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Trapping of Reactive Intermediates to Study Reaction Mechanisms in Cellulose Chemistry

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Abstract Reaction with specific scavenger agents, so-called *trapping*, is a direct way to prove the occurrence of reactive intermediates in a reaction system, and thus to elucidate the underlying reaction mechanisms. After an introduction on chemical intermediates, chemical trapping and the peculiarities of trapping methodology in the presence of cellulose, four chapters from cellulose chemistry were selected to illustrate how trapping can be used to determine reactive intermediates, to prove the occurrence of reactive intermediates in the respective reaction system, and to finally help establish the reaction mechanism. The four topics are: radical and ionic intermediates in Lyocell dopes that cause cellulose degradation, the chemistry of cellulose in DMAc/LiCl solutions, aging of alkali cellulose under steeping conditions, and cellulose degradation during carbanilation in dimethyl sulfoxide (DMSO) mixtures.

Keywords Cellulose · Trapping · Reactive intermediates · Reaction mechanism

Abbreviations

DMAc	*N*,*N*-dimethylacetamide
DMSO	dimethyl sulfoxide
DP	degree of polymerization
EPR	electron paramagnetic resonance
GPC	gel permeation chromatography
HPCE	high-performance capillary electrophoresis
IR	infrared
NMMO	*N*-methylmorpholine-*N*-oxide
NMR	nuclear magnetic resonance
SOMO	single occupied molecular orbital
THF	tetrahydrofuran
TLC	thin-layer chromatography

1 Reactive Intermediates and Trapping Reactions

1.1 Chemical Intermediates

A chemical intermediate is a species that is neither starting material nor product and occurs only in multi-step reactions. The term chemical intermediate should not be mixed up with the term transition state. While the latter portrays the geometry of highest potential energy along the reaction coordinate of an elementary reaction step, the former describes an individual, albeit short-lived, chemical compound with transition states leading to and from it. When generated in a chemical reaction, intermediates will quickly con-

vert into another, more stable, molecule. Most chemical reactions consist of more than one elementary step, and thus inevitably involve chemical intermediates. The series of elemental steps makes up the reaction mechanism. The knowledge on each single step is thus necessary to formulate the complete mechanism of the overall reaction.

If the example reaction A + B → C is considered, it may proceed according to the separate steps A + B → X and X → C; in this case X is the chemical intermediate. The amount of an intermediate present in a reacting system at any instant of time will depend on the rate of the step by which it is formed and the rate of its subsequent reaction. A qualitative indication of the relationship between intermediate concentration and the kinetics of the reaction can be gained by comparing the rate constants of the reactions for intermediate production and consumption, as shown in the following for the most general two-step mechanism: reactants $\xrightarrow{k1}$ intermediate $\xrightarrow{k2}$ products. In some reactions, the situation $k1 > k2$ exists. Under these conditions, the concentration of the intermediate will build up, and the reactants are consumed faster than the products are formed. It will be possible to isolate, or at least to observe, the intermediate. In most reactions, the opposite case $k2 > k1$, or the case that both constants are very large, is found. Only a very small concentration of the intermediate will exist at any time. The reaction proceeds too rapidly to permit isolation of the intermediate, which will thus be a rather transient or short-lived species. Often, the term reactive intermediates – which is also preferred in the following – is used to distinguish such species from the isolable and more stable chemical intermediates in the case $k1 > k2$.

Examples for frequently encountered intermediates in organic reactions are: carbocations (carbenium ions, carbonium ions), carbanions, *C*-centered radicals, carbenes, *O*-centered radicals (hydroxyl, alkoxyl, peroxyl, superoxide anion radical etc.), nitrenes, *N*-centered radicals (aminium, iminium), arynes, to name but a few. Generally, with the exception of so-called persistent radicals which are stabilized by special steric or resonance effects, most radicals belong to the class of reactive intermediates.

1.2 Spectroscopic Detection of Intermediates

Identification of the intermediates in a multi-step reaction is the major objective of studies of reaction mechanisms. It is most useful to study intermediates present in low concentrations without chemical interference with the reacting system, i.e. by rapid spectroscopic methods. The most common methods in organic chemistry include ultraviolet–visible (UV-VIS), IR, and EPR spectroscopy. In principle, all other spectroscopic methods for the detection of reaction intermediates are also applicable provided that they are fast enough to monitor the intermediate and able to provide sufficient structural information to assist in the identification of the transient species.

UV-VIS and IR spectroscopy are often combined with the technique of fast cooling to detect and identify highly unstable intermediates. The quickly decreasing temperature drastically decreases reaction rates and mobility so that it becomes more likely to get a spectroscopic snapshot of the intermediate. An extreme example of this technique is called matrix isolation. In this method, the intermediate is trapped in a solid inert matrix, usually argon or another inert gas, at very low temperatures. Because each molecule is surrounded by inert gas atoms, there is no possibility for further intermolecular reactions and the rates of intramolecular reactions are slowed down by the low temperature. Matrix isolation is a very useful method for characterizing intermediates in photochemical or gas-phase reactions.

Free radicals and other intermediates with unpaired electrons can be detected in extremely low concentrations by electron paramagnetic resonance (EPR). This technique measures the energy absorbed to reorient an electronic spin in a magnetic field. It provides structural information on the basis of splitting of the signal by adjacent nuclei, much as in NMR. EPR is not only very sensitive but also very specific: as diamagnetic molecules present give no signals, the possibility for interference is greatly decreased. The method can only be applied to homolytic reactions, i.e. processes involving paramagnetic intermediates. Because of its sensitivity, it is important to demonstrate that any paramagnetic species detected are true intermediates rather than being involved only in minor pathways.

In the use of all spectroscopic methods, it must be remembered that the simple detection of a species does not prove that it is an intermediate. It must also be shown that the species is converted to the product. Therefore, it is necessary in most cases to determine the kinetics of the production and consumption of the intermediate and to demonstrate that this is consistent with the species being an intermediate, which in most cases is rather difficult.

1.3 Trapping of Reactive Intermediates

In contrast to the spectroscopic techniques, which in most cases provide only an indication for the occurrence of the intermediate but no unambiguous proof, trapping experiments – if successful – are capable of providing solid evidence for the occurrence of a reactive intermediate. In addition, the chemical structure of the intermediate will become evident. For trapping a reactive intermediate, a compound that is expected to react specifically with the intermediate in a well-defined manner is added to the reaction system. This reagent stops or slows down the reaction to the usual reaction product by competitively converting the intermediate into a different product. The intermediate is thus diverted from its normal reaction course, and evidence for the existence of the intermediate is obtained if the structure of the trapped

product is consistent with expectation. Occurrence of the expected trapping product confirms the intermediacy, clarifies the structure of the intermediate, and proves the stepwise nature of the overall reaction.

The particular reasons for employing trapping methodology can be manifold:

- if it is not possible to isolate a chemical species or to detect it by spectroscopic means,
- if the concentration of the intermediate is very small and below the detection limit,
- if the occurrence of a species is assumed but not verified,
- if the observed outcome of a reaction needs to be related to an intermediate compound,
- if a reaction takes an unexpected course that must be clarified, or
- if the intermediate concentration at a certain point of time needs to be quantified.

The most prominent application of trapping methodology is to prove the occurrence of chemical species in a reacting system. From this knowledge, the processes leading to the intermediate and its subsequent reactions can be deduced, and the presence of the intermediate can be correlated with the experimental observations. Eventually, this will lead to clarification of the reaction mechanism of the sequence in which the intermediate is involved.

As the whole breadth of chemistry is found for reactive intermediates, the same must in principle be true for trapping agents. However, the well-defined action of trapping agents allows the definition of some general rules as to their chemical and physical properties. An ideal trapping agent should perform the following tasks and exhibit the following properties:

- selective reaction with the intermediate,
- formation of stable trapping products which do not undergo subsequent conversions,
- no parallel reactions with other species in the reaction system,
- much faster reaction rate of the trap with the intermediate than that of the intermediate to the usual products,
- formation of trapping products that unambiguously report the presence of the intermediate (no other reaction that the trapping reaction of the specific intermediate must lead to the trapping product),
- formation of a trapping product that can be separated from the reaction mixture.

1.4 Trapping Methodology in Cellulose Chemistry

In general, all the above characteristics of trapping agents also apply to reactions involving cellulose. However, there are some peculiarities if trapping

methodology is to be applied in cellulose chemistry, which make the approach even more intricate than in conventional organic chemistry.

- Reactions of intermediates with cellulose will be polymer-analogous reactions. The reaction will occur more or less randomly along the polymer chain and will thus likely be difficult to prove or to relate to specific locations along the polymer chain.
- Typical reactions of cellulose, such as oxidation or chain cleavage, can be caused by many different reagents and conditions. It will thus be difficult to relate the reaction outcome to the presence of a specific intermediate.
- In the case of cellulose solutions, the reaction mixture will be rather viscous, which limits the intimate admixing of the trapping agent and quick reaction with the species to be trapped.
- In heterogeneous reactions involving cellulose, the accessibility for the trapping agent is a major problem.
- In both homogeneous and heterogeneous mixtures involving cellulose, the system is likely to be rather complex, so that separation and identification of trapping products might prove difficult.

In the following, four selected chapters from cellulose chemistry will illustrate how trapping was used in the hunt for reactive intermediates.

The first section covers the chemistry of cellulose solutions in an amine *N*-oxide solvent (NMMO), the so-called Lyocell chemistry, as encountered in the industrial production of cellulosic Lyocell material. The system is characterized by high reaction temperatures, the presence of a strong oxidant and high complexity by multiple (homolytic and heterolytic) parallel reactions. Trapping was used to address the questions that reactive intermediates are present in Lyocell solutions and are responsible for the observed side-reactions and degradation processes of both solvent and solute.

The second chapter deals with cellulose solutions in yet another solvent system for cellulose, namely DMAc/LiCl, which is not used on an industrial scale as is NMMO, but on the laboratory scale for analytical purposes. The presence of the somewhat exotic reaction medium poses special requirements on trapping methodology that was used to clarify the mechanisms of different degradation processes. This issue was of importance since maintenance of cellulose integrity is the key prerequisite for any analytical procedure which should report the polymer characteristics of the genuine cellulosic material.

The third chapter is concerned with the detection of a highly reactive intermediate, hydroxyl radicals, upon alkalization of cellulose. This processing step is frequently used in cellulose chemistry, especially in industrial-scale production of cellulose ethers and viscose. The presence of hydroxyl radicals with their inherent high reactivity and low selectivity would have implications as to the appropriate choice of reaction conditions and the underlying reaction mechanisms. However, the extreme conditions – working in concentrated lye – made application of trapping methodology especially challenging.

The final section addresses degradation and oxidation reactions in a commonly used derivatization system for cellulose, a mixture of DMSO and phenyl isocyanate to achieve cellulose carbanilation, e.g. for analytical purposes. Mechanistic studies were aimed at verifying the assumed oxidative action of this reaction system, and trapping methodology was employed to detect responsible intermediates.

2
Cellulose Solutions in NMMO (Lyocell)

2.1
Cellulose and NMMO Degradation in Lyocell Dopes

N-Methylmorpholine-*N*-oxide monohydrate, a tertiary, aliphatic amine *N*-oxide, is able to dissolve cellulose directly, i.e. without chemical derivatization, which is used on an industrial scale as the basis of the Lyocell process [1, 2]. This technology only requires a comparatively low number of process steps compared for instance to traditional viscose production. Cellulose material – mainly fibers – are directly obtained from the cellulose solution in NMMO; no chemical derivatization, such as alkalization and xanthation for rayon fibers, is required [3]. The main advantage of the Lyocell process lies in its environmental compatibility: very few process chemicals are applied, and in the idealized case NMMO and water are completely recycled, which is also an important economic factor. Even in industrial production systems NMMO recovery is greater than 99%. Thus, compared with cotton and viscose the Lyocell process pertains a significantly lower specific environmental challenge [4]. Today, Lyocell fibers are produced on an industrial scale, and other cellulosic products, such as films, beads, membranes and filaments, are also currently being developed or are already produced commercially.

As NMMO is a solid at room temperature, dissolution and processing of the spinning dope require elevated temperatures of about 100 °C. The dope is spun into an air gap and water, where cellulose is regenerated and NMMO is washed out. After purification and evaporation of the water, the amine *N*-oxide is reintroduced into the system and used again for cellulose dissolution.

Ideally, dissolution of cellulose in the amine *N*-oxide is supposed to be an entirely physical process without any chemical changes of pulp or solvent. However, in real-world processes there are several chemical processes observed, which cause formation of appreciable amounts of byproducts. A strong discoloration of the solution due to chromophore formation has been observed, which is accompanied by degradation of both the solute cellulose and the solvent NMMO at the elevated process temperatures, which in turn can provoke very severe effects, such as degradation of cellulose, temporary or permanent discoloration of the resulting fibers, decreased product

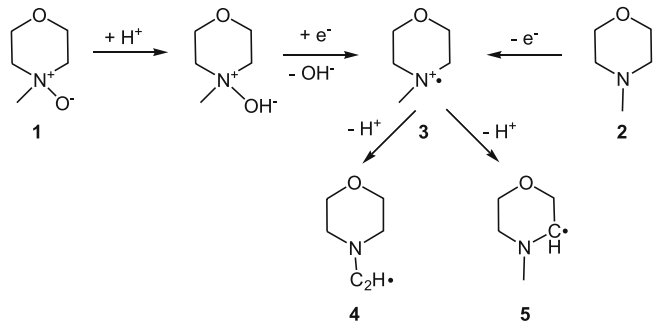
performance, accelerated decomposition of NMMO and increased consumption of stabilizers. The most drastic effect of side-reactions are degradation processes that become uncontrollable, in the literature often denoted with the euphemistic terms "fast exothermic process" or "thermal runaway reaction" [5–7]. The question of the chemical stability of the system has always been a crucial issue for the development of Lyocell technology, and is still a major concern today as it is related to safety at work and integrity of the whole production line. Research on degradation processes in NMMO/cellulose mixtures in different industrial companies have therefore largely focused on the empirical search for new and better stabilizers for Lyocell dopes.

It was our aim to study the chemistry of NMMO and Lyocell solutions in order to put the prevention of undesired side-effects on a more scientific foundation [8, 9]. The improved understanding of the individual chemical processes in Lyocell solutions today allows an accurate deduction of the different tasks of optimum Lyocell stabilizers. The question of which reactive intermediates are involved in the degradation processes of both NMMO as the solvent and cellulose as the solute was a key issue in the studies of Lyocell chemistry.

2.2
NMMO-derived Radical Intermediates

2.2.1
Formation and Occurrence of NMMO-Derived Radicals

The positive effect of classical phenolic antioxidants on the stability of Lyocell solutions suggested that radicals were involved in the degradation processes. Analogous to tertiary amine oxides in general [10, 11], the primary radical species derived from NMMO was assumed to be the *N*-centered cation radical **3**, which is generated by cleavage of the N – O bond. For this breakage to occur, activation of the *exo*-oxygen by protonation and concomitant one-electron reduction is required, finally producing **3** and a hydroxyl anion. The same species is obtained by one-electron oxidation of the corresponding tertiary amine, in this case *N*-methylmorpholine (**2**). Aminium cation radicals such as **3** are generally very labile and have a pronounced tendency towards mesolytic cleavage of the $C_\alpha - H_\beta$ bond. Mesolysis, in addition to the well-known terms homolysis and heterolysis, denotes a bond cleavage in radical ions that separates the charge from the single electron [12]. This extremely fast process results in uncharged *C*-centered α-amino radicals [13, 14]. Hence, also the primary cation radical **3** was expected to produce immediately neutral carbon-centered radicals by release of a β-proton, either from the exocyclic *N*-methyl group leading to **4**, or from the ring *N*-methylene leading to **5**. In accordance with general amine and amine *N*-oxide chemistry, cation



Scheme 1 Primary radical species derived from NMMO

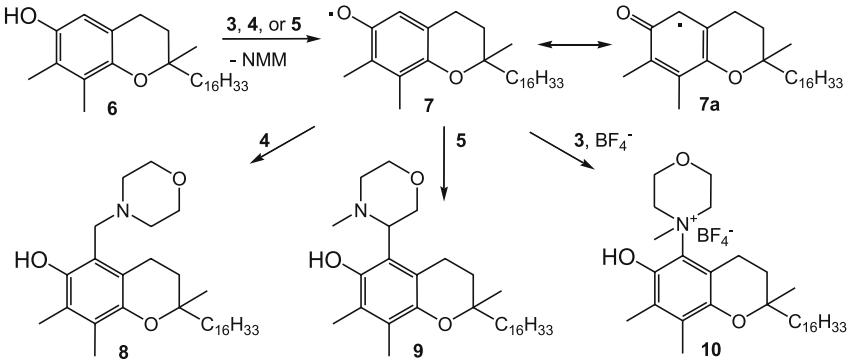
radical **3**, the *exo*-centered radical **4**, and the ring-centered radical **5** are the three main initial intermediates in homolytic reactions of NMMO (Scheme 1).

Cation radicals of tertiary amines without steric hindrance around the nitrogen, such as **3**, are rather intricate to investigate by EPR spectroscopy. The detection mostly requires UV or γ-irradiation in inert matrices at low temperatures and provides only badly resolved spectra [15, 16]. EPR was therefore considered inappropriate for the identification of radicals present in NMMO reaction mixtures.

2.2.2 Trapping of NMMO-Derived Radicals

The application of conventional spin traps, such as substituted pyrroline-*N*-oxides, nitrones, or sterically hindered phenols, has been reported to fail in the presence of large amounts of tertiary amine oxides [10, 11]. For successful trapping of the radicals, γ-tocopherol (**6**), a component of natural vitamin E, was used as the specific trapping agent. Both the trapping agent and its products offer the advantage of supreme extractability into apolar solvents, such as *n*-hexane or petrol ether, due to the strongly lipophilic isoprenoid side-chain. Thus, even from very complex mixtures, they can readily be separated. From the chemical point of view, the well-defined coupling reaction was a clear benefit, as was the near absence of self-coupling reactions, in contrast to other phenolic spin traps.

The interaction of γ-tocopherol (**6**) with radicals generates the relatively stable γ-tocopheroxyl radical (**7**). While the *O*-centered form of the γ-tocopheroxyl radical has a lower affinity towards other radicals and forms relatively labile tocopheryl ether products, its *C*-centered resonance structure **7a**, with the radical being located at C-5, readily recombines with other radicals present in the mixture to give stable compounds. This way, trapping products of all three radicals **3**, **4**, and **5** were isolated and fully analytically characterized (Scheme 2) [17].



Scheme 2 Trapping of the NMMO-derived radicals **3**, **4** and **5** with the trapping agent γ-tocopherol (**6**)

The production of the radicals was carried out by reduction of NMMO with Fe(II) or by oxidation of *N*-methylmorpholine with Fe(III), at different temperatures. Other reductants and oxidants gave nearly identical results. The similar outcome of NMMO reduction and NMM oxidation was already a clear indication that the structure of the radical intermediates was correctly proposed – apart from the definite proof by the chemical structure of the trapped radical intermediates.

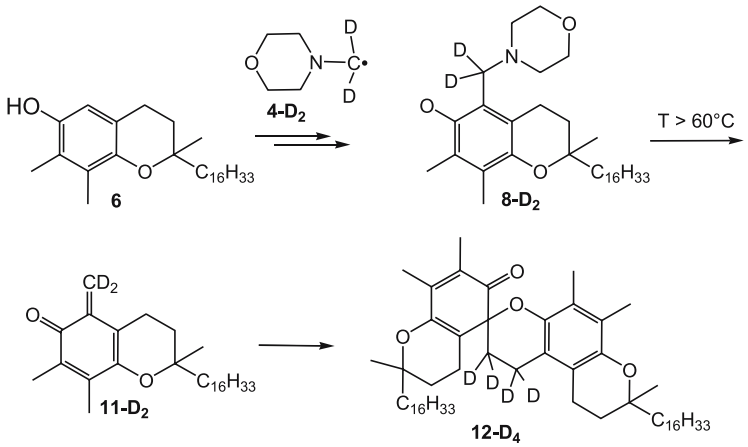
Compound **8**, the major trapping product, originated from coupling of radical **4** with **7a**. Trapped **5** was also observed, however in significantly smaller amounts. This agreed very well with theoretical considerations based on computations on the ab initio level, which predict a lower stability of **5** compared to **4**. Also the trapping product of the primary cation radical **3**, the quaternary ammonium cation **10**, was isolated. Only very small amounts of **10** were obtained, and purification was possible by precipitation as the corresponding tetrafluoroborate salt. The rather low yield of **10** was due to three reasons: first, the stability of **3**, and thus its equilibrium concentration, is very low as it readily loses a β-proton to give the more stable **4** or **5**. Second, tertiary amine cation radicals recombine rather slowly with γ-tocopheroxyl radicals: while the recombination of γ-tocopheroxyl radicals with carbon-centered radicals is a diffusion-limited process, with the rate being largely independent of the nature of the radical, the rate constant for the recombination with amine cation radicals is about three orders of magnitude smaller [18]. At third, the trapping product is extremely thermolabile and sensitive towards oxidation. Even short exposure to air at ambient conditions was sufficient to cause complete oxidative conversion into red 5,6-tocopheryldione, so-called α-tocored.

Care has been taken to rule out that the coupling products could have formed according to heterolytic (nonradical) pathways involving Mannich intermediates. In short, a modified trapping agent, γ-tocopherol methyl ether,

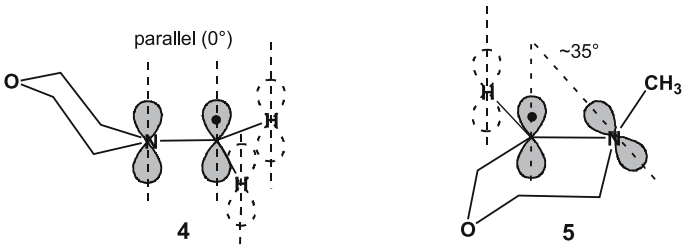
was used which would exclusively react by electrophilic substitution, but not homolytically as from the blocked phenolic OH group neither the phenoxyl radical nor the *C*-centered resonance form could form. The fact that no trapping products were found in this case demonstrated that the formation of **8–10** was indeed caused by homolytic reactions.

The trapping reaction with γ-tocopherol (**6**) was also employed to prove the occurrence of the NMMO-derived radicals directly under Lyocell conditions, and not only in organic solutions of NMMO at ambient temperatures or below. While the trapping product of the *N*-centered radical was too labile under the prevailing conditions, trapping product **9** from radical **5** was indeed detected. For trapping *C*-centered radical **4**, the procedure was modified since trapping product **8** was thermally unstable above 60 °C, eliminating morpholine to produce the *ortho*-quinone methide **11** which immediately dimerized to spiro-dimer **12** (Scheme 3). Both **11** and **12** are typical products in the chemistry of α-tocopherol which differs from the employed trapping reagent γ-tocopherol by an additional methyl group in position 5. In the trapping product **8** as well as in *ortho*-quinone methide intermediate **11** and spiro-dimer **12** the additional carbon atoms originated from the *exo*-CH_2 group of the radical **4**. This was demonstrated by applying selectively deuterated NMMO (**1-D$_3$**) as the starting material [19]. Coupling of the corresponding radical **4-D$_2$** produced the bisdeuterated coupling product **8-D$_2$** which finally gave the tetradeuterated dimer **12-D$_4$**. Since the deuterium can only arise from the methyl group in the starting material NMMO, the occurrence of the labeled product is a direct proof of **4** as the intermediate.

Ab initio computations predicted the *exo*-centered radical **4** to be more stable by 2.3 kJ/mol (energy of formation) than the ring-centered radical **5**. With



Scheme 3 Modified trapping procedure for the detection of NMMO-derived radical **4** under Lyocell conditions



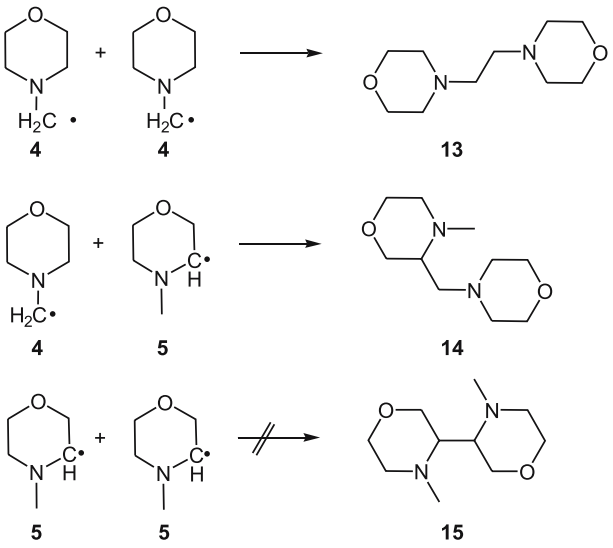
Scheme 4 Illustration of hyperconjugative stabilization and approximate geometries, leading to higher stability of radical **4** compared to radical **5**

the calculated activation energy difference $\Delta(\Delta E^{\#})$, the equilibrium ratios of **4** and **5** are given by $N_5/N_4 = \exp - (\Delta(\Delta E^{\#})/RT)$, assuming an irreversible formation reaction for **4** and **5**. The theoretical values calculated from this equation were in superb agreement with the experimental ones determined by measuring the ratios between these two radicals in the form of their trapping products at different temperatures.

Optimum hyperconjugative stabilization in **4** and the lack of steric strain account for its higher stability compared to **5**. Generally, aminyl radicals experience hyperconjugative stabilization of the SOMO by neighboring orbitals. The *p*-orbital SOMO in **4** can fully overlap with the two pseudo-*p* orbitals of the remaining two methylene protons and with the nitrogen *n*–*p* orbital, so that the hyperconjugative stabilization reaches its optimum. In contrast, in **5** there is only one pseudo-*p* orbital at the ring proton, and the nitrogen *n*–*p* orbital overlaps less effectively (34.6°) with the SOMO, so that the stabilization effect is much smaller. Furthermore, the spin-bearing carbon – as an sp^2 hybrid with a singly occupied *p* orbital – has nearly planar geometry. This means no steric strain at the *exo*-carbon of **4**, but severe twisting of the chair conformation for the ring-centered radical **5**, rendering the latter energetically unfavorable (Scheme 4). These effects account for the smaller stability of **5**, which is reflected experimentally by the fact that the trapping product of **4** dominated over that of **5** in all cases.

2.2.3
Radical Recombination of NMMO-Derived Radicals

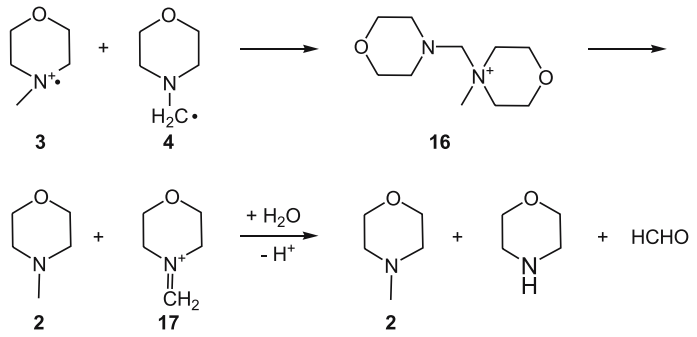
The reaction of two radicals can be seen as a type of self-trapping, with one molecule of the radical species consuming another one in a recombination process. For this process to be observed, the radical concentration must be sufficiently high that the probability of two radicals encountering one another is increased and the recombination products are accumulated to detectable amounts. In the case of the *C*-centered NMMO-derived radicals **4** and **5**, two of the three possible recombination products were identified (Scheme 5).



Scheme 5 Radical recombinations with C – C bond formation, involving the NMMO-derived *C*-centered radicals **4** and **5**

The proof of their structure was again provided by separation and analytical characterization of the pure compound. The symmetrical coupling product 1,2-bis(4-morpholino)ethane (**13**) was formed by recombination of two molecules of **4**. By analogy, **4** and **5** yielded 3-(4′-morpholinomethyl)-4-methylmorpholine (**14**). Compound **15**, as the self-trapping product of the ring-centered radical **5**, was not found [17]. Although likely to have formed, it was present only in concentrations too small for detection: first, the absolute concentration of **5** and thus the probability of two molecules of **5** to meet were rather low and, second, the steric conditions for the recombination of two secondary radicals were much more demanding than for the reaction between **4** and **4**, or **4** and **5**, respectively.

In the literature, the simultaneous formation of the major NMMO degradation products *N*-methylmorpholine, morpholine and formaldehyde [20] is always attributed to the disproportionation of the primary aminyl radical **3**, as a – not further defined – redox process between two molecules of **3**, in which one is reduced to *N*-methylmorpholine (**2**) and the other oxidized to *N*-(methylene)morpholinium cation (**17**), which upon addition of water, forms morpholine and formaldehyde. Also this disproportionation can be rationalized as a radical coupling reaction which proceeds through recombination of *N*-centered **3** and *C*-centered **4**, via the ammonium aminal intermediate **16** as the actual recombination product (Scheme 6). The intermediacy of this species was indeed confirmed by isolation from the reaction mixture and full characterization [17]. Compound **16** is quite labile and immediately de-

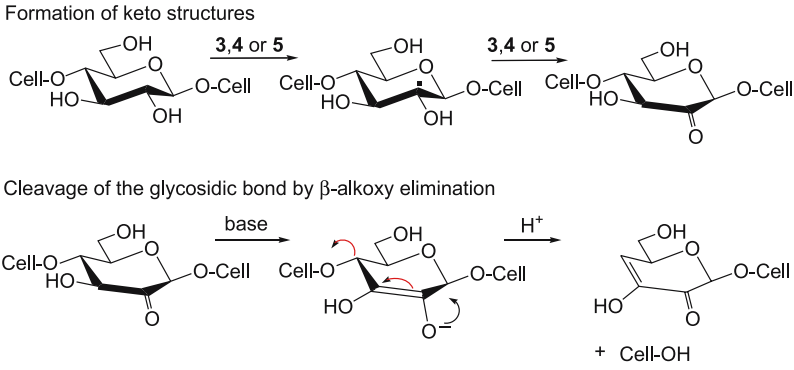


Scheme 6 Disproportionation of the NMMO-derived radicals

composed in quantitative yields into *N*-methylmorpholine, morpholine and formaldehyde when entering aqueous media – exactly the macroscopically observed outcome of the disproportionation.

2.2.4
Reactions of the NMMO-Derived Radicals with Cellulose

The NMMO-derived radicals are strongly electron-deficient and thus strongly oxidizing species. By analogy to hydroperoxyl radicals, they will react with electron-rich positions in cellulose or model compounds. The preferred positions for attack will be the CH-acidic groups in the α-position to carbonyl functions. Trialkylaminyl radicals react with α-hydroxyacids to give α-ketoacids, and with aldoses to furnish 2-ketoaldoses [21]. The main result of the action of NMMO-derived radical **3**–**5** on pulp will be the random introduction of keto groups into the 2-position of the anhydroglucose repeating



Scheme 7 Cellulose-chain scission as a consequence of homolytic reactions involving NMMO-derived radicals

units of cellulose, finally leading to chain cleavage by β-elimination and thus, a decreased DP (Scheme 7).

Typical values given in the literature for Lyocell dopes without stabilizers added are DP losses from 472 to 177 over 6 hours at 105 °C [22], or from 570 to 185 over 2 hours at 90 °C [23]. The activation energy for the cellulose chain cleavage in NMMO at temperatures above 115 °C was determined to be 69 kJ/mol. This observation strongly supported the hypothesis that the actual rate-determining step of the cellulose chain cleavage was a β-alkoxy elimination, with an activation energy of 67–72 kJ/mol [24, 25].

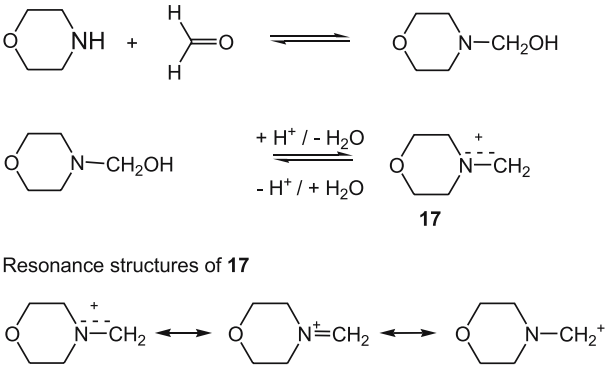
2.3 NMMO-Derived Ionic Intermediates

2.3.1 Formation and Trapping of Carbenium-iminium Ions

In the early phases of Lyocell research, degradation reactions of NMMO and cellulose solutions in NMMO were mainly thought to be homolytic (radical) processes, mostly sustained by the beneficial action of antioxidant additives, such as propyl gallate, which were assumed to act merely as a radical scavenger. However, the radical pathways could hardly account for uncontrollable degradation reactions, which on one hand would occur rather unpredictably also in the presence of stabilizers and on the other hand were not inducible by typical radical initiators. With the finding of nonradical, autocatalytic decomposition processes and *Polonowski*-type degradation reactions [26, 27], studies in Lyocell chemistry turned to those heterolytic (ionic) degradation processes, which were established as the cause of the observed exothermic processes – showing the system of side-reactions in the Lyocell system to be much more complex than commonly thought.

To prove the presence of formaldehyde and NMMO-derived carbenium-iminium ions under Lyocell mixtures was a key issue here, as the occurrence of the latter is critical with regard to autocatalytic degradation and instabilities of Lyocell solutions. Again, trapping methodology was used for this purpose, it served also to investigate the general chemistry of the NMMO-derived carbenium-iminium ions.

Formaldehyde is the aldehyde with the highest carbonyl reactivity: it reacts rather fast with any suitable coreactant present, for instance with cellulose, causing the formation of *O*-hydroxymethyl groups and methylene crosslinks. The critical process with regard to NMMO degradation is reaction with the NMMO-degradation product morpholine to form *N*-(methylene)morpholinium cations (**17**) via *N*-hydroxymethylmorpholine in neutral and acidic media, cf. Scheme 8. *N*-(Methylene)morpholinium cations (**17**) belong to the compound class of carbenium-iminium ions or so-called *Mannich* intermediates, they induce the autocatalytic decomposition of NMMO



Scheme 8 The role of formaldehyde in the formation of carbenium-iminium ion **17** and resonance stabilization of the latter

and other tertiary amine *N*-oxides [26]. The detection of formaldehyde as one precursor of **17** was a prerequisite in confirming the decisive role of carbenium-iminium ions in Lyocell chemistry.

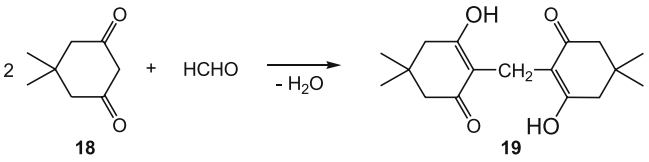
The determination of HCHO in the NMMO/water/cellulose reaction system was unusually difficult as all commonly employed reactions to determine aldehydes were unsuitable since either the trapping reagents were unstable under the prevailing reaction conditions, or they reacted with the carbohydrates present in the system. It should be recalled that working under Lyocell conditions meant performing the reactions in a viscous melt of a relatively strong oxidant in the presence of about 10% dissolved cellulose at temperatures of about 100 °C. Dilution of the system with water followed by determination of formaldehyde in the resulting aqueous mixture was not feasible, since determination of HCHO would not necessarily prove its presence in the Lyocell dope, but only in the aqueous extracts: there remained the possibility that the HCHO originated from hydrolytic reactions. A good trapping agent for HCHO had to react specifically with HCHO immediately upon its formation, to be sufficient stable under the drastic reaction conditions, and to form stable and separable products.

The trapping of formaldehyde in Lyocell dopes under processing conditions was performed using the trapping agent 5,5-dimethylcyclohexa-1,3-dione (dimedone, **18**) in a two-phase system with *o*-dichlorobenzene as the organic phase and the cellulose/water/NMMO mixture as the "aqueous" phase [28]. Dimedone reacts with aldehydes in a well-defined reaction [29, 30]. It is insoluble in *o*-dichlorobenzene, whereas its reaction product with HCHO is soluble in this solvent and is thus continuously extracted and prevented from side reactions with NMMO. *o*-Dichlorobenzene has a sufficiently high boiling point (180 °C) to have a negligible vapor pressure at the Lyocell working temperature, and it is completely inert under the reaction conditions so

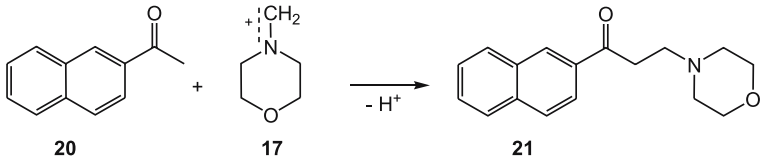
that it does not interfere with the processes in the cellulose/water/NMMO layer in any way. Addition of dimedone into the Lyocell dope (0.5% relative to NMMO*H_2O) resulted in the formation of the dimedone–formaldehyde adduct **19**, which upon formation was immediately extracted into the organic phase (Scheme 9). The solution characteristics were so favorable that only trace amounts of other compounds besides the desired product **19** were extracted. This was also reflected by the fact that the organic phase remained nearly colorless while the NMMO phase quickly turned dark in the reaction.

After having established the presence of HCHO in Lyocell dopes, trapping methodology was used once more to demonstrate the presence of *N*-(methylene)morpholinium cations (**17**). A Mannich-type conversion [31, 32] was certainly the most specific reaction of carbenium-iminium ions to be used for this task: the carbenium-iminium ions needed in this reaction would not be formed by separate reaction between secondary amine and aldehyde, but would already be present in the system as intermediates to be trapped. The actual trapping agent thus needed to be a suitable methylene-active carbonyl compound. However, the above described restrictions to the selection of a trapping reagent apply analogously, and first of all the trapping reagent must be stable under Lyocell conditions. This requirement eliminated the application of aliphatic aldehydes as trapping reagents. In addition, the products of the reaction, usually named Mannich bases, had to be stable and easily isolable. This turned out to be a major impediment as many Mannich bases readily eliminate the secondary amine group to form an α,β-unsaturated carbonyl compound.

After testing several arylmethylketones, 2-acetonaphthone (**20**) was found to be a very suitable reagent, which was used to demonstrate the in situ formation of *N*-(methylene)morpholinium cations in NMMO solutions of cellulose by formation of the Mannich base 3-(4-morpholino)propionaphthone (**21**), see Scheme 10 [28]. This trapping product did not eliminate morpholine at temperatures below 120 °C and was easily extractable into chloroform due to the relatively lipophilic naphthene structure. Although the yield of the trapping reaction was rather low depending on the respective conditions – between 0.1 and 5% relative to applied trapping agent – the ease of isolation of the compound made the trapping procedure quite reliable and reproducible so that different Lyocell dopes or different reaction conditions could be com-



Scheme 9 Trapping of formaldehyde with dimedone (**18**) under Lyocell conditions in the two-phase system Lyocell dope/*o*-dichlorobenzene

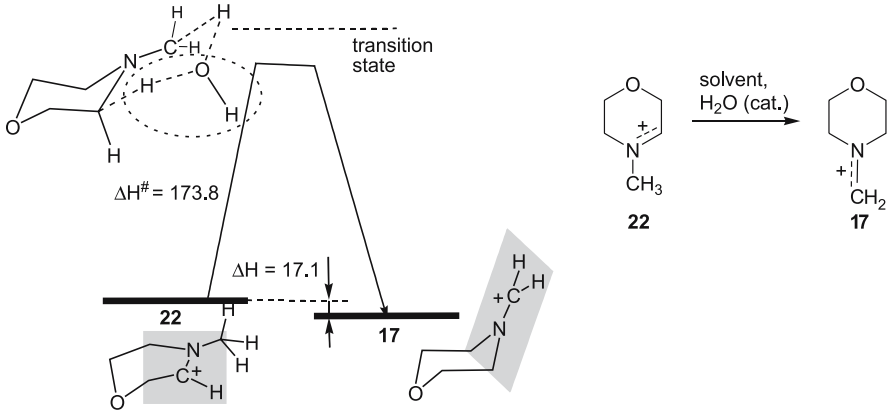


Scheme 10 Trapping of *N*-(methylene)morpholinium cations (**17**) in Lyocell dopes by 2-acetonaphthone (**20**)

pared with regard to the content of **6** by determining the amounts of trapping product formed.

2.3.2
Interconversion of NMMO-Derived Carbenium-iminium Ions

Trapping with 2-acetonaphthone was also used to clarify a peculiar interconversion reaction between carbenium-iminium ions derived from NMMO [33]. According to theory, two such species were to be expected, the *exo*-centered carbenium–iminium ion **17** and the *ring*-centered carbenium–iminium ion **22** (Scheme 11). Even though **22** might appear more stable as its ring-centered positive charge seems better accommodated at a secondary position than the "exposed" charge in **17**, it was the latter which occurred predominantly in all different types of side-reactions starting from NMMO. In fact, the intermediate **17** was produced exclusively in NMMO reaction mixtures containing water – thus also under Lyocell conditions, whereas in nonaqueous solutions



Scheme 11 Carbenium-iminium ion conversion of **22** into **17**: schematic representation of the computed reactant and transition state geometries as well as reaction energies. The trigonal planar environments of the carbenoid carbons are *shaded in gray*. The water molecule participating in the transition state is *circled by a dotted line*

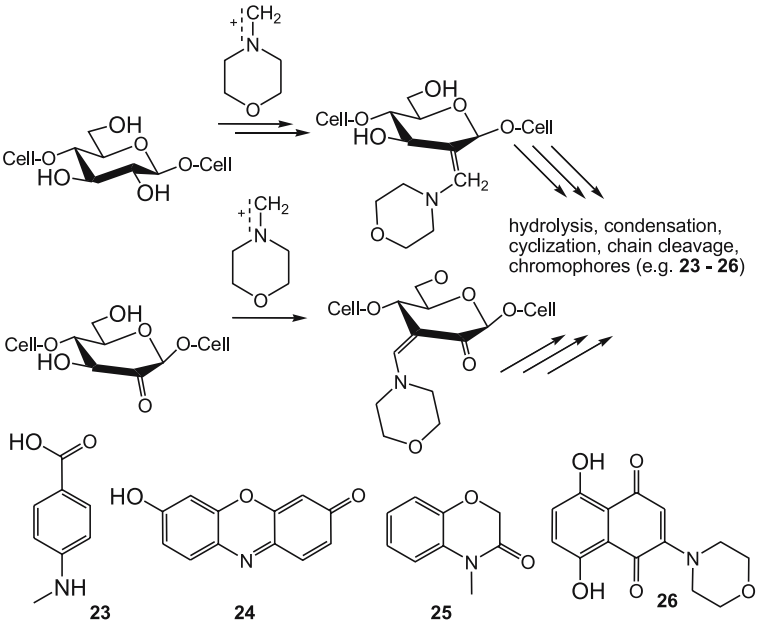
of NMMO smaller amounts of **22** were also found. Thus, both the presence of water and higher temperatures generally seemed to promote the consumption of **22** in favor of **17**.

Besides the trapping methodology, a combined approach consisting of isotopic labeling, kinetic studies, and computations on the density-functional theory (DFT) level was used to clarify the mechanism (Scheme 11) [33]. The NMMO-derived *ring*-centered carbenium-iminium ion **22** is energetically disfavored by ring strain imposed by the trigonal planar geometry of the carbenium carbon. In the presence of water it is rearranged into its counterpart, *N*-(methylene)morpholinium cation (**17**), which has no ring strain as the carbenium center is exocyclic. The reaction is an endothermic, bimolecular process proceeding via a highly organized transition state that involves one molecule of water. The reaction was the first example of a carbenium-iminium ion interconversion reported, which in addition was in complete agreement with the empirical data from Lyocell process chemistry as it explained the nearly complete absence of **22** and the observed predominance of **17**.

2.3.3
Reactions of NMMO-Derived Carbenium-iminium Ions with Cellulose

From the observation that *N*-(methylene)morpholinium cations (**17**) induced the autocatalytic decomposition of tertiary amine *N*-oxides in combination with the proof that these intermediates were actually present in Lyocell dopes, the question arose why Lyocell solutions were stable at all. The answer is found in the fact that carbenium-iminium ions generated are immediately consumed by reaction with water and carbohydrate structures as the most abundant and most reactive nucleophiles present. Only when the local concentration of **17** increases to such a high level that the consumption by reaction with water or cellulose cannot compensate for its production, does the reaction with NMMO become uncontrollable and lead to an exothermic event. The pulp used in the Lyocell process acts as a quasi-stabilizer for the solvent NMMO, albeit with the drawback of increased chromophore generation.

The strongly electrophilic *N*-(methylene)morpholinium cation attacks CH-acidic positions in cellulose, mainly neighboring a keto, acetal or eneamine structure, which basically constitutes a classical Mannich reaction. With α-hydroxy-carbonyl compounds, among them aldoses, ketoses and the anhydroglucose units in cellulose, Mannich intermediates react according to a multi-step sequence that formally exchanges the hydroxyl group with a formyl group to produce 1,3-dicarbonyl compounds, see Scheme 12 [34–36]. These highly reactive species will immediately undergo subsequent reactions, especially under the drastic conditions of Lyocell processing, which eventually cause formation of deeply colored compounds (**23–26**),



Scheme 12 Reactions of *N*-(methylene)morpholinium cations (**17**) with cellulose and oxidized structures in cellulose and formation of Lyocell-specific chromophores (**23–26**)

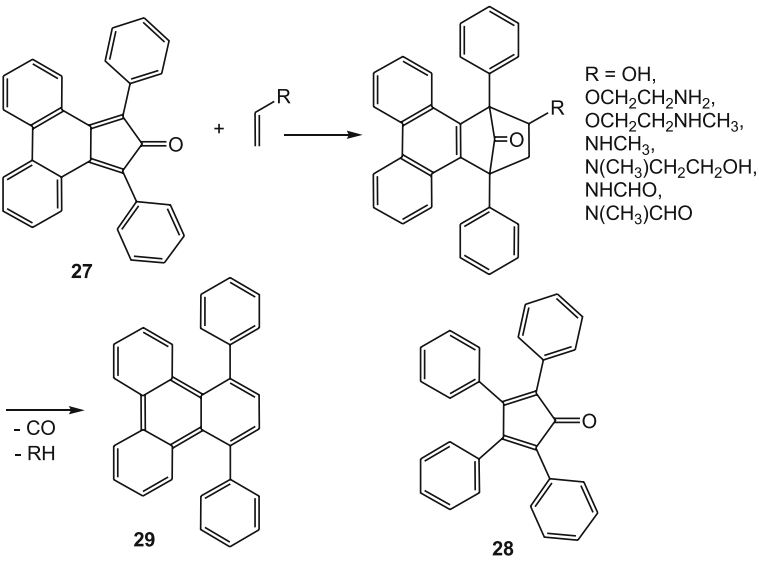
see Scheme 12. These chromophores are either released into the NMMO as the solvent or remain attached to the cellulose. Indeed, such chromophores as condensation products of NMMO degradation compounds and cellulose degradation compounds were isolated from Lyocell fiber material according to a novel chromophore analysis procedure [37, 38]. Compounds **23–26** proved generally the participation of NMMO or NMMO-derived intermediates in the formation of colored degradation products, since the latter contained nitrogen, of which NMMO was the only possible source. Naphthoquinone **26** even included an intact morpholine ring that indicated the likely participation of the carbenium-iminium ion **17** in the formation.

2.4 Trapping of Unsaturated Intermediates Upon Thermal Degradation of NMMO

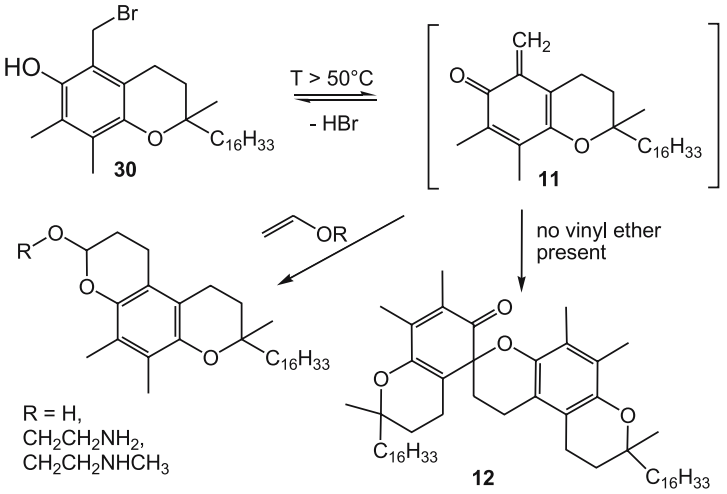
The mechanism of the thermal decomposition of NMMO and Lyocell solutions is extremely complex since the reaction, initiated by the action of carbenium-iminium ions, quickly enters an uncontrollable course. A central question was whether the heterocyclic ring of NMMO was cleaved during the reaction and whether products of this cleavage, having either vinyl ether or enamine structures, could be detected. Employing the trapping agents

phencyclone (**27**) and tetracyclone (**28**) several vinyl ether and enamine-type compounds were trapped in situ in the reaction mixture during thermal degradation of Lyocell dopes (Scheme 13) [39]. These trapping reagents represent electron-deficient dienes, which would react with electron-rich dienophiles, such as the degradation products, in a Diels–Alder type [4 + 2]-cycloaddition. The reagents are relatively inert and suitable also for use under rather drastic conditions. The reaction products again offer good extractability into aromatic solvents, from which the products can be separated and identified. At the high temperatures present, the primary addition products undergo elimination and decarbonylative aromatization to a substituted triphenylene **29**, so that in the trapping mixture both the primary adducts and the aromatization products were found. The trapped olefinic intermediates originated from cleavage of the O – C and N – C bonds, respectively, of the morpholine ring and thus proved its destruction during exothermic events in Lyocell dopes.

Vinyl ether structures from the ring fragmentation of NMMO have also been identified in the gaseous phase from uncontrolled degradation reactions under Lyocell conditions, again by trapping methodology [8]. For this purpose, the hot reaction gases were introduced into an ethanolic solution of 5a-bromo-α-tocopherol (**30**). The local heating by the gas caused local formation of the *ortho*-quinone methide **11** as the actual trapping reagent. In the absence of vinyl-type structures, dimerization to the spiro-dimer **12** occurred. If vinyl ethers were present, corresponding trapping products were



Scheme 13 In situ trapping of vinyl ether and enamine structures in the mixture of uncontrolled thermal decomposition of NMMO



Scheme 14 Uncontrolled thermal decomposition of NMMO: in situ trapping of vinyl ether structures in the gas phase of the reaction

obtained (Scheme 14), which were readily extracted into *n*-hexane due to the lipophilic side chain. No reaction occurred with enamine double bonds. This way, the low-molecular-weight vinyl ethers in the gas phase of uncontrolled degradation reactions of NMMO were demonstrated to be similar to those found directly in the degradation mixture by trapping with the cyclone reagents. The application of 5a-bromo-α-tocopherol (**30**) directly in the reaction mixture instead of the phencyclone (**27**) or tetracyclone (**28**) traps – and not just for the gaseous phase – was not feasible as the reagent is degraded to the *ortho*-quinone methide intermediate **11** at temperatures above 50 °C, much lower than the temperatures of the degradation. Before eventually reaching the degradation temperatures, the trapping reagent would have been completely consumed and converted into the spiro-dimer **12**, which possessed no further trapping ability.

Origin and formation pathways of the different vinyl ether and enamine structures in mixtures from the uncontrolled NMMO degradation were difficult to assess, since the high temperatures during such processes also allowed disfavored decomposition processes to proceed, which are thermodynamically forbidden or disfavored under the usual Lyocell process conditions.

2.5 Summary

In summary, trapping methodology helped to confirm the presence of the three main NMMO-derived radical species, the nitrogen-centered radical cation **3** and the carbon-centered radicals **4** and **5** in Lyocell dopes. Trapping

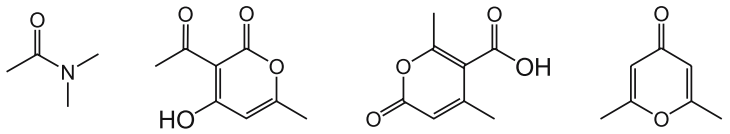
was not only performed by externally added trapping agent, but products from radical recombination reactions as a kind of internal trapping were also observed. The occurrence of NMMO-derived carbenium-iminium ion **17** and formaldehyde as its precursor compound were shown by trapping under Lyocell conditions. Trapping methodology was also used to study carbenium-iminium ion interconversions. Also intermediate vinyl ether and enamine-type degradation products in thermal decomposition mixtures of NMMO and the exhausted gases were detected by trapping.

3
Cellulose Solutions in DMAc/LiCl

3.1
Degradation of Solvent and Cellulose

N,*N*-Dimethylacetamide (DMAc, **31**) 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 very frequently used in polysaccharide chemistry [40, 41, 43]. First of all, it has become a standard solvent for gel permeation chromatography (GPC) measurements of cellulosics [44–49]. For dissolving pulps and low-molecular-weight pulps, dissolution occurs neatly. As paper pulps and some higher-molecular-weight dissolving pulps are largely insoluble in DMAc/LiCl, several activation procedures have been proposed, which aim to accelerate the dissolution in the case of soluble pulps, and to make dissolution possible at all in the case of initially insoluble pulps. All activation treatments are thought to cause intra- and intercrystallite swelling, breaking of hydrogen bonds and increased accessibility. Among those activation procedures are the treatment with liquid ammonia [50, 51], swelling in water followed by solvent exchange to ethanol and DMAc [52, 53], freeze-drying [54], or swelling in 0.1 M LiCl followed by a number of extraction steps [55].

A very common protocol is also heating or refluxing the cellulose samples in DMAc, or in DMAc containing low concentrations of LiCl [56, 57]. A yellowing of the heated mixture has been noticed, sometimes accompanied by a yellowish discoloration of the activated pulp sample. The chemistry of heated cellulose solutions in DMAc and DMAc/LiCl was investigated, and once more intensive use of trapping methodology was made. After having shown in previous work that the discoloration was caused by chromophores formed in LiCl-catalyzed condensation reactions from DMAc, such as dehydroacetic acid (**32**), isodehydroacetic acid (**33**), and 2,6-dimethyl-γ-pyrone (**34**) [58], see Scheme 15, the question of whether – and if so how – cellulose was degraded by the activation treatment became the key issue. If cellulose degradation indeed occurred, the common heating treatment would be



31 32 33 34

Scheme 15 Chromophoric condensation products of DMAc (**31**) formed by prolonged heating of DMAc or DMAc/LiCl

unsuitable for all processes which rely on an unchanged molecular weight distribution, such as GPC of pulps.

GPC measurements with initially soluble pulps demonstrated unambiguously that cellulosic material suffered a loss in average degree of polymerization (DP) upon heating in DMAc/LiCl. Already at temperatures as low as 80 °C there was a slow, linear, but noticeable decrease in molecular weight. At temperatures between 120 °C and the boiling point of DMAc (164 °C) the kinetics changed to an exponential decay, and the molecular weight degradation became rather severe and fast. The two degradation modes were observed for all pulps, although the degradation rate differed slightly for pulps of different providence.

The well-known fact that heating of initially insoluble pulps in DMAc/LiCl improves solubility or increases the dissolution rate of the material had thus to be attributed to pronounced cellulose degradation. The observed improved solubility was evidently accompanied by a progressive DP loss of the pulp. The solubility gain was thus not an activation of the pulp, but mainly a degradation process to material of lower molecular weight which naturally exhibited a higher solubility in the cellulose solvent.

From the GPC results it was clear that heating in DMAc/LiCl significantly influenced the molecular-weight distribution of the pulps. Consequently, GPC results from pulps which had undergone such an "activation" treatment did not reflect the data of the genuine cellulosic starting material. However, the actual degradation mechanism and the species causing this effect remained to be clarified. The two degradation processes that contribute to the DP loss have been identified: an *endwise peeling* reaction causing a rather slow decrease in the molecular weight at lower temperatures, and a random cleavage of glycosidic bonds, which is responsible for a much faster DP loss, at temperatures above 120 °C.

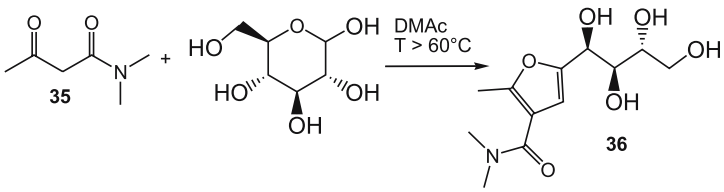
3.2
Slow "Thermal Endwise Peeling" of Cellulose in DMAc/LiCl

Thermal treatment of DMAc/LiCl caused the formation of *N*,*N*-dimethylacetoacetamide (**35**), independent of the presence of pulp [58]. This species is a highly reactive 1,3-dicarbonyl compound that readily undergoes subsequent

conversions, such as aldol condensations. The first step in these processes is the addition of the highly activated, CH-acidic methylene group of **35** to a carbonyl function. To prove the presence of this reactive intermediate in heated DMAc/LiCl, glucose was used as a trapping reagent, which was neatly converted into UV-active furan derivative **36** (Scheme 16), which was isolated and comprehensively characterized. C1 and C2 of the aldose and C2 and C3 of the acetoacetamide were incorporated into the furan heterocycle.

Surprisingly, furan **36** was not just formed upon trapping with glucose, but also when cellulosic pulps were heated in DMAc or DMAc/LiCl, and the formation was continuous over time following zero-order kinetics. The formation of **36** from pulp was strongly accelerated when excess *N*,*N*-dimethylacetoacetamide (**35**) was added to the mixture. From these results it became evident that not only the reducing ends were derivatized forming furan structures, but the derivatized terminal anhydroglucose units were continuously cleaved and released in the form of condensation product **36**. Thus, a cellulose chain with *n* anhydroglucose units formed the corresponding furan derivative, which was subsequently peeled off as **36** leaving behind the (*n* – 1)-cellulose chain with a "new" reducing end, which again reacted with acetoacetamide **35** and was once more cleaved. *N*,*N*-Dimethylacetoacetamide (**35**), the main thermal condensation product of DMAc, thus eventually caused a thermal endwise peeling of the pulp with concomitant release of furan **36**.

This peeling mechanism was confirmed by reaction of **35** with cellotetraose. The cellotetraose acted here as a type of repetitive trapping agent as it produced aldose molecules capable of trapping **35** as the respective furan structures. While the formation of endwise furan structures started at temperatures as low as 80 °C, the subsequent peeling steps required higher temperatures of about 95 °C to proceed at a noticeable rate. Cellotetraose formed first the corresponding furan derivative, which was then cleaved to give cellotriose and furan **36**, as followed by TLC and HPCE [59]. The cellotriose reacted immediately with **35** to give the corresponding end-derivatized furan, from which again **36** was peeled off under formation of cellobiose. Cellobiose, eventually, was converted into the corresponding endwise furan, and then finally cleaved into two molecules of **36**. Thus, the starting oligosaccharide



Scheme 16 Reaction of the main thermal condensation product of DMAc, *N*,*N*-dimethylacetoacetamide (**35**), with glucose to furan **36**

reacted four times as a quasi-trap for *N*,*N*-dimethylacetoacetamide (**35**), and was neatly converted into four molecules of furan **36** without significant formation of byproducts. As pulp and also cellotetraose formed exclusively **36**, but no other furan structures or condensation products, it was clear that the degradation had progressed from the reducing end. Cleavage of glycosidic bonds other than the respective proximal ones did not occur.

The mechanism of thermal endwise peeling of cellotetraose can be summarized as in Eq. 5, with the Eqs. 1–4 describing the consecutive, stepwise character of furan formation:

$$(\mathrm{Glc})_4 + \mathbf{35} \rightarrow (\mathrm{Glc})_3 + \mathbf{36} \quad (1)$$

$$(\mathrm{Glc})_3 + \mathbf{35} \rightarrow (\mathrm{Glc})_2 + \mathbf{36} \quad (2)$$

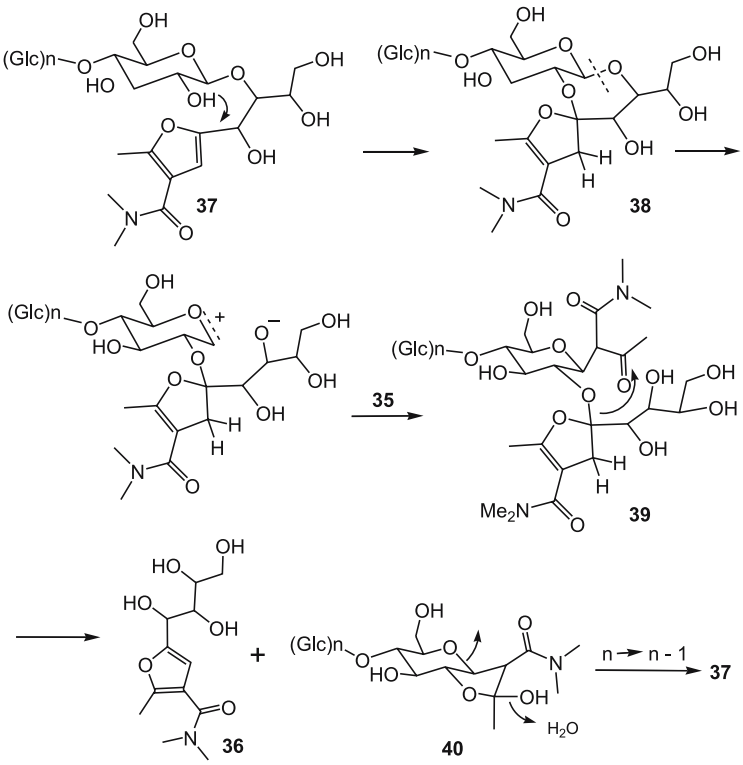
$$(\mathrm{Glc})_2 + \mathbf{35} \rightarrow \mathrm{Glc} + \mathbf{36} \quad (3)$$

$$\mathrm{Glc} + \mathbf{35} \rightarrow \mathbf{36} \quad (4)$$

$$(\mathrm{Glc})_4 + \mathbf{35}\ (\text{Eq. 4}) \rightarrow \mathbf{36}\ (\text{Eq. 4})\ . \quad (5)$$

A plausible mechanism for the observed thermal endwise peeling reaction was proposed based on computational chemistry. In its minimum conformation, C-2 of the furan ring at the terminal anhydroglucose unit of a derivatized cellulose molecule **37** is placed in close proximity to the C-2 hydroxyl group of the $(n - 1)$ non-reducing anhydroglucose unit. This preorganizational effect facilitates the addition of the hydroxyl group to the furan ring. The addition is an endothermic process and a reversible reaction; addition/elimination reactions of alcohols or hydroxyl ions to/from furans are well known in organic chemistry [60, 61]. The resulting seven-membered-ring structure **38**, a perhydro-1,4-dioxepane derivative, will most likely fragment back into the starting material. However, ring opening by cleavage of the glycosidic bond between C-1′ and O-1′ is a competitive pathway with relatively low activation energy and high overall exothermicity. The intermediate, a resonance-stabilized oxonium cation, reacts immediately with water to a new reducing end, or directly with **35** to form **39** in which two molecules of acetoacetamide are bound to the cellulose at the same time. Elimination of O-2 releases furan **36** into the surrounding medium. After ring closure to tetrahydrofuran derivative **40** the whole reaction cycle starts again with the cellulose chain shortened by one glucose unit (Scheme 17).

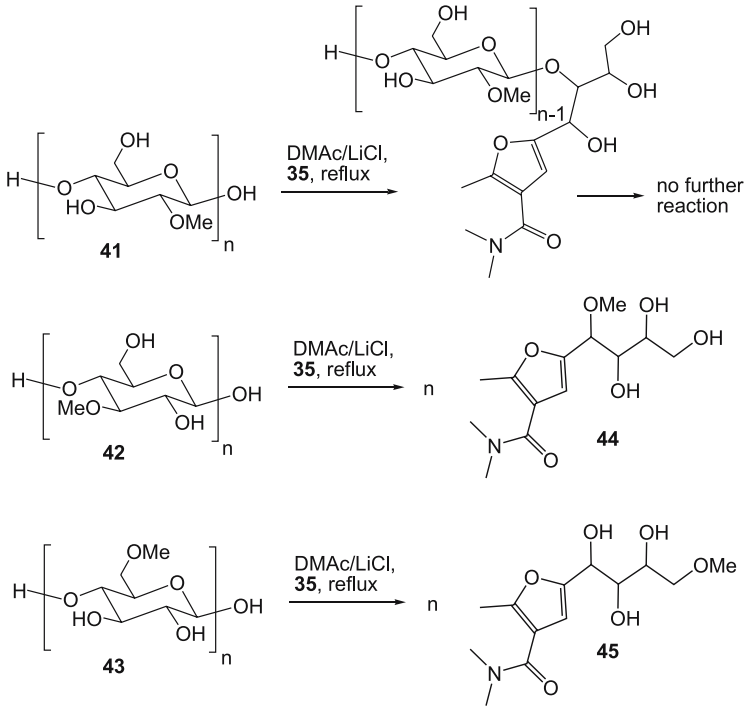
Following from the computations, the formation of furan derivatives from the reducing end of cellulose thus represents a neighbor-group assisted reaction. According to the proposed mechanism, only cleavage of the glycosidic bond that is adjacent to the proximal furan structure occurs, in agreement with experimental data. All other glycosidic bonds are stable under the prevailing conditions as no neighboring, activating furan structures are available. The crucial effect of the neighboring C-2 hydroxyl group was experimentally confirmed. Selectively 2-*O*-methylated cellulose (**41**), obtained chemically by cationic ring-opening polymerization [62–64], was shown to



Scheme 17 Mechanism of the slow thermal endwise peeling of cellulose in heated DMAc/LiCl under release of furan **36**

be completely inert towards *N*,*N*-dimethylacetoacetamide (**35**), even upon prolonged reflux in DMAc. As this material contained no free 2-OH group, addition to the terminal furan structure was prevented, and further thermal endwise peeling could not proceed. In contrast, selectively 3-*O*-methylated cellulose (**42**) and 6-*O*-methylated cellulose (**43**) – similarly synthesized by ring-opening polymerization – underwent the furan peeling reaction by complete analogy to cellulose (Scheme 18). These cellulose derivatives produced the respective monomethoxy derivatives **44** and **45**, respectively, as the peeling products, instead of furan **36.**

A final conformation of the computationally predicted mechanism was provided by the use of isotopically labeled material. *N*,*N*-Dimethylacetoacetamide-2-^{13}C was used to produce a snapshot of the reaction intermediates present during reaction with cellotetraose as a model compound, taken by ^{13}C NMR. A series of consecutive spectra produced a kinetic record how the positions with isotopic enrichment were distributed among different intermediates. From the prominent resonance in the starting material, the



Scheme 18 Thermal behavior of selectively substituted methyl celluloses (**41–43**) in refluxing DMAc/LiCl

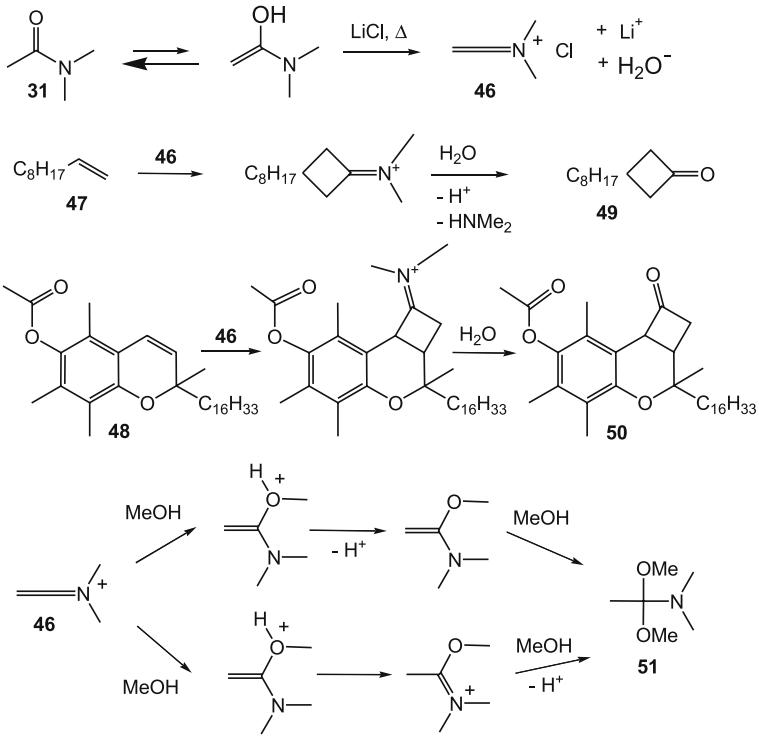
spectrum soon displayed four different resonances in agreement with the intermediates **38–40** in Scheme 17, and changed back to a single resonance of final furan product **36**.

3.3 Fast Degradation of Cellulose in DMAc/LiCl Due to Random Cleavage of Glycosidic Bonds by Keteniminium Ions

The thermal endwise peeling mechanism could not explain the drastically increased degradation of cellulosic material in heated DMAc at temperatures above 120 °C. If the decrease in molecular weight was only due to endwise peeling, large amounts of peeled-off furan structures **36** should be present, but only minute amounts were found. Thermal endwise peeling by furan structures and cleavage of glycosidic bonds along the cellulose chain were thus two separate parallel processes, which both caused a decrease in molecular weight of the pulp heated in DMAc, the first one proceeding only slowly, the latter one rather fast.

As *N*,*N*-dimethylacetoacetamide (**35**) alone induced only the slow endwise peeling pathway, and the other thermally formed byproducts of DMAc (**32**–**34**) did not effect a chain cleavage at all, an even more reactive species, which was responsible for the chain cleavage, was likely to be present. This intermediate was identified as *N*,*N*-dimethylketeniminium cations (**46**) by trapping reactions (Scheme 19) [65, 66].

Keteniminium salts are extremely reactive compounds; they are more electrophilic than ketenes and do not dimerize as most ketenes do [67, 68]. To prove the intermediacy of this species we used a typical reaction of keteniminium ions (and ketenes), the reaction with non-activated olefins to cyclobutanes in a thermal, i.e. suprafacial–antarafacial, [2 + 2]-cycloaddition. In order to be able to separate the trapping products from the DMAc medium with its high solvation power, strongly lipophilic trapping reagents were chosen that allowed extraction into apolar solvents. 1-Decene (**47**) and 3,4-dehydro-α-tocopheryl acetate (**48**) were chosen as the olefinic traps, the latter having the additional advantage of a high boiling point so that it can be used also in refluxing DMAc without yield penalty. The intermediacy of **46**

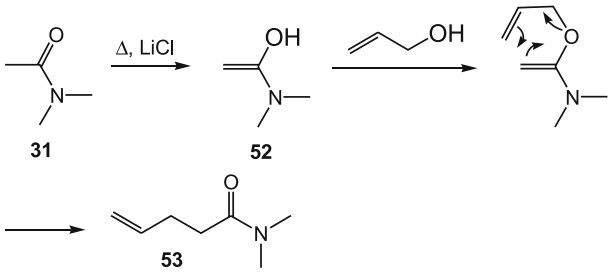


Scheme 19 Formation of *N*,*N*-dimethylketeniminium ions (**46**) from DMAc (**31**) and their trapping in [2 + 2]-cycloadditions and by consumption with methanol

in DMAc/LiCl of varying composition at temperatures above 120 °C was then unambiguously proven by isolation of the trapping products 3-octylcyclobutanone (**49**) from **47**, and cyclobutanone **50** from the tocopherol trap **48**, respectively. The regioselectivity of the addition reaction, e.g., the selective formation of the 3-octylcyclobutanone as compared to the 2-octyl derivative starting from **47**, is exclusively determined by steric factors as usual in thermal [2 + 2]-cycloadditions. The trapping of keteniminium **46** succeeded in DMAc/LiCl solutions independent of the presence of dissolved cellulose. In its presence, however, the amount of trapping product obtained was significantly lower, which indicated that also the pulp consumed the reactive intermediate, thereby being degraded.

The equilibrium concentration of **46** is determined by the endothermicity of the formation 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, for instance by reaction with pulp or by trapping, they are continuously regenerated according to the equilibrium constant. Addition of methanol to the respective DMAc/LiCl mixture was the most simple way of consuming *N*,*N*-dimethylketeniminium ions, which were converted into 1-dimethylamino-1,1-dimethoxy-ethane (**51**) (Scheme 19). Alternatively, the reaction with methanol can be seen as a trapping of the reactive intermediate **46** with methanol as the trapping agent. The formation reaction proceeded in a neat way, and the working procedure was quite convenient: product **51** was simply distilled off together with excess methanol. Keteniminium **46** was continuously regenerated in the reaction mixture and converted to the trapping product **51** by methanol. The capacity of DMAc/LiCl to generate **46** was quite large, ranging in the 1–5 percent range upon refluxing for 3 hours, depending on the amount of LiCl present. From the mechanistic point of view, the trapping started with methanol nucleophilically attacking the keteniminium carbon. This was followed by two competitive reaction sequences that both lead to the same trapping product **51**: first, proton loss produced an enol ether intermediate (an *O*-methylated ketene-semiaminal) which added a second equivalent of methanol to produce **51**, or second, a [1,3]-sigmatropic proton shift gave an iminium salt that reacted with methanol to provide the same product after proton release (Scheme 18). Both pathways differed in whether the second molecule of methanol is added to a C = C double bond or to the C = N double bond.

The *N*,*N*-dimethylketeniminium cation (**46**) is not formed directly from DMAc, but via its enol form (**52**), see Scheme 19. The formation of the enol form (imine form) is strongly facilitated by the presence of lithium ions, which coordinate to the amide oxygen. Also the intermediacy of enol precursor **52** was proven by means of trapping reactions: in the presence of allyl alcohol as the trap, the enol **52** formed an allyl enol ether, which at the prevailing elevated temperatures immediately underwent a *Claisen*-type rearrangement to produce 4-pentenoic acid *N*,*N*-dimethylamide (**53**) (Scheme 20). This



Scheme 20 Trapping of the enol form of DMAc (**52**) as the precursor of *N*,*N*-dimethylketeniminium cations (**46**)

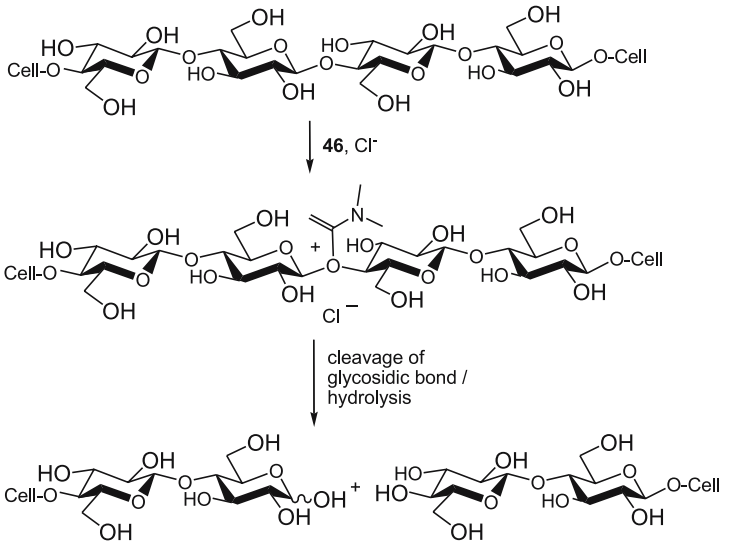
amide, which was again detected both in the presence and absence of pulp, was isolated from the reaction mixture by extraction with ethyl acetate after addition of water. The rearrangement was quite convenient as a trapping reaction as it proceeded neatly without byproduct formation.

3.4
Reactions of the DMAc-Derived Keteniminium Ions with Cellulose

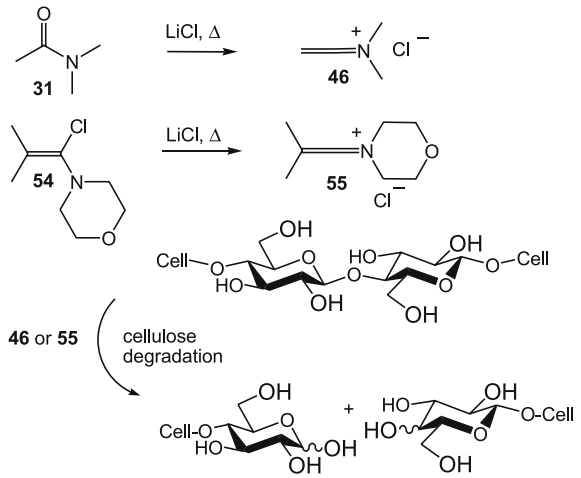
The absolute amount of keteniminium ions present in heated DMAc/LiCl solutions is rather low. However, due to the extreme high reactivity of this intermediate and due to its continuous regeneration upon consumption, these small amounts were evidently sufficient to cause the observed pronounced cellulose degradation. Keteniminium salts are known as reagents to effect mild cleavage of ethers, even nonreactive diaryl ethers, acetals, and ketals [67, 69, 70]. In the first step, the keteniminium ion attacks the ether oxygen electrophilically, followed by ether bond cleavage. In solutions containing electrolytes, such as ammonium salts or soluble alkali salts, hydroxyl groups and amino groups do not significantly interfere with the reaction, as these structures in ionic solutions are surrounded by a solvent shell (*ion cloud*) and blocked by strong hydrogen bonds, thus being shielded from attack.

An analogous mechanism was assumed for the cleavage of glycosidic bonds in cellulosic pulp. The strongly electrophilic *N*,*N*-dimethylketeniminium ion (**46**) attacked the glycosidic oxygen, followed by cleavage of the glycosidic bond under formation of a ketene-semiaminal derivative, which underwent secondary hydrolytic reactions, shown in Scheme 21 for a cellotetraose section of a cellulose molecule.

In heated DMAc/LiCl, the keteniminium ions are generated in situ from the solvent. When the degrading agent was added externally in the form of a keteniminium precursor, cellulose degradation was even more pronounced. The thermolabile keteniminium precursor compound 4-(1-chloro-2-methylpropenyl)morpholine (**54**) immediately releases keteniminium ions **55** upon thermal treatment (Scheme 22) [71]. Addition of the precursor in very small



Scheme 21 Cleavage of glycosidic bonds in cellulose by *N*,*N*-dimethylketeniminium ions (**46**)



Scheme 22 Cellulose degradation by keteniminium ions being either generated in the reaction mixture or added externally

amounts to a solution of pulp in heated DMAc/LiCl at 125 °C caused degradation of the cellulose down to oligomers (DP < 30) within less than 1 h. This was an additional illustrative proof of the detrimental action of keteniminium species on cellulose.

3.5 Summary

Two thermal degradations mechanisms of cellulose dissolved in DMAc/LiCl have been clarified. The lower-temperature process consists of an endwise peeling under release of furan structures induced by the thermal condensation product of DMAc, *N*,*N*-dimethylacetoacetamide (**35**). The high-temperature mechanism for cellulose degradation is based on DMAc-derived *N*,*N*-dimethylketeniminium ions (**46**), the presence of which in heated DMAc/LiCl, independent of the presence of pulp, was confirmed by trapping. Also the occurrence of a precursor enol intermediate (**52**) was demonstrated by trapping methodology. The general degrading effect of keteniminium ions on cellulose was experimentally shown in addition.

4 Cellulose in NaOH (Alkali Cellulose)

4.1 Aging of Alkali Cellulose

Alkalization of cellulose – often also called alkaline steeping – is a central process step in the production of many cellulose derivatives, most notably xanthation in the viscose process [72] or etherification in the production of carboxymethyl celluloses or alkyl celluloses [73]. In viscose rayon production, alkalization is not only used for activation of the hydroxyl groups towards xanthation, but also to free the pulp from impurities, such as hemicelluloses and cello-oligosaccharides. The alkalization step involves treatment of dissolving pulp with strong alkali hydroxides – mostly 18% NaOH – which converts cellulose into sodium cellulose I. The alkalization step is followed by the (pre-)ripening procedure: excess sodium hydroxide is pressed off and the press cake is left at temperatures slightly above ambient in the presence of air for several hours. In this stage, the appropriate pulp viscosity, i.e. the cellulose DP, is adjusted for further processing to viscose. It is known that the changes in the molecular-weight distribution are brought about by oxidative processes [74, 75], which involve introduction and conversion of oxidized functions, such as keto and aldehyde groups [76], in addition to chain shortening.

Mechanistic aspects of the alkaline degradation of cellulosic materials have mainly been addressed by research groups in the 1950s and 1960s [77–79]. Chain cleavage was shown to be predominantly caused by introduction of keto groups followed by β-elimination. As early as 1949, a radical chain mechanism for the aging of alkali cellulose was proposed [80, 81]. The formation of hydrogen peroxide during aging of alkali cellulose under oxygen was demon-

strated [82], as well as the formation of a number of low-molecular-weight acids. Thus, reactive oxygen species, namely hydroperoxyl, alkylperoxyl and hydrogen peroxide along with the respective radical anions, play a key role in the aging of alkali cellulose. The question of whether also the extremely reactive hydroxyl radicals were involved was controversially discussed. On one hand, the formation of hydroxyl radicals from peroxides and other reactive oxygen species should proceed relatively easily, on the other hand, hydroxyl radicals – if present in reasonably high concentrations – should cause much more pronounced chain degradation than usually observed.

Problems concerning the presence of a distinct radical species are usually addressed by specific trapping [83], employing spin traps that react with transient single-electron species to form stable radicals, which are subsequently analyzed by EPR or UV spectrometry. Such approaches have been widely and successfully used for a large variety of structurally different radicals, employing numerous special spin traps. Almost all of these applications have been concerned with the detection of radicals under physiological conditions or conditions coming close to those in living systems. The number of spin traps remaining operational under extreme conditions, i.e. at high temperatures or in the presence of concentrated acids, bases or other aggressive chemicals, is extremely limited. This was the reason, for instance, why a nonconventional spin trap had to be used to clarify the chemistry in Lyocell dopes (see above). For the detection of OH radicals during alkalization of celluloses the extreme conditions posed a similar problem.

4.2
Development of a Hydroxyl Radical Trap Working in Alkali Cellulose

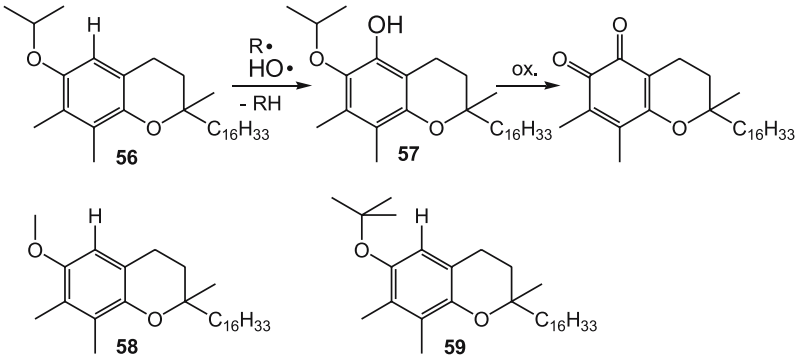
There have been reports on spin traps working under alkaline bleaching conditions [84, 85], and a literature report on a colorimetric determination of OH radicals in weakly alkalized cellulose samples using *N*,*N*′-(5-nitro-1,3-phenylene)bisglutaramide [86], but these approaches were not viable for application in the case of alkali cellulose. Generally, there was no spin trap known to work under the drastic conditions of cellulose alkalization, a reaction essentially carried out in concentrated aqueous NaOH. Recovery of the spin traps and separation from the alkalization byproducts remained as additional obstacles. In most cases, both the starting trap and the trapping product cannot withstand the concentrated alkaline medium. Therefore, aromatic hydroxylation was chosen as another means to report the presence of hydroxyl radicals. Aromatic systems are converted into hydroxyaromatics (phenols) in the presence of hydroxyl radicals. Usually, salicylic acid or phenylalanine are used as aromatic traps in hydroxylation assays under physiological conditions [87]. However, application to alkali cellulose posed the problem of retrieving spin trap and trapping products, as the mixture was rather complex and contained a nearly inseparable blend

of aromatic degradation products from low-molecular-weight celluloses and hemicelluloses.

γ-Tocopheryl-*iso*-propyl ether (**56**) was introduced as a new hydroxyl-selective spin trap to work under conditions of cellulose alkalization [88]. The reagent was synthesized according to a facile Williamson etherification procedure starting from γ-tocopherol (**6**) and 2-bromo-propane. The reagent is stable under ambient conditions, but should be kept in the dark under inert gas for long-term storage. The trapping reagent offered the advantage of only one aromatic position free for hydroxylation, which limited the number of possible hydroxylation products and facilitated subsequent analysis. Furthermore, the spin trap and its reaction products are strongly lipophilic and thus readily extractable into apolar solvents, a fact that had already been exploited and mentioned repeatedly in the case of tocopherol-based trapping agents. Even from the semi-solid cellulose alkalization mixture, retrieval of trapping agent and problems posed no problems.

The selectivity of the trap towards hydroxyl radicals was demonstrated by several control experiments using different radicals, showing that the formation of the respective hydroxylation product, 5-hydroxy-6-*O*-*iso*-propyl-γ-tocopherol (**57**), was caused exclusively by hydroxyl radicals, but not by hydroperoxyl, alkylperoxyl, alkoxyl, nitroxyl, or superoxide anion radicals. These radicals caused the formation of spin adducts from standard nitrone- and pyrroline-based spin traps, whereas a chemical change of spin trap **56** was only observed in the case of hydroxyl radicals. This result was independent of the use of monophasic, biphasic, or micellar reaction systems: in all OH radical generating test systems, the trapping product **57** was found. For quantitation, compound **57** was extracted with petrol ether, separated by adsorption onto basic alumina and subsequently oxidized in a quantitative reaction to α-tocored, the deeply red-colored 5,6-tocopheryldione, which was subsequently determined by UV spectrophotometry (Scheme 23).

The trapping selectivity of γ-tocopheryl-*iso*-propyl ether (**56**) was due to a combination of both electronic and steric effects. The aromatic part in tocopherols is electron-rich, which is the prerequisite for a high trapping efficiency towards electrophilic radicals. The electron density is increased by the mesomeric effects of the two oxygens at C-6 and C-8a and the inductive influence of the alkyl groups. γ-Tocopheryl-methyl ether (**58**) can be regarded as a model trap in which only the electronic contributions are active, since the methyl substituent is sterically innocent, exerting no influence on the neighboring non-substituted aromatic position. Compound **58** reacted also with hydroperoxyl, alkylperoxyl and alkoxyl radicals besides hydroxyl radicals: the high selectivity for hydroxyl radicals as found in **56** was evidently lost by exchanging the isopropyl for a methyl group. On the other hand, the *iso*-propyl group was still small enough to allow hydroxyl radicals approaching the neighboring aromatic position. A *tert*-butyl structure as in γ-tocopheryl-*tert*-butyl ether (**59**), carrying only one CH_3 group more than trap **56**, had



Scheme 23 Hydroxyl radical-selective trapping reaction with γ-tocopheryl-*iso*-propyl ether (**56**) and γ-tocopheryl ether derivatives (**58, 59**) showing different reactivity towards radicals

apparently lost this property, as hydroxyl radicals attacked this molecule almost randomly, with only a slight preference remaining for the reactive, but now largely inaccessible position 5.

4.3 Hydroxyl Radical Trapping in Alkali Cellulose During Aging

By application of hydroxyl radical trap **56**, the presence of hydroxyl radicals during ripening of alkali cellulose was proven for the first time. Aging of alkali cellulose was performed under conditions of industrial relevance, over a time of 19 h at two temperatures, 35 °C and 40 °C. The spin trap was added during the initial shredding of the alkali cellulose, and samples were taken over the reaction time. The samples were extracted with petrol ether to remove all tocopherol products, and the trapping product quantified as described above. The obtained data corresponded to the amount of hydroxyl radicals trapped during the respective time, which is an integral value, reflecting the amount of hydroxyl radicals trapped from the beginning of the aging process to a specific time rather than a snapshot of the radical concentration at the respective point of sampling time.

OH-radical production was quite intense in the initial phase of alkali cellulose aging, whereas in the later stages radical production gradually slowed down. The leveling off at longer reaction times could not be attributed to a diminished trap reservoir, as approximately 70% of the trap remained unchanged after completion of alkalization. About 15% of the added reagent was converted within the first three hours, nearly 30% at the end of the aging procedure after 19 °C. Thus, about one half of the trapped OH radicals were generated in the first sixth of the overall aging time. This allowed the interesting conclusion that hydroxyl radicals were mainly active in the initial phases

of cellulose aging, but involved little in later stages. This appeared reasonable as alkalization of cellulose under oxygen is well-known to produce a variety of low-molecular-weight (aromatic) compounds and semi-stable radicals from cello-oligosaccharide and xylo-oligosaccharide degradation products, all of which act as competitive substrates trapping hydroxyl radicals [89–93]. The concentrations of these species are low in early aging phases, so that hydroxyl radicals predominantly react with the tocopherol-derived trap **56**. In later stages, the reaction with the condensation products becomes increasingly competitive as their concentration increases, so that less hydroxyl radicals react with spin traps or with cellulose.

4.4
Cellulose Degradation During Steeping of Alkali Cellulose

The course of hydroxyl radical generation agreed very well with the observed cellulose chain degradation. The DP loss was pronounced in the early alkalization stage, and slowed down with longer reaction times, parallel to the activity of hydroxyl radicals as detected through the trapping approach. For instance, cellulose of an initial DP of approximately 1400 suffered a DP loss of 400–500 within the first three hours, whereas the DP loss in the remaining 16 h was only about 300–400 DP units more. The hydroxyl radicals present – this applies to other radicals as well – appeared to attack the alkali cellulose mainly in the early phases of the aging procedure; in later phases competitive reactions of the radicals with low-molecular-weight products became increasingly dominant, so that aging cellulose degradation could be assumed to be increasingly caused by ionic rather than radical processes.

Also with trap **56** no quantification of the total amount of generated hydroxyl radicals could be performed – as is the case with any other trapping method – since hydroxyl radicals are overly aggressive chemical species, reacting with any structure in their immediate chemical environment. However, aging of alkali cellulose in the absence and presence of the radical trap was compared and showed that the presence of γ-tocopheryl isopropyl ether (**56**) in aging alkali cellulose evidently slowed down the chain cleavage of cellulose and thus impeded the rate of the DP loss. The differences in the aging kinetics were related to the trapped hydroxyl radicals, with the missing amount of OH radicals corresponding to the amount of hydroxylation product isolated. However, the contribution of OH radicals to the overall cellulose degradation, approximately 100 DP units, was comparatively small, the larger part was attributable to the action of different radicals, reactive oxygen species, and heterolytic processes. Also OH radicals, which hydroxylated the trap, would in the absence of the trap not necessarily attack and cleave the cellulose chain directly, but rather initiate a complex set of reactions, which as a whole resulted in chain degradation. These processes, for instance, might consist of the generation of secondary radicals which attack the cellulose,

or the introduction of oxidized functionalities into the cellulose chain followed by base-induced cleavage (β-elimination). The aging temperature had the expected strong effect; the cellulose degradation proceeded faster with increasing temperature.

4.5 Summary

The presence of OH radicals during aging of alkali cellulose – as performed in the ripening step of viscose production – was proven for the first time by application of a newly developed, tocopherol-derived trapping agent **56**. The action of OH radicals was shown to be especially pronounced in the earlier phase of the aging reaction, in later stages the effect of OH radicals was increasingly attenuated by competitive reactions with (aromatic) carbohydrate degradation products.

5 Cellulose Carbanilation in DMSO

5.1 Cellulose Carbanilation in Different Solvents

Cellulose tricarbanilate, obtained by reaction of cellulose with phenyl isocyanate – mostly in DMSO or pyridine as the solvents – has been used widely for the determination of analytical parameters of celluloses by gel permeation chromatography (GPC) in organic solvents, such as THF.

Carbanilation offers some advantages over direct dissolution, e.g. in DMAc/LiCl, or over preparation of other derivatives for analytical purposes, such as cellulose nitrates. For instance, carbanilates are quite stable and can be stored over extended periods of time [94], and the eluants used in GPC of carbanilates – mostly THF – are much less exotic than, for instance, DMAc/LiCl or transition-metal complexes. The increase of the polymer mass by carbanilation in combination with the large refractive index increment dn/dc accounts for increased sensitivity upon light-scattering and refractive-index detection, respectively. In addition, the introduction of aromatic moieties upon derivatization allows for monitoring by UV detection. Carbanilates are also suitable derivatives for the analysis of partially substituted celluloses, such as cellulose ethers or esters. After derivatization of the remaining free hydroxyl groups by carbanilation the degree of substitution in relation to the molecular weight can be assessed without a cleavage of the primary substituents [94, 95].

One obstacle to a broad application in cellulose analytics is a certain discrimination effect: low-molecular-weight parts are lost in precipitation and

purification steps. The main disadvantage, however, is cellulose degradation upon carbanilation, and the lack of suitable means to prevent this negative effect, so that a reliable polymer-analogous derivatization could not be performed so far. Many derivatization procedures for cellulose tricarbanilates have been reported [96–105]. In most protocols, DMSO was used as the derivatization solvent, sometimes pyridine or mixtures of both solvents. Cellulose degradation was found to occur in both solvents, but was described to be more pronounced in DMSO [102–104]. The degradation in DMSO was assumed to be due to an oxidizing effect of the solvent in combination with isocyanate, similar to Moffat oxidation systems [106], which would introduce carbonyl structures that subsequently cause chain cleavage by β-elimination procedures. The latter was also assumed to be the cause of cellulose degradation in pyridine as the carbanilation solvent.

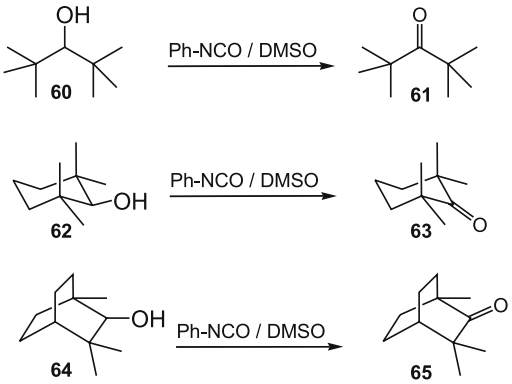
It was the main goal of our studies to verify the existence of an oxidizing effect of DMSO-based carbanilation mixtures on cellulose, and – if this effect existed – to clarify the responsible reactive intermediates. Trapping reactions were again the key elements in these mechanistic studies.

5.2
Oxidizing Effects of Carbanilation Mixtures Containing DMSO

The oxidative power of carbanilation mixtures containing DMSO and isocyanates was concluded from cellulose degradation in these mixtures. The mechanism of cellulose degradation was proposed to be a combination of oxidation and subsequent chain cleavage at the oxidized positions according to a β-elimination mechanism triggered by auxiliary bases [106].

Three carbinol model compounds with a $\alpha,\alpha,\alpha',\alpha'$-tetraalkyl substitution pattern were applied to screen for oxidizing DMSO-derived species: 2,2,4,4-tetramethylpentan-3-ol (**60**), 2,2,6,6-tetramethylcyclohexanol (**62**), and fenchyl alcohol (**64**) the latter being closer to the structure of cellulosic anhydroglucose units by having a similar six-membered ring in chair conformation. The main advantage of the model compounds was their inability to form carbanilates due to steric crowding. For instance, 2,2,4,4-tetramethylpentan-3-ol (**60**) can also be termed di-*tert*-butyl-carbinol – a name that better reflects the steric hindrance. Using classical Swern oxidation conditions, it was confirmed that small molecules, such as sulfonium ylides, could still approach this site to perform oxidation, whereas steric hindrance around the hydroxyl groups would prevent larger molecules – such as isocyanates – from reacting. Thus, the chosen model compounds would make oxidation observable without carbanilation as a competitive process. Furthermore, the three product ketones were inert towards the carbanilation mixtures and thus were not further consumed by side-reactions.

Indeed, the oxidizing effect of a DMSO/PhNCO mixture under standard cellulose carbanilation conditions, i.e. reaction times of 2–3 d at tem-



Scheme 24 Proving the oxidizing effect of DMSO/phenyl isocyanate mixtures under conditions used for carbanilation of cellulose by means of sterically hindered alcohol model compounds

peratures between 40 °C and 90 °C and a molar DMSO/isocyanate ratio of about 100 : 1, was demonstrated by means of the model compounds. All three alcohols were converted into the corresponding ketones, 2,2,4,4-tetramethylpentan-3-one (**61**), 2,2,6,6-tetramethylcyclohexanone (**63**) and fenchone (**65**), and no alcohol-derived byproducts, especially no carbanilates, were found (Scheme 24). In the presence of cellulose as a competitive substrate, the model alcohols were still oxidized, but at a much slower rate. This confirmed that the oxidative effect of the DMSO/PhNCO mixture was still active and not suppressed by the cellulose, and implied that cellulosic hydroxyls were oxidized to keto functions similar to the hydroxyls of the model alcohol probes. As the model compounds used were strongly sterically hindered, it was moreover likely that the oxidizing effect on the relatively easily accessible cellulosic hydroxyls was even more pronounced.

5.3 Carbanilation in the Presence of Trapping Agents

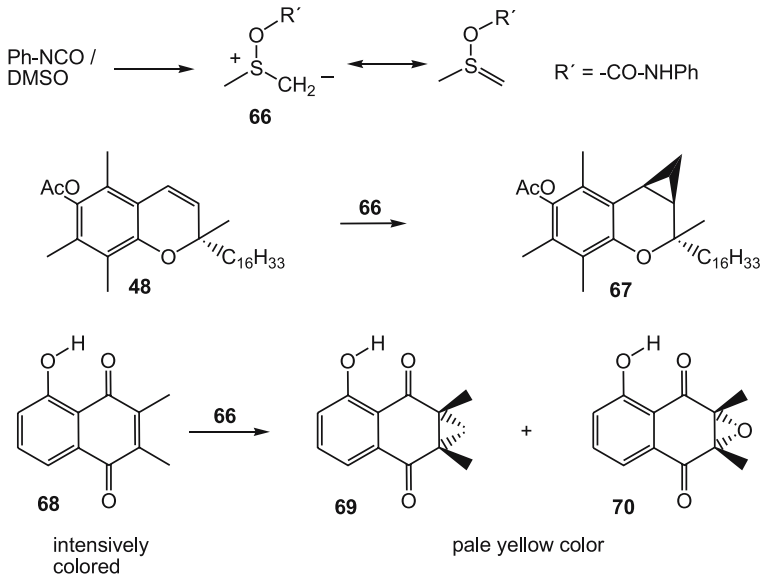
The proof of the oxidizing power of the DMSO-based carbanilation did not answer the question of which chemical species were actually causing the oxidation. It was very likely that these species were sulfonium ylides (**66**) by analogy to Moffat-type and Swern-type oxidations. Apart from their action mode as oxidants, sulfonium ylides are able to react with double bonds to cyclopropanes or epoxides, depending on whether the coreactant is an olefin, an α,β-unsaturated ketone, or an α,β-unsaturated ester. This chemical behavior was employed in a trapping approach to prove the presence of sulfonium ylide species.

From the apparent wealth of unsaturated compounds as coreactants, very few seemed appropriate as trapping agent for sulfonium ions or ylides, since

the trapping approach once more sets special requirements: the reaction products – possibly formed in minute amounts only – had to be separated from the cellulose carbanilation mixture, purified, and identified. For this reason, once more a tocopherol derivative, 3,4-dehydro-α-tocopheryl acetate (**48**), was chosen due to its strong lipophilicity which guaranteed supreme extractability into apolar media, such as *n*-hexane or petrol ether, also from complex and heterogeneous carbanilation mixtures. The apolar extraction medium contained only the trapping agent and its products; all other components were too hydrophilic to enter the alkane phase.

Carbanilation in the presence of the trapping agent and subsequent extraction into *n*-hexane provided a mixture of non-reacted trap and a main product, the corresponding cyclopropa[c]chromanol derivative **67**, indicating that the double bond of the trapping agent had undergone cyclopropanation (Scheme 25). The cyclopropane derivative was separated, purified and fully analytically characterized, and its structure additionally confirmed by comparison with an authentic sample.

The trapping product constituted unambiguous evidence for the presence of dimethylsulfonium ions and the derived sulfonium ylide in the carbanilation mixture consisting of DMSO/PhNCO/cellulose. These sulphur-containing species – known to be strongly oxidizing as the actual oxidants in Moffat-type and Swern-type procedures – cause the oxidative effect of the



Scheme 25 Generation of methylsulfonium ylides in DMSO-based cellulose carbanilation mixtures, trapping by 3,4-dehydro-α-tocopheryl acetate (**67**), and quick color testing for their presence by naphthoquinone derivative **69**

DMSO/isocyanate carbanilation medium on cellulose. It should be noted that the oxidation per se does not cause chain cleavage and cellulose degradation, but only the introduction of carbonyl functionalities along the cellulose chain. However, these groups constitute points of pronounced chemical instability where subsequent cleavage, mainly under basic conditions in β-elimination processes, will readily occur.

A second proof of the presence of the cellulose-damaging sulfonium ylide **66** was provided by employing 5-hydroxy-2,3-dimethyl-[1,4]-naphthoquinone (**68**) as the trapping agent. This compound, which dissolved with a dark-blue, almost black, color – was similarly attacked at the quinoid double bond, and converted into a mixture of the cyclopropane derivative 1a,7a-dihydro-1*H*-cyclopropa[b]naphthalene-2,7-dione (**69**) and the epoxide derivative 1a,7a-dihydro-1-oxa-cyclopropa[b]naphthalene-2,7-dione (**70**) in an approximate 3 : 1 ratio (Scheme 25). As both of the products lacked the strongly chromophoric benzoquinoid system, the solution turned increasingly light during the reaction, finally reaching a pale-greenish hue.

Besides the direct proof of the presence of the oxidizing sulfonium species, this reaction offered a surprisingly easy and convenient way to check whether certain carbanilation conditions will cause oxidative damage of cellulose or whether they are safe to perform with regard to cellulose integrity. For this purpose, the naphthoquinone **68** was used as a quasi-color indicator in very low concentrations, just enough to cause a visible coloration of the solution. If the reaction mixture exerted an oxidizing effect due to dimethylsulfonium ions, the color faded; if no oxidizing sulfonium species were present, the color remained unchanged. With the finding of this probe, it became readily possible to monitor the effect of different influencing factors, such as temperature, isocyanate type, concentration, cosolvents, auxiliaries and others, on the oxidative power of the carbanilation system, in order to minimize oxidative damage to the cellulose and subsequent DP losses.

5.4 Summary

The oxidative effect of the DMSO/PhNCO system on cellulose was confirmed by means of alcoholic model compounds (**60**, **62**, **64**) that were neatly oxidized into the corresponding ketones. The presence of the active species, the oxidatively acting sulfonium ylide **66**, in the cellulose carbanilation mixture was proven by trapping with two reagents, a tocopherol-based compound (**48**) and a naphthoquinone (**68**) that was also used in a facile color test to estimate the degrading effect of certain carbanilation mixtures and conditions on cellulose.

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