation, i.e. swelling or breaking of hydrogen bonds; but also due to a degradation of the high-molecular weight pulps. Heating in DMAc/LiCl significantly influences the molecular weight distribution of the pulps. Consequently, GPC results from pulps which have undergone such an activation treatment will not reflect the data of the genuine cellulosic starting material.

The degradation process was also investigated by the CCOA method [12], which affords carbonyl group profiles relative to the molecular weight, based on fluorescence labeling. Although an increase in carbonyl groups with increasing heating times (Fig. 2) was observed, this is mainly due to the higher amount of reducing end groups present in samples with decreased molecular weight. Thus,

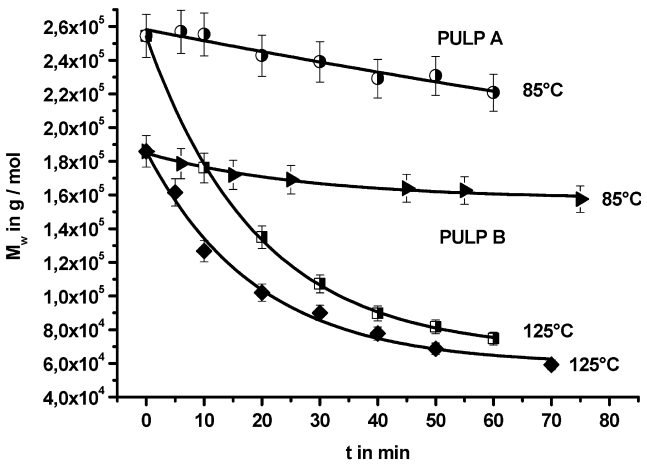


Fig. 1. Degradation of two different pulps upon heating in DMAc/LiCl (9% w/v) at different temperatures. Pulp (A) Beech sulphite pulp; pulp (B) Eucalyptus prehydrolysis kraft pulp, error bars 5%.

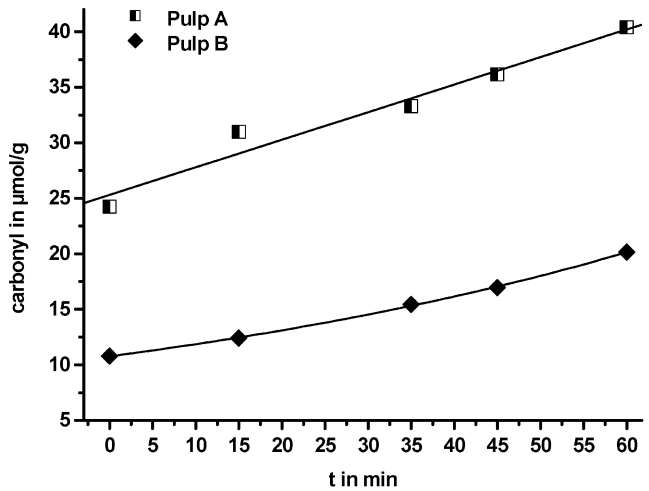


Fig. 2. Changes in the carbonyl content of two pulps upon heating in DMAc/LiCl (9% w/v) at 125 °C. Pulp (A) Beech sulphite pulp; pulp (B) Eucalyptus prehydrolysis kraft pulp.

the degradation of pulps in heated DMAc/LiCl is largely not of oxidative origin. The changes in carbonyl content relative to molecular weight (carbonyl DS plots) and the differential molecular weight distributions at different heating times are given in Fig. 3.

Two degradation processes, which contribute to the DP loss, have been identified and will be discussed in the following: an 'endwise peeling' reaction causing a rather slow decrease in the molecular weight, and a cleavage of glycosidic bonds by keteniminium ions, which is responsible for a much faster DP loss.

3.2. 'Thermal endwise peeling' under formation of furan structures

As described in Part I of this work, thermal treatment of pulp in DMAc/LiCl causes the formation of *N*,*N*-dimethylacetoacetamide (**2**), which is a highly reactive 1,3-dicarbonyl compound readily undergoing subsequent

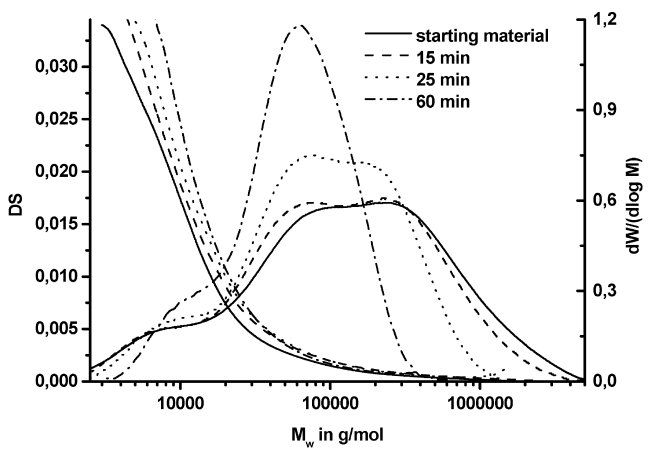


Fig. 3. Cellulose degradation of pulp A by heating in DMAc/LiCl (9% w/v) at 125 °C. Changes in the differential molecular weight distribution and carbonyl DS at different heating times.

conversions. The first step in these processes is the aldol-type reaction between the highly activated, CH-acidic methylene group of **2** and the aldehyde structure of a reducing end group. The reaction with glucose caused formation of furan derivative **3**, with C1 and C2 of the sugar and C2 and C3 of the acetoacetamide being incorporated into the heterocycle.

Surprisingly, **3** was also formed when pulp was heated in DMAc, and the formation was rather continuous over time. The formation of **3** from pulp was strongly accelerated when excess **2** was added to the DMAc. From these results, it became evident that not only the reducing ends are derivatized forming furan structures, but these structures are subsequently cleaved and released as **3**. In summary, a cellulose chain with n anhydroglucose units forms the corresponding furan derivative, which is subsequently peeled off as **3** leaving behind the $(n-1)$-cellulose chain with a 'new' reducing end, which again reacts with **2** and is once more cleaved. *N*,*N*-Dimethylacetoacetamide, the main thermal condensation product of DMAc, thus eventually causes a thermal endwise peeling of the pulp.

This peeling mechanism was confirmed with cellotetraose. While formation of the furan structures started at temperatures as low as 80 °C, the subsequent peeling steps required temperatures above 110 °C to proceed. Cellotetraose thus formed first the corresponding furan derivative, which was then cleaved to give cellotriose and **3** (as controlled by TLC). The cellotriose reacted immediately to give the corresponding furan from which again **3** was peeled off under formation of cellobiose. Cellobiose, eventually, was cleaved into two molecules of **3**. Thus, the starting oligosaccharide was neatly degraded to four molecules of furan **3** without formation of byproducts (TLC, NMR) within 4 h at 130 °C. This mechanism of thermal endwise peeling of cellotetraose can be summarized as in Eq. (4), with Eqs. (1)–(3) describing the consecutive, step-wise character of furan formation:

$$(\mathrm{Glc})_4 + \mathbf{2} \rightarrow (\mathrm{Glc})_3 + \mathbf{3} \quad (1)$$

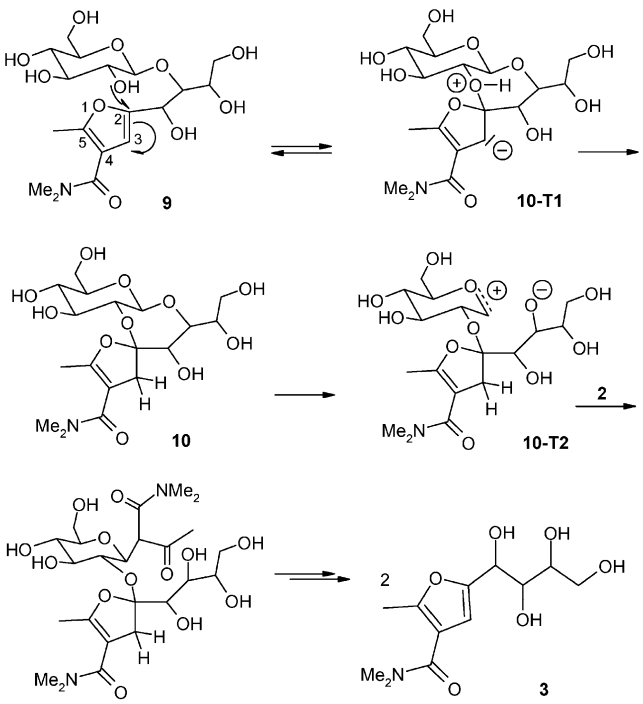
$$(\mathrm{Glc})_3 + \mathbf{2} \rightarrow (\mathrm{Glc})_2 + \mathbf{3} \quad (2)$$

$$(\mathrm{Glc})_2 + \mathbf{2} \rightarrow \mathbf{3} + \mathbf{3} \quad (3)$$

$$(\mathrm{Glc})_4 + \mathbf{2}(4\ \mathrm{eq.}) \rightarrow \mathbf{3} \quad (4)$$

As pulp and also cellotetraose formed exclusively **3**, but no other furan structures, the degradation mechanism must be progressing from the reducing end. Cleavage of glycosidic bonds other than the proximal one does not occur.

A possible explanation of the observed reaction behavior was found by computational chemistry. The approach involved conformational search, localization of transition state structures, and computation of reaction energetics performed on the furan derivative of cellobiose (**9**), details of which will be published elsewhere. In its minimum conformation, C-2 of the furan ring is placed in close proximity to the C-2 hydroxyl group of the non-reducing anhydroglucose unit (Scheme 1). This pre-organization



Scheme 1.

effect facilitates the addition of the hydroxyl group to the furan ring via a zwitterionic transition state (**10**-**T1**). The addition is an endothermic process with a free reaction enthalpy of +68 kJ/mol and a relatively large activation energy of +115 kJ/mol at 393 K. Moreover, it is a reversible reaction; addition/elimination reactions of alcohols or hydroxyl ions to/from furans are well-known from organic chemistry [17,18]. The resulting seven-membered ring structure **10**, a perhydro-1,4-dioxepane derivative, is labile and will most likely fragment into the starting material **9**. This elimination of the O-2 from the dihydrofuran structure under regeneration of **9** is exothermic by −68 kJ/mol. However, ring opening by cleavage of the glycosidic bond between C-1′ and O-1′ becomes a competitive pathway with relatively low activation energy (82 kJ/mol) to form the corresponding zwitterionic transition state (**10**-**T2**). This pathway is additionally energetically favored by its high overall exothermicity (−164 kJ/mol), originating in concomitant formation of a second furan structure by reaction with the acetoacetamide **2**, so that eventually two molecules of furan derivative **3** are formed.

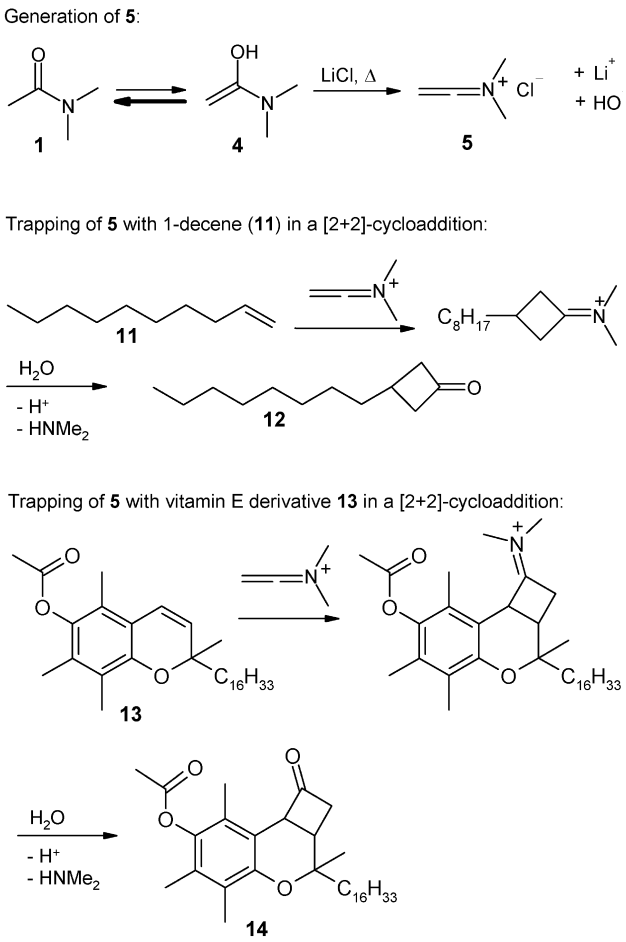
Thus, in summary cellobiose was converted by two molecules of **2** to two molecules of furan derivative **3** in a neighbor-group assisted reaction. According to the proposed mechanism, cleavage of the glycosidic bong occurs only on that glycosidic bond which is in close proximity of the downstream, proximal furan structure in agreement with experimental data. All other glycosidic bonds are stable under the prevailing conditions as no neighboring, activating furan structures are available. The rate-determining step of the reaction is the addition of the C-2 hydroxyl group to the furan structure with formation of **10**. The endothermicity and high activation energy of this process explain that relatively high temperatures are required for the reaction to proceed at noticeable rate. The calculation provides a rational explanation for the observed regioselectivity of the bond cleavage, i.e. the thermal endwise peeling in form of furan **3**, and for the activating effect of the furan structure. Experimental verification of the mechanism, for instance by using cellobiose carrying a methoxy group at C-2 (which would not undergo addition to the furan and thus would not peel off **3** from the reducing end), was not produced so far.

In the case of pulps, the molecular weight changes effected by the thermal peeling are negligible as compared to those described in the following.

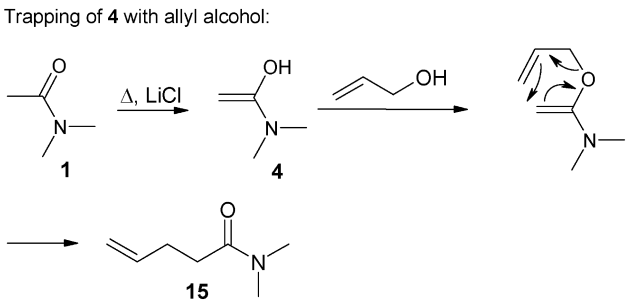
3.3. Cleavage of glycosidic bonds by keteniminium ions

The observed molecular weight degradation of cellulosic material in heated DMAc must be caused by a cleavage of glycosidic bonds along the cellulose chains, as the endwise peeling by furan structures cannot account for such a pronounced DP loss: if the decrease in molecular weight were only due to endwise peeling, large amounts of peeled-off furan structures **3** should be present, but only minute amounts were found. Thermal endwise peeling by furan structures and cleavage of glycosidic bonds along the cellulose chain are thus two separate parallel processes, which both cause a decrease in molecular weight of the pulp heated in DMAc, the first one proceeding only slowly, the latter one rather fast.

The question how the chain cleavage was accomplished was difficult to answer at first, as *N*,*N*-dimethylacetoacetamide (**2**) causes only the slow endwise peeling, and the other thermally formed byproducts of DMAc (see Part I) do not effect a chain cleavage at all. This lead us to the assumption that another, even more reactive species, might be present as intermediate. By means of trapping reactions we were able to confirm that *N*,*N*-dimethylketeniminium cations (**5**) are present in DMAc/LiCl (0.5 wt%) at temperatures above 80 °C (Scheme 2). Keteniminium salts are extremely reactive compounds, they are more electrophilic than ketenes and do not dimerize as most ketenes do [19,20]. For proving the occurrence of this intermediate we used a typical reaction of keteniminiums (and ketenes), the reaction with non-activated olefins which produces cyclobutanes in a thermal, i.e. suprafacial–antarafacial, [2 + 2]-cycloaddition. Lipophilic trapping reagents offer the advantage that they can be readily extracted even from complex mixtures. 1-Decene (**11**) and 3,4-dehydro-α-tocopheryl acetate (**13**) were chosen as the olefinic traps, the latter has the advantage of a high boiling point so that it can be used also in refluxing DMAc without yield penalty. The intermediacy of **5** was then unambiguously proven by isolation of the trapping product 3-octylcyclobutanone (**12**), and cyclobutanone **14** (Scheme 2). The regioselectivity of



Scheme 2.



Scheme 3.

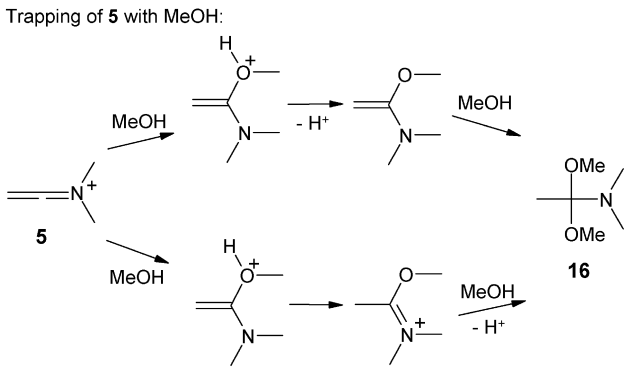
the addition reaction, e.g. the selective formation of the 3-octylcyclobutanone as compared to the 2-octyl derivative starting from **11**, is exclusively determined by steric factors as usual in thermal [2 + 2]-cycloadditions. The trapping of **5** succeeded also in DMAc/LiCl solutions containing dissolved pulp. However, the amount of trapping product obtained was significantly lower, which is indicative of the fact that also the pulp exerts a trapping effect (and is thereby degraded).

The *N*,*N*-dimethylketeniminium cation (**5**) is formed from the imine form (enol form) of DMAc (**4**). The formation of the enol form is strongly facilitated by the presence of lithiums ions, which coordinate to the amide oxygen (cf. Part I of these studies). Also the presence of precursor **4** was proven by means of trapping reactions: in the presence of allyl alcohol, **4** forms an allyl enol ether, which at the prevailing elevated temperatures immediately underwent a *Claisen*-type rearrangement to produce 4-pentenoic acid *N*,*N*-dimethylamide (**15**) (Scheme 3). The amide, which was again found both in the presence and absence of pulp, can be isolated from the reaction mixture by extraction with ethyl acetate after addition of water. The rearrangement is very suitable as trapping reaction as it proceeds neatly without byproduct formation when employed in synthesis.

It should be noticed that the formation of **5** from the enol form of DMAc (**4**) is a thermal elimination, which implies that a hydroxyl anion is released directly. Under non-thermal conditions, elimination of hydroxyl would occur only after protonation, which converted the hydroxyl group into a better leaving group, and lead to *N*,*N*-dimethylaminoethyne. The thermally eliminated hydroxyl ion becomes immediately surrounded by oppositely charged lithium cations, which prevents the immediate reverse reaction [21]. Simultaneously, the chloride anions act as counterions to the keteniminium ions. Thus, a dynamic equilibrium between the keteniminium ions **5**, lithium cations, hydroxyl anions and chloride anions is established, which form a highly polar 'broth' of ionic species [22,23]. The thermal formation of keteniminium salts from unsubstituted amides in organic solutions in the presence of tetrafluoroborates and hexafluorophosphate salts has been known from the literature [24,25], but has never before been reported to occur in DMAc/LiCl mixtures.

The equilibrium concentration of **5** is determined by the endothermicity of the elimination process and the sum of strong ionic interactions in the solution, and is usually very low. However, if keteniminiums are removed from the reaction system, e.g. by a competitive reaction with pulp or by trapping, they are continuously regenerated according to the equilibrium constant. Addition of methanol to the respective DMAc/LiCl mixture is a simple way of trapping *N*,*N*-dimethylketeniminium, which is converted into 1-dimethylamino-ethane-1,1-diol (**16**), which can be seen as dimethylketal of DMAc or dimethylaminoderivative of methyl orthoacetate (Scheme 4). The formation reaction is an electrophilic attack of the keteniminium at the oxygen in methanol. This is followed by two competitive pathways, which both lead to the same product **16**: first, proton loss produces an *O*-methylated ketene-semiaminal intermediate which adds a second equivalent of methanol to give **16**, or second, a [1,3]-sigmatropic proton shift gives an iminium salt which reacts with methanol to provide the same product after proton release. Both pathways correspond to whether the second molecule of methanol is added to the C=N double bond or to the C=C double bond (Scheme 4).

Addition of methanol under efficient stirring converts the



Scheme 4.

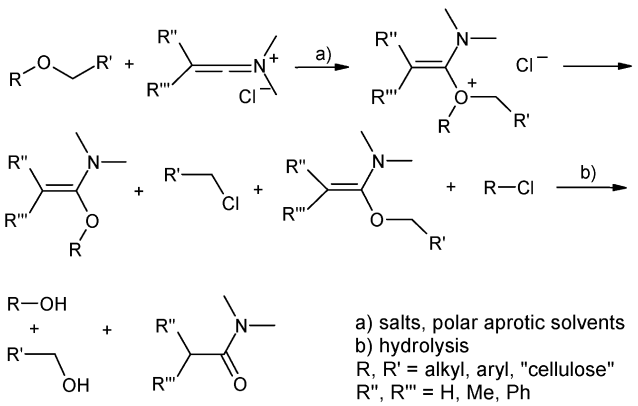
intermediate keteniminium **5** quantitatively into **16**, which is distilled off together with unreacted methanol. **5** will be regenerated in the reaction mixture and again be converted to the trapping product by methanol. In DMAc/LiCl (0.5 wt%) heated to 140 °C for 3 h, as much as 1.3% of the DMAc are converted to **16** via the *N*,*N*-dimethylketeniminium cations (**5**). This means that the capacity of the DMAc/LiCl system to generate **5** is quite large.

It can be safely assumed that the concentrations of all possible coreactants (DMAc, LiCl, MeOH) are much larger than the concentration of **5**, and can be considered constant during the reaction. On understanding that the formation of the keteniminiums is the slowest, rate-determining step in the trapping reaction, a pseudo zero-order rate law for the formation of 1-dimethylamino-ethane-1,1-diol (**16**) results. The amount of **16** obtained at different reaction temperatures at defined reaction times (Table 1) thus allowed roughly estimating the activation energy for the formation process according to the Arrhenius equation, which yielded a value of 137.5 kJ/mol.

This relatively high activation energy of 137.5 kJ/mol corresponds to a slow process whose rate increases strongly with increasing temperature as experimentally observed. The total amount of keteniminiums formed is rather low. However, due to the extreme high reactivity of this intermediate and due to its continuous regeneration upon consumption, these amounts are evidently sufficient to cause the observed cellulose degradation.

Table 1
Formation of trapping product **16** from intermediate *N*,*N*-dimethylketeniminium ions (**4**) and methanol in 100 ml of DMAc/LiCl (0.5 wt%) after 3 h reaction time

T in K	**16** Formed in g	Remarks
80	0	
90	0.002	
100	0.009	
115	0.056	
130	0.187	Yellowish discoloration of the reaction mixture
145	1.01	Yellow discoloration of the reaction mixture
160	3.52	Strong yellow discoloration of the reaction mixture

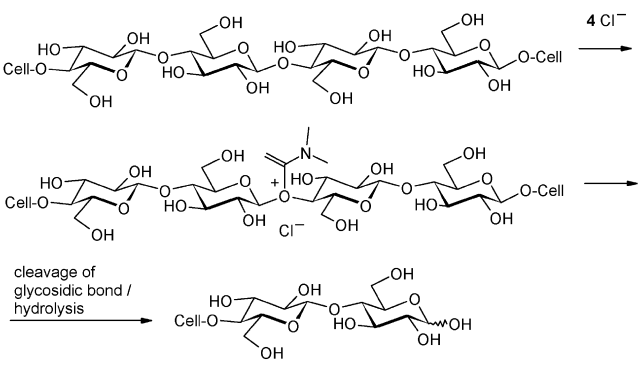


Scheme 5.

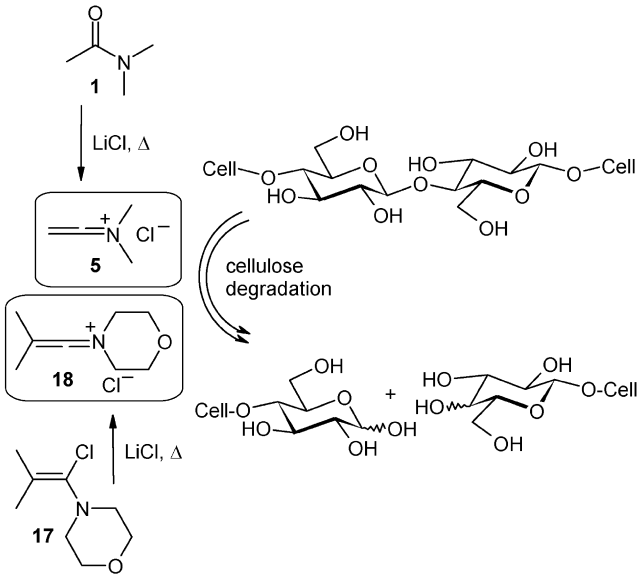
Keteniminium salts—in contrast to the less electrophilic ketenes—are known as reagents to effect mild cleavage of ethers, even of non-reactive diaryl ethers, acetals and ketals [19,26,27] (Scheme 5). In solutions containing electrolytes, such as ammonium salts or soluble alkali salts, hydroxyl groups and amino groups do not interfere with the reaction, as these structures in strongly ionic solutions are surrounded by a solvent shell ('ion cloud'), and are thus shielded from attack by the strongly electrophilic keteniminium reagent.

An analogous mechanism must be assumed for the cleavage of glycosidic bonds in pulp. The strongly electrophilic *N*,*N*-dimethylketeniminium ion attacks the glycosidic oxygen, followed by cleavage of the glycosidic bond under formation of a ketene-hemiaminal derivative and a chlorinated compound, which both undergo secondary hydrolytic reactions. This is shown in Scheme 6 for a cellotetraose section of a cellulose molecule.

Keteniminium ions evidently exert a detrimental effect of on the integrity of cellulosic pulps. In heated DMAc/LiCl, the corresponding transient species are generated in situ from the solvent. However, the degrading agent can also be added externally in the form of a keteniminium precursor: 4-(1-chloro-2-methylpropenyl) morpholine (**17**), for instance, immediately releases keteniminium ion **18** upon thermal treatment (Scheme 7) [28]. When **17** (0.1% relative to pulp) was added to a solution of pulp in DMAc/LiCl (9%, w/v) heated to 125 °C, the cellulose was degraded to oligomers (DP < 50) within 30 min.



Scheme 6.



Scheme 7.

Since the pulp degradation proceeds also in the absence of LiCl (albeit much slower than in its presence), it is likely that besides the presented pathways there are additional minor competitive degradation mechanisms. Moreover, the presented degradation mechanisms cannot account for the observed differences in the sensitivity of pulps toward degradation in DMAc/LiCl. It can reasonably be assumed that these reactivity differences are caused by the different provenience of the pulps materials, i.e. differences in hemicellulose content and degree of oxidative damage. Oxidized positions, e.g. carbonyl groups, act as 'hot spots' for chain cleavage, especially under the thermal conditions used.

3.4. Reactivity of heated DMAc/LiCl: coalescence temperature of DMAc

The rotation around the C–N bond in DMAc is restricted due to its partial double bond character, as in all amides, (see formulae in Fig. 4) [29]. Internal rotation around the C–N bond leads to an intramolecular exchange of the methyl groups, which is slow at room temperature, but is gradually accelerated with increasing temperature. In ^{1}H NMR spectroscopy, the two *N*-methyl groups exhibit different resonance frequencies, ν_a and ν_b. The two signals of the *N*-methyl groups are sharp lines at room temperature, broaden with increasing temperature, and finally fall together to a broad single line at the coalescence temperature T_c.

Below T_c, the perpendicular p_z orbital of the sp^2-hybridized amide carbon interacts with both a p-orbital of the oxygen—which constitutes the classical C=O double bond—and with the perpendicular p_z-orbital of the sp^2-hybridized amide nitrogen, which can be visualized by a double bond between N and C. The *N*,*N*-disubstituted amide is thus best described as resonance hybrid of two mesomeric

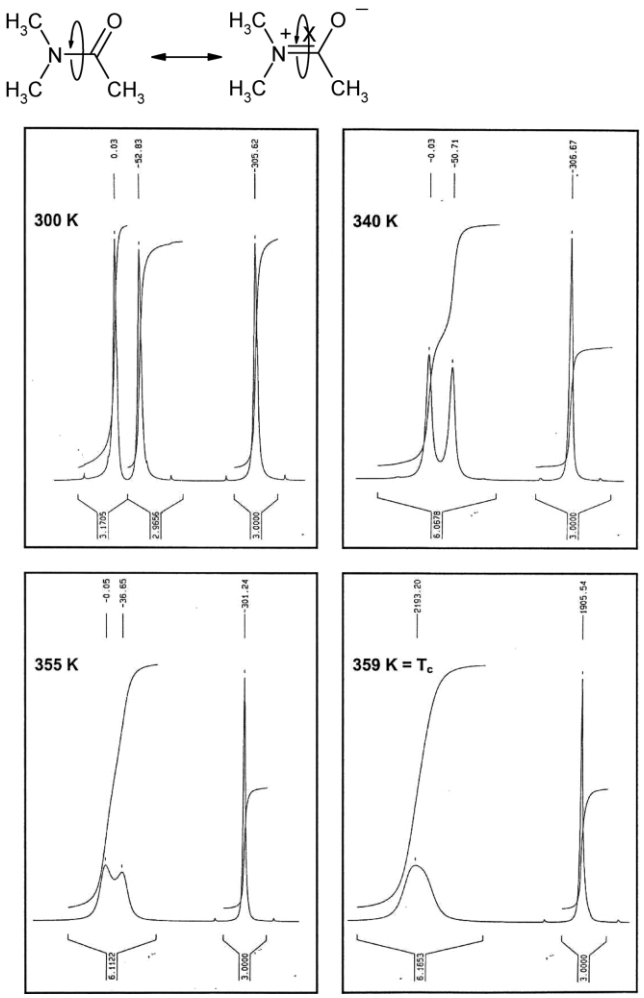


Fig. 4. Determination of the coalescence temperature T_c of DMAc by dynamic NMR: example spectra showing the temperature-independent, sharp singlet of the CH_3–CO–methyl group (right signal) and the signals of the N–CH_3 groups broadening and coming closer with increasing temperature and eventually falling together at T_c.

structures, in which the N–C bond possesses partial double bond character, and the O–C bond partial single bond character. From this structure follows a rather small carbonyl reactivity, which is responsible for the low reactivity of DMAc (and amides in general) in aldol-type reactions and for their stability towards hydrolysis. Before the amide is able to undergo a carbonyl reaction, the double bond must be 'fixed' to either O or N. The anchoring, with the double bond being placed between C and O rendering the C–N bond a freely rotable single bond, occurs at increased temperatures at and above the coalescence temperature T_c. Thus, from the chemical point of view, the reactivity of DMAc (and of amides in general) is strongly increased above the coalescence temperature. While it is very small below T_c, it becomes much higher—comparable to medium reactive esters—at T_c and above.

The coalescence temperature of DMAc and DMAc containing different LiCl concentrations was determined by dynamic NMR experiments. In addition, the rate constant

for the rotation process k_r and the free activation enthalpy ΔG_r of the rotation was obtained according to Eqs. (5)–(7), by recording the shift difference $\Delta\nu = \nu_{b-}\nu_a$ in dependence on the temperature [30].

$$k_r = \frac{\pi}{\sqrt{2}}\Delta\nu\,(\mathrm{Hz}) \tag{5}$$

$$\Delta G_r = \ln\left(\frac{k_B}{h}\right)RT_c + \ln\left(\frac{T_c}{k_r}\right)RT_c \tag{6}$$

$$\Delta G_r = 8.314T_c\left(23.76 + \ln\frac{T_c}{k_r}\right)(\mathrm{J/mol}) \tag{7}$$

The results of the dynamic NMR experiments are summarized in Table 2, four exemplary ^{1}H NMR spectra of pure DMAc recorded at different temperatures are given in Fig. 4. The coalescence temperature of dry DMAc was determined to be 86 °C. T_c increases with increasing LiCl content reaching 96 °C at 8% LiCl. The resulting rate constant for the rotation around the C–N bond at the coalescence temperature in pure DMAc was calculated to be 117 Hz, which corresponds to an appreciably high activation energy of 74.25 kJ/mol. This is in excellent agreement with quantum chemical computations on the ab initio level (6-31G* basis set), which predict a value of 78.5 kJ/mol.

These results demonstrate that formation of *N*,*N*-dimethylketeniminium ion **5** occurs to a significant extent only at and above the coalescence temperature of DMAc. Generation of keteniminium requires an intermediate imide with a 'fixed' single bond between C and N to be formed, which can proceed only above T_c when the resonance stabilization is suppressed.

4. Conclusions

N,*N*-dimethylacetoacetamide (**2**), the main thermal condensation product of DMAc, reacts with the reducing ends in pulp to produce furan structures at temperatures above approx. 80 °C. At higher temperatures above 130 °C, these furan structures are released as *N*,*N*-dimethyl-[2-methyl-5-(1,2,3,4-tetrahydroxybutyl)-3-furyl]formamide (**3**) under cleavage of the proximal glycosidic bond. The newly formed reducing end will again undergo reaction with **2** followed by release of **3**, so that *N*,*N*-dimethylacetoacetamide (**2**) with pulp effects a slow thermal endwise peeling under release of furan structure.

The coalescence temperatures T_c of DMAc and DMAc/LiCl mixtures, ranging between 86 and 96 °C, were determined by dynamic NMR. At and above the coalescence temperature, the reactivity of amides is drastically increased. It was demonstrated by means of trapping reactions that DMAc/LiCl, heated above the coalescence temperature, contains *N*,*N*-dimethylketeniminium ions (**5**) as highly reactive intermediates, both in the absence and in the presence of suspended pulp. Two readily extractable trapping agents were used, which reacted with intermediate **5** to cyclobutanone derivatives in thermal [2 + 2]-cycloadditions. Analogously, methanol was used to convert **5** into 1-dimethylamino-ethane-1,1-diol (**16**).

Also the presence of the precursor of keteniminium ion **5**, the enol form of DMAc (**4**), was proven. This time, allyl alcohol was employed as the trapping agent, which converts **4** into an intermediate ketenaminal which immediately undergoes a *Claisen*-type rearrangement to 4-pentenoic acid dimethylamide (**15**).

Keteniminium ions are known to effect the cleavage of ether and acetal structures by electrophilic attack, which must be assumed as the main pathway for the observed cleavage of glycosidic bonds of pulp in heated DMAc. The degradation of the pulp is strongly accelerated in the presence of LiCl, which promotes the formation of the harmful intermediate **5**.

The observed degradation of pulps is thus a superposition of two main pathways, a slow endwise peeling process, which forms furan structures from a thermal condensation product of DMAc, and a random cleavage of glycosidic bonds by highly reactive keteniminium intermediate formed from DMAc by thermal elimination. The observed increase in carbonyl groups can mainly be attributed to the increasing number of reducing end groups generated upon cleavage of glycosidic bonds.

From our studies, it must be concluded, that heating or refluxing pulp in DMAc or DMAc/LiCl is not appropriate as an activation procedure to achieve better solubility. The heating procedures pronouncedly change the molecular weight of the pulp. Subsequent GPC measurement will thus report an altered molecular weight distribution and not produce the data of the original, genuine cellulosic material.

Acknowledgements

We would like to thank Gertrud Linsberger for practical

Table 2
Results of dynamic NMR measurements on DMAc and DMAc/LiCl

Composition	T_c (°C/K)	$\Delta\nu$ (Hz)	k_r (Hz)	ΔG_r (kJ/mol)
DMAc (10% D)	86/359	52.83	117.4	74.25
DMAc (10% D), 1% LiCl	88/361	55.11	122.4	74.56
DMAc (10% D), 5% LiCl	93/366	57.34	127.3	75.51
DMAc (10% D), 8% LiCl	96/369	59.58	132.4	76.04
Theoretical (computed) value	/			78.5

assistance, as well as Dr Andreas Hofinger and Dr Jürgen Röhrling for recording the NMR spectra. The financial support by the Christian–Doppler Research Society and the Lenzing AG, Austria, is gratefully acknowledged.

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