Russian Chemical Reviews **79** (1) 63 – 75 (2010) © 2010 Russian Academy of Sciences and Turpion Ltd

DOI 10.1070/RC2010v079n01ABEH004074

Nitroxide-catalyzed selective oxidation of alcohols and polysaccharides

I Yu Ponedel'kina, E A Khaibrakhmanova, V N Odinokov

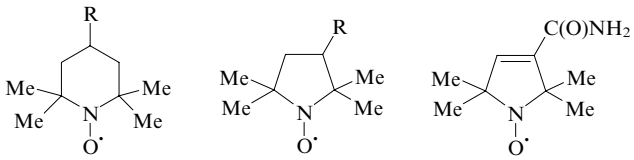
Contents

I. Introduction	63
II. Oxidation of alcohols involving 2,2,6,6-tetramethylpiperidine-1-oxyl	64
III. Selective oxidation of polysaccharides	68

Abstract. The use of nitroxide radicals in the selective oxidation of alcohols is considered. Attention is focused on the oxidation of polysaccharides as a method of preparation of polyuronic acids, aldehydes and hemiacetals. The bibliography includes 146 references.

I. Introduction

The oxidation of primary hydroxyl groups in neutral polysaccharides represents one of the most important directions of their modification that produces practically valuable polyuronic acids, aldehydes, hemiacetals to be later used as glues, thickeners, adsorbents, additives to foodstuffs and cosmetics, dyes and drugs.[1–3] The oxidation of polysaccharides involved the use of nitrogen oxides,[4–7] alkali metal nitrites and nitrates,[8,9] ozone,[10] hydrogen peroxide,[11–13] oxygen (in the presence of Pt),[14–16] different oxygen-containing halogen compounds (NaOCl, $NaClO_2$, $NaClO_3$, $NaBrO_3$, ClO_2).[17–22] However, the use of nitrogen dioxide resulted in the formation of polysaccharide nitrates as side products[4–6] while the degree of conversion of polysaccharides in the oxidation under the action of O_2, H_2O_2, O_3 and ClO_2 is low, and this is accompanied by a substantial decrease in their molecular masses due to the cleavage of glycosidic bonds.[10–16,21] The majority of known oxidants are chemically non-specific and, hence, capable of oxidizing secondary OH groups of polysaccharides in addition to their primary hydroxyl groups. The selective oxidation of the primary OH groups in the presence of secondary ones was achieved in reactions catalyzed by cyclic sterically hindered nitroxide radicals such as 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (**1**), its 4-substituted derivatives (**2**–**11**), 2,2,5,5-tetramethylpyrrolidine-1-oxyl (**12**), its 3-substituted derivatives (**13**, **14**) and 3-carbamoyl-2,2,5,5-tetramethyl-3-pyrroline-1-oxyl (**15**).[23–25]



1–**11** **12**–**14** **15**

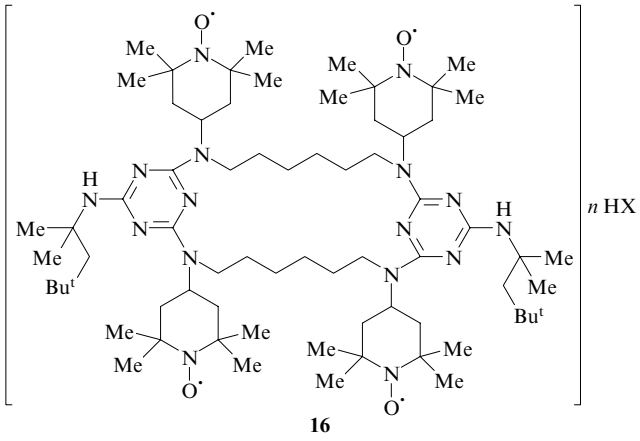
R = H (**1**, **12**), NHAc (**2**), CO_2H (**3**, **13**), NH_2 (**4**), OH (**5**), O^- (**6**), OMe (**7**), $NHC(O)CH_2Br$ (**8**), PO_4H_2 (**9**), OAc (**10**), OSO_2Me (**11**), $C(O)NH_2$ (**14**).

The synthesis, properties and chemistry of nitroxide radicals were comprehensively considered in numerous publications.[23,26–32] Sterically hindered nitroxides are characterized by the stability that is uncommon for radicals; this is associated with the absence of α-hydrogen atoms in their structures, which precludes disproportionation of these radicals.[26] Nitroxide radicals were used as antioxidants,[33,34] free radical scavengers,[35] spin labels in studying biological systems,[26,36] inhibitors of chain polymerization processes,[37] radical initiators of certain reactions.[38] Nitroxide radicals have found application in organic synthesis for the oxidation of alcohols, amines (including anilines), phosphines and phenols.[23,39,40]

Innobilization of TEMPO derivatives onto polymeric matrices, such as polystyrene,[41,42] polyacetylene,[43] poly(ethylene glycol) [44,45] has made possible their recycling. Grafting of TEMPO on graphene-coated magnetic cobalt nanoparticles[46] enabled easy recovery of the catalyst from the reaction mixture by magnetic decantation. This radical was incorporated into a cyclic oligomer (**16**),[47] an ionic liquid (**17**)[48] and bound to polystyrene microencapsulated in a polyurea shell (**18**) (the microcapsule is conditionally shown by a circumference).[49] Multiple triazole moieties and perfluoroalkyl chains attached to TEMPO favour emulsion formation in a two-phase system, the catalyst **19** is highly active for the oxidation of alcohols and easily recoverable.[50]

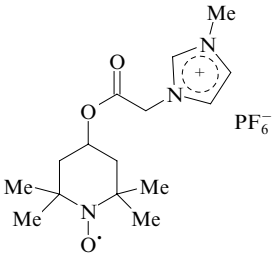
I Yu Ponedel'kina, E A Khaibrakhmanova, V N Odinokov Institute of Petrochemistry and Catalysis, Russian Academy of Sciences, prosp. Oktyabrya 141, 450075 Ufa, Russian Federation. Fax/tel. (7-347) 284 27 50, e-mail: ink@anrb.ru

Received 12 May 2009
Uspekhi Khimii **79** (1) 65 – 77 (2010); translated by T Ya Safonova

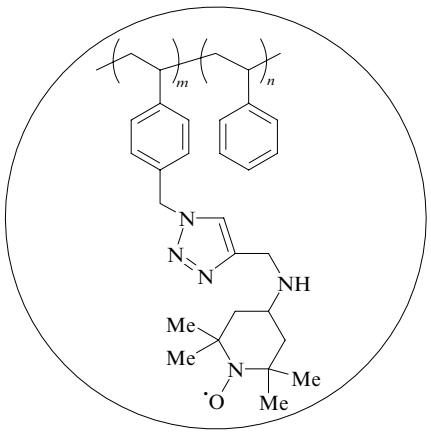


16

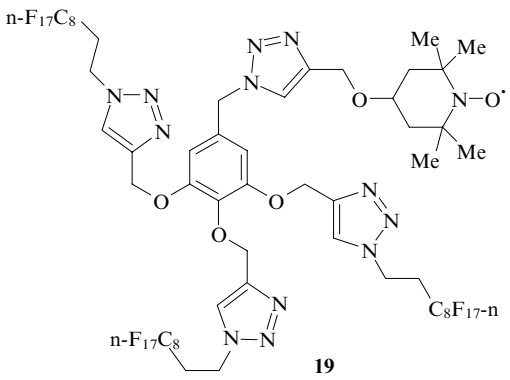
HX is an organic or inorganic acid, $n = 0-4$.



17



18

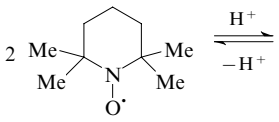


19

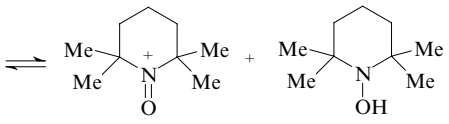
Despite the diversity of nitroxide radicals, it is the water-soluble TEMPO radical (**1**) that was used most often in the selective oxidation of alcohols and polysaccharides, which is mainly due to its ready accessibility.

II. Oxidation of alcohols involving 2,2,6,6-tetramethylpiperidine-1-oxyl

The use of the TEMPO radical as a component of oxidation systems is related to its ability of easy oxidation to the 2,2,6,6-tetramethyl-1-oxopiperidinium cation (**20**) and reduction to 1-hydroxy-2,2,6,6-tetramethylpiperidine (TEMPOH, **21**).[51, 52] For TEMPO (**1**) and its derivatives, the reversible acid-catalyzed disproportionation reaction is also typical.[51, 53]



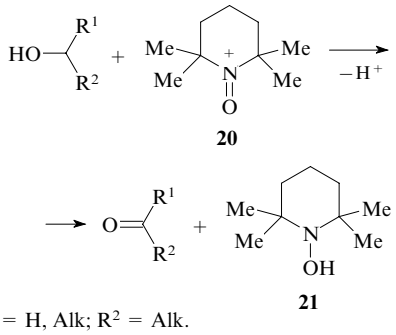
1



20 **21**

Both nitroxides and oxoammonium salts were used as the oxidants. Certain examples where stoichiometric amounts of nitroxide radicals oxidized different substrates (without involvement of oxoammonium salts) were described in a review.[32]

Oxoammonium salt **20** is a stronger oxidant than original radical **1**, hence, the latter is transformed to salt **20** upon disproportionation or a reaction with a strong oxidant (*e.g.*, chlorine or ClO_2, see Ref. 26). Oxidation of alcohols with oxoammonium salt **20** afforded the corresponding carbonyl compound, while salt **20** was reduced to hydroxylamine **21**.[54]



20 **21** (1)

R^1 = H, Alk; R^2 = Alk.

Examples of oxidation of alcohols with oxoammonium salts can be found in several reviews.[23, 24, 32, 51, 54] It is beyond doubt that the pioneers in this field are the Russian scientists, Golubev *et al.*, who were the first to study the mechanism of oxidation of alcohols and aldehydes with the oxoammonium cations.[51, 54]

Of the greatest concern is the catalytic oxidation of alcohols with such oxidants as sodium hypochlorite, organic peroxy acids, O_2, *etc.* and TEMPO radical (**1**) as the catalyst ($\sim$1 mass % of the substrate) rather than with stoichiometric amounts of the oxoammonium salts.[23, 25, 32] The active form in the catalytic cycle was assumed to be oxoammonium cation **20** formed from TEMPO [or from its reduced forms, namely, 2,2,6,6-tetramethylpiperidine[55] or hydroxylamine TEMPOH (**21**)] under the action of the oxidant. Having oxidized the alcohol, cation **20** transforms to hydroxylamine **21** [reaction (1)]; the latter is oxidized to

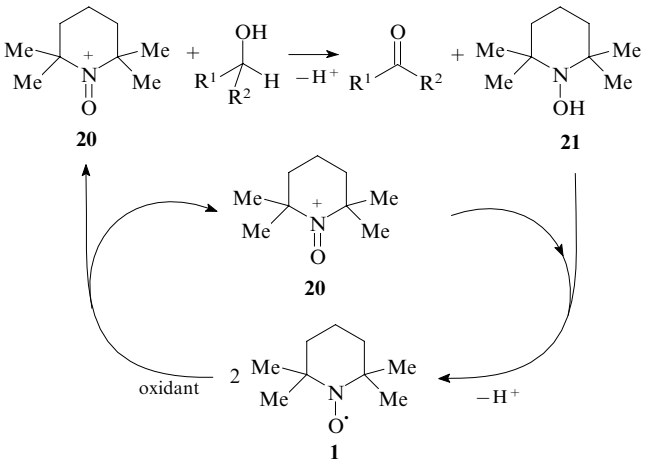
oxoammonium cation **20** under the action of the oxidant and returns to the cycle. For the first time, this scheme was proposed by Golubev *et al.*[56] in the context of their studies of oxidation of alcohols with hypochlorous acid in the presence of 2,2,6,6-tetramethyl-1-oxopiperidinium perchlorate (0.4 mol % – 7.5 mol % with respect to the substrate, pH 7.6).

$$\mathbf{20} + RCH_2OH \longrightarrow \mathbf{21} + RCHO + H^+,$$

$$\mathbf{21} + HOCl \longrightarrow \mathbf{20} + H_2O + Cl^-.$$

This process involved no transient formation of a nitroxide radical in the regeneration of TEMPOH (**21**) to cation **20** by hypochlorous acid.[57] When ClO_2 was used as the oxidant, the regeneration of oxoammonium cation **20** from hydroxylamine **21** proceeded *via* a radical species.[26] The concepts on the TEMPO transformations in catalytic oxidation, which considered its ability to undergo reversible acid-catalyzed disproportionation, were used to propose schemes that took no account of the oxidant nature or properties of the oxoammonium salts. Examples of such schemes that describe the TEMPO redox reactions as a function of pH can be found in reviews.[23,25] At pH > 3, radical **1** was transformed under the action of an oxidant into oxoammonium cation **20**. The latter was consumed both in the oxidation of alcohols being reduced to hydroxylamine **21** and in the oxidation of TEMPOH (**21**) to the original radical **1** (Scheme 1).[23,25]

Scheme 1

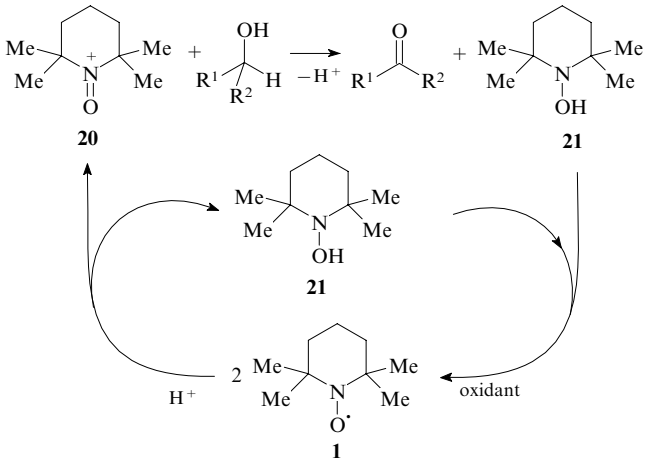


R^1 = Pr^n, n-C_5H_{11}, n-C_6H_{13}, Ph, Bn, PhCH=CH;
R^2 = H, Me, Et; $R^1 - R^2$ = $(CH_2)_4$, *etc.*

At pH < 2, the TEMPO radical (**1**) disproportionates to hydroxylamine **21** and oxoammonium cation **20**; the latter oxidizes the alcohol and is reduced to hydroxylamine **21**. Under the action of the oxidant, the hydroxylamine transforms into the original radical **1** (Scheme 2).[23]

The majority of studies concerning the use of hypochlorite in an alkaline medium as a stoichiometric oxidant of alcohols and polysaccharides presume that the transformations of the TEMPO radical (**1**), cation **20** and TEMPOH (**21**) in the catalytic cycle are the same as shown in Schemes 1 and 2. At present, it is known that oxoammonium salts are unstable in solutions and quickly reduced to the original nitroxide in aqueous[51] and aqueous alkaline media[58,59] and in the presence of NaOCl and NaOBr (pH 10.2) (according to EPR data).[60] Following oxidation of starch[61] or glucopyranose 1-phosphate[62] with sodium

Scheme 2



R^1 = Pr^n, n-C_5H_{11}, n-C_6H_{13}, Ph, Bn, PhCH=CH;
R^2 = H, Me, Et; $R^1 - R^2$ = $(CH_2)_4$, *etc.*

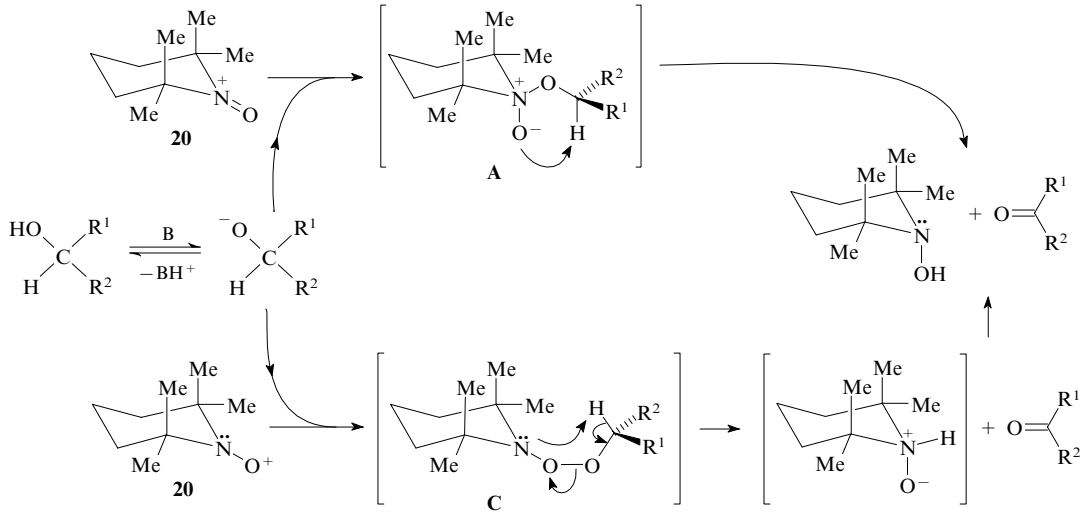
hypochlorite (5 mol % – 6 mol % of TEMPO with respect to substrate, H_2O, pH 9, 1 – 1.5 h), TEMPO was isolated from the reaction mixture by azeotropic distillation with water and its activity in the third cycle of substrate oxidation remained virtually unchanged. No detailed characteristics of the recovered catalyst were presented in these studies.

It should be noted that no careful attention was paid to the effect of TEMPO on the stoichiometric oxidants conventionally used in the oxidation of alcohols. A study[55] that showed that the decomposition of *m*-chloroperoxybenzoic acid in the presence of TEMPO was accelerated under the action of an alcohol, as well as some our observations on the TEMPO-catalyzed decomposition of NaOCl that presumably resulted in the formation of oxygen and the ClO and ClO_2 radicals[60] are the exceptions. For deeper insight into the mechanism of oxidation of alcohols and the role played by the TEMPO radical it is necessary to comprehensively study these oxidant systems in the same manner as, for example, for the system $NaClO_2$ – manganese porphyrin complex, which has been used in the oxidation of cyclohexane in a water – organic medium (pH 11). In this system, the catalytic disproportionation of chlorite yields reactive oxygen in amount sufficient to support the autoxidation mechanism.[63]

In the oxidation of alcohols in the presence of TEMPO (and, as conventionally believed, in the generation and regeneration of oxoammonium cations in the catalytic cycle), various oxidants and oxidation systems were used, namely, O_2 – Cu salts,[64] $O_2 - CuO - MnO_2$,[65] $O_2 - FeCl_3 - NaNO_2$,[66] $Ca(OCl)_2$,[67] NaOCl – NaBr,[68] $NaClO_2 - NaOCl$,[69] *N*-chlorosuccinimide,[70] $K_3[Fe^{III}(CN)_6]$ (Ref. 71), $PhICl_2$,[72] trichloroisocyanuric acid,[73] I_2,[74] $O_2 - Br_2 - NaNO_2$,[75] $O_2 - NaNO_2$ – 1,3-dibromo-5,5-dimetylhydantoin,[76] $O_2 - Mn(NO_3)_2 - Co(NO_3)_2$ or $Mn(NO_3)_2 - Cu(NO_3)_2$,[77] $H_2O_2 - HBr - MeReO_3$,[78] IO_5,[79] $O_2 - HBr - Bu^tNO_2$,[80] as well as oxidants in combination with enzymes (O_2 with laccase[81] and H_2O_2 with horseradish peroxidase[82]). With the same purpose, the electrochemical oxidation was used,[83] including its version in ionic liquids.[84,85]

The reaction medium acidity had a substantial effect on the rate of oxidation of alcohols in the presence of TEMPO and on the composition of the reaction products. At pH < 8, the primary and secondary alcohols were oxidized at the same rates that were lower than at pH > 8. With an

Scheme 3



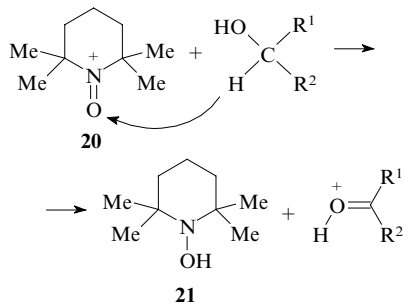
B is a base.

increase in pH of the reaction mixture, the selectivity of oxidation of primary alcohols increased.[23, 25]

In organic solvents, primary alcohols were preferentially oxidized to aldehydes,[86] in water–organic media, in addition to aldehydes, carboxylic acids were formed and became the main reaction products in the case of oxidation in the presence of a phase-transfer catalyst.[87]

The high selectivity of the oxidation of alcohols in the presence of TEMPO was rationalized by invoking an ionic mechanism,[23, 51, 88] which was also substantiated by theoretical calculations.[89] According to this mechanism, the oxidation of alcohols in an alkaline medium could begin with a nucleopilic attack of an alkoxide on the nitrogen or oxygen atom of the strongly polarized N=O bond of cation **20**, which results in complex **A** or **C**, respectively (Scheme 3). According to calculations, the energy of bipolar complex **A** is lower; hence, the oxidation of alcohols *via* peroxide complex **C** is less probable. The intramolecular transfer of two electrons from the C–H bond to the nitrogen atom in complex **A** leads to a carbonyl compound and hydroxylamine TEMPOH (**21**).[89] The high selectivity of the oxidation of primary alcohol was explained by, first, the higher stability of the respective intermediates and, second, the higher concentration of primary alkoxide groups in solutions (at the same pH value) as compared with secondary alkoxide groups due to the higher acidity of primary alcohols.[90]

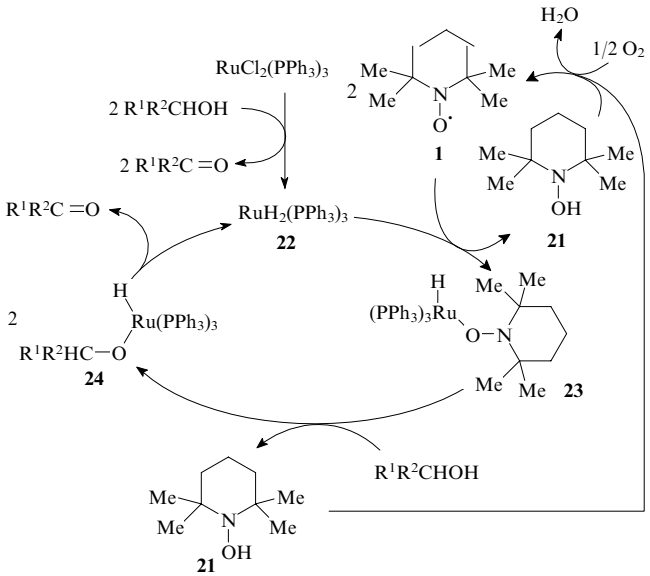
Oxidation in neutral and acidic media involved the intermolecular transfer of a hydride ion from the α-carbon atom of the alcohol to the oxygen atom of the oxoammonium cation **20** to afford hydroxylamine **21** and the protonated form of an aldehyde or ketone.[89]



R^2 = H: R^1 = Me, Et, Pr^i, *etc.*

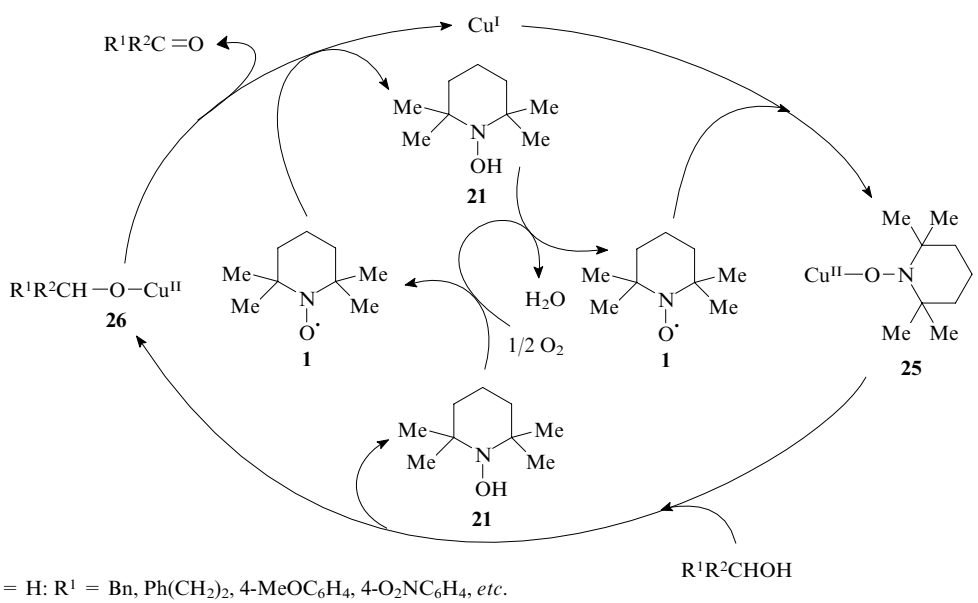
In combination with metal complex catalysts (Ru or Cu complexes), in the aerobic oxidation of alcohols, the TEMPO radical acted as the mediator of the hydrogen atom transfer, the involvement of the oxoammonium salt **20** as the active oxidant was ruled out. In the postulated[91] hydridometal mechanism, the catalyst represented a dihydride species $RuH_2(PPh_3)_3$ (**22**) formed from $RuCl_2(PPh_3)_3$ in the initial stage of the reaction with an alcohol (chlorobenzene as a solvent). Dihydride **22** reacted with two TEMPO molecules to form a single TEMPOH molecule (**21**) and complex **23**. The proton transfer from the alcohol to the piperidinoxy ligand in complex **23** led to complex **24**, which involved the liberation of another TEMPOH molecule (**21**). In complex **24**, elimination of a hydrogen atom to form a carbonyl compound and dihydride **22** occurred. In the aerobic process, both TEMPOH molecules were oxidized to the original TEMPO, which thus returns to the cycle (Scheme 4). This mechanism, *i.e.*, the oxidation of alcohols through a dehydrogenation stage (a one-electron oxidation process), was confirmed by the kinetic isotope effect observed in the oxidation of α-deuterated *p*-methyl-

Scheme 4



R^1 = n-C_7H_{15}, Ph, 4-$NO_2C_6H_4$; R^2 = H, Me; R^1–R^2 = $(CH_2)_7$, *etc.*

Scheme 5



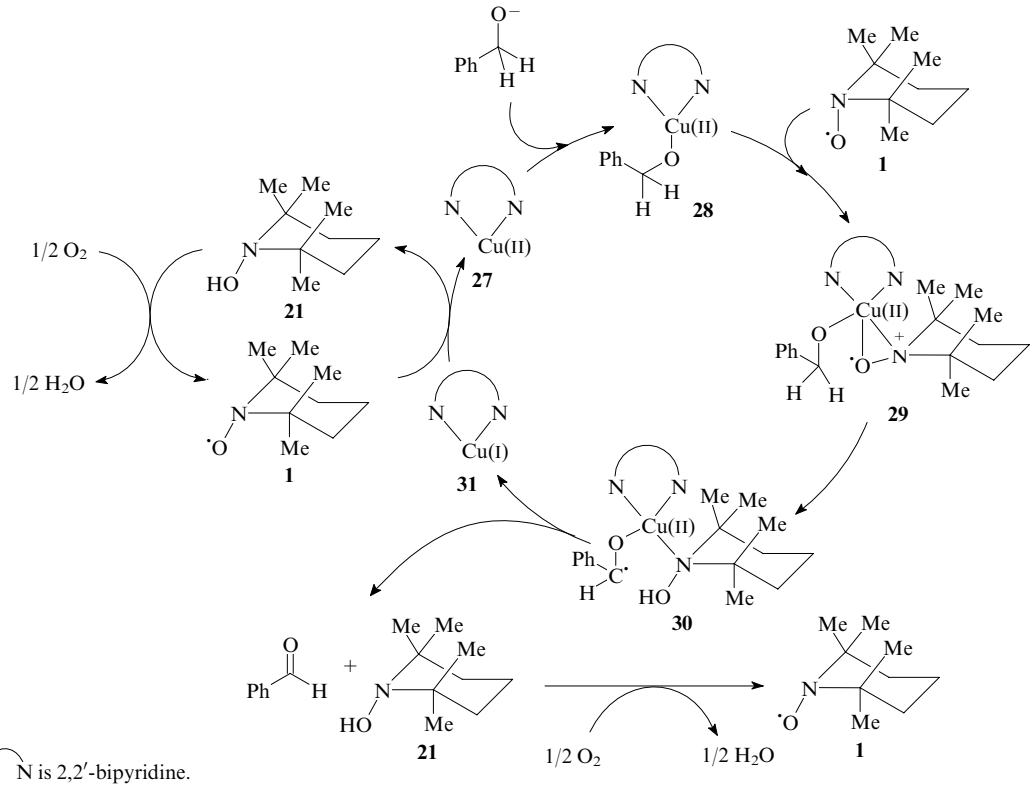
R^2 = H: R^1 = Bn, $Ph(CH_2)_2$, 4-$MeOC_6H_4$, 4-$O_2NC_6H_4$, *etc.*

benzyl alcohol, namely, $k_H/k_D = 3.4$ (100 °C) and 5.1 (25 °C).[91,92] When benzyl alcohols were oxidized with oxoammonium cations, the values k_H/k_D were lower, namely, 1.7–2.3 (25 °C).[88]

A similar interpretation[92,93] was given for the oxidation with the O_2–CuCl–TEMPO system by a mechanism in which the reaction of CuCl with radical **1** generated complex salt Cu(II)–TEMPO (**25**) as confirmed by experiments with stoichiometric amounts of reactants. The reaction of complex **25** with an alcohol (with the transfer of a proton from the alcohol to the complex) afforded TEMPOH (**21**) and alkoxycopper(II) complex **26**. The reaction of the latter with a second molecule of TEMPO produced a carbonyl compound with the formation of another molecule of TEMPOH and the recovery of Cu(I). In the presence of O_2, both TEMPOH molecules were reoxidized to TEMPO, thus completing the catalytic cycle (Scheme 5).[92,93]

Aerobic oxidation of primary alcohols in aqueous acetonitrile (MeCN : H_2O = 2 : 1, pH 13–13.5) with a catalytic system $CuBr_2$–TEMPO–Bu^{t}OK–bipy (bipy is 2,2′-bipyridine) was considered[94] as a process that involved the formation of radical intermediates. According to the proposed mechanism, in an alkaline medium an alcohol reacted with Cu^{II}(bipy) complex (**27**) to form alkoxy complex **28**, which later coordinated TEMPO (**1**). In the resulting complex **29**, α-hydrogen of the alcohol migrated to the O-radical centre to afford C-radical intermediate **30**; the intramolecular one-electron transfer in the latter resulted in its

Scheme 6



N N is 2,2′-bipyridine.

decomposition to aldehyde, TEMPOH (**21**) and Cu^{I}(bipy) (**31**). The latter compound was oxidized in the reaction with TEMPO to Cu^{II}(bipy) (**27**). Under the effect of atmospheric oxygen, the resulting TEMPOH (**21**) was transformed into TEMPO (Scheme 6).[93, 94]

The oxidation of benzyl alcohol and its *ortho*-, *meta*- and *para*-substituted derivatives with the system O_2–Cu–TEMPO ($MeCN : H_2O = 2 : 1$, pH 13) proceeded according to an analogous scheme. It should be noted that virtually no oxidation of aliphatic alcohols (octan-2-ol and 2-phenylethanol) occurred. This difference was due to the ability of benzyl alcohols to stabilize radical intermediate **30** (see Scheme 6).[95]

Presumably, the aerobic oxidation of primary alcohols in an ionic liquid $[bmpy]^+PF_6^-$ (bmpy is 1-butyl-4-methylpyridinium) in the presence of copper perchlorate, 4-(dimethylamino)pyridine and 4-acetamido-TEMPO (**2**) proceeds by the same scheme that involves radical intermediates.[96]

Thus, to interpret the results of the oxidation of alcohols with involvement of TEMPO and its analogues, the ionic, hydridometal and radical mechanisms have been proposed.

III. Selective oxidation of polysaccharides

The oxidation of hydroxymethyl groups in carbohydrates in the presence of TEMPO was initially accomplished for partially protected monosaccharides in the CH_2Cl_2–H_2O two-phase system under the action of NaOCl.[97]

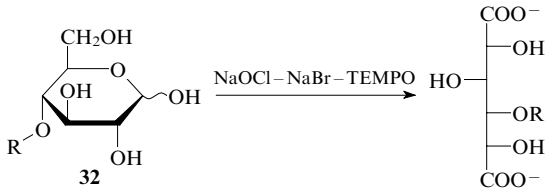


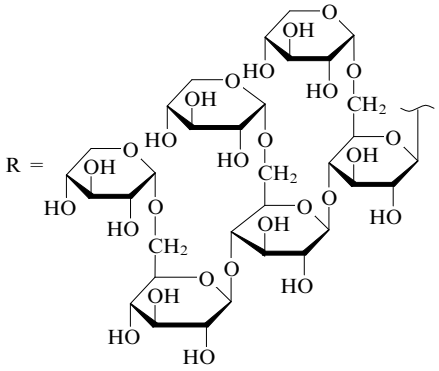
R^1 = Me, R^2 = Bn: R^3 = Ac, Bn; $R^2 = R^3$ = H: R^1 = Me, n-C_8H_{17}.

Later, this reaction was studied in an aqueous medium by the example of methyl α-D-glucopyranoside. The intermediate methyl α-D-*gluco*-hexodialdo-1,5-pyranoside hydrate (the maximum concentration 10%) detected by the high resolution anion-exchange chromatography rapidly oxidized to uronic acid.[98]

It was only relatively recently that the TEMPO-mediated oxidation found application in the chemistry of polysaccharides.[68] It is characterized by the high selectivity in the oxidation of primary alcohol groups in the presence of secondary ones that require no protection. The terminal reducing unit in the heptasaccharide fragment (**32**) of xyloglucan was oxidized to glucaric acid (**33**).[99]

The oxidation of polysaccharides under the action of NaOCl was usually carried out in alkaline aqueous media in the presence of TEMPO (0.5 mol % – 4 mol % with respect to substrate) and NaBr (5 mol % – 30 mol %) as the catalysts.[25] The addition of NaBr was required for generating sodium hypobromite, which is a stronger oxidant than NaOCl.[19, 68] With the substitution of different oxidants (O_2 or H_2O_2,[100] oxoammonium salts[101]) for NaOCl, the yields of uronic acids substantially decreased. It was found that amides and imides accelerated the reaction,[102] whereas amines interacted with TEMPO thus inhibiting the oxidation.[32, 62] The reaction was as a rule carried out at 0 – 30 °C, its selectivity decreasing with the increase in the temperature.[68] The increase in the NaBr and TEMPO concentrations accelerated oxidation but reduced the selectivity of the process.[68]

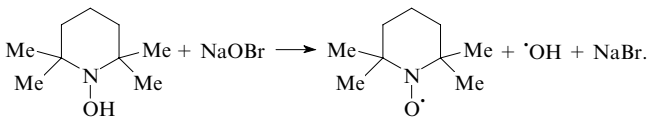




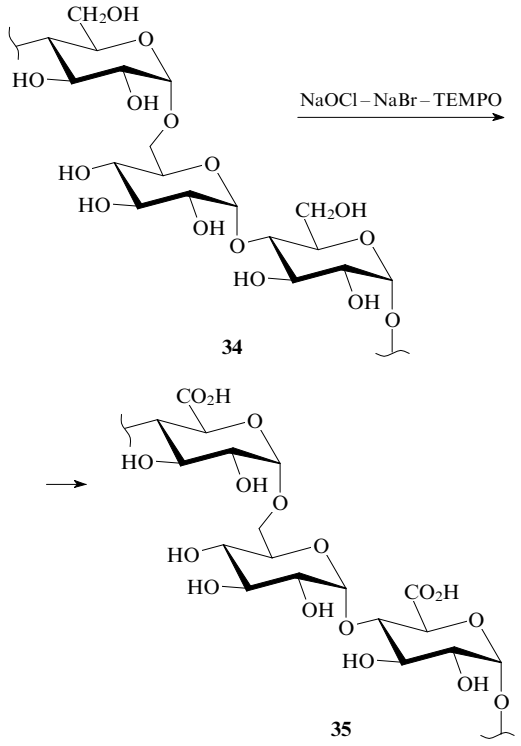
The use of the NaOCl–NaBr–TEMPO system under mild conditions (H_2O, pH 9 – 11, 0 – 30 °C) made it possible to selectively oxidize virtually all water-soluble and -insoluble polysaccharides, namely, starch, amylopectin, amylodextrin, cellulose and its modifications, pullulan, galactomannan (guaran), inulin, xyloglucan, chitin, chitosan, *etc*.[25]

The oxidation of linear water-soluble polysaccharides to the corresponding polyuronic acids proceeded with high selectivity, whereas the oxidation of branched polysaccharides was less selective.[25] In the oxidation of starch, which represents a mixture of linear amylose and branched amylopectin, by a system NaOCl–NaBr–TEMPO the cleavage of α-(1→6)-glycosidic bonds in amylopectin to produce linear α-(1→4)-polyglucuronic acid was the main side reaction.[103]

Cellouronic acid prepared by TEMPO-mediated oxidation of cellulose underwent partial depolymerisation when treated with each of the reagents of the TEMPO–NaBr–NaClO system at pH 11, which was attributed to the formation of hydroxyl radicals capable of cleavage of the molecules.[104]



The degree of polysaccharide degradation depended on their structure, pH of the reaction medium and the nature of the nitroxide radical. Thus in the oxidation of pullulan (**34**) by a system NaOCl–NaBr–TEMPO to afford product **35**, the optimal pH value was 9.2 – 9.7; at pH 6 – 8, the selectivity decreased, and at pH 10 – 11, substantial depolymerization of polysaccharide **34** was observed.[105] The degree of depolymerization was lower for substituted radicals **2**, **7**, **10** and **11**.[106]

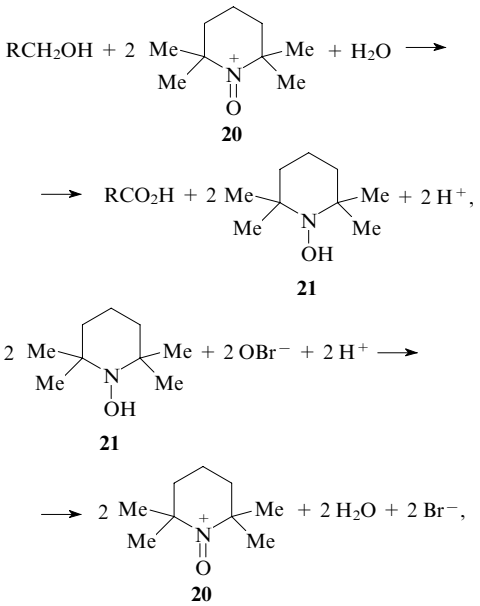


34

35

In the oxidation of polysaccharides with a system NaOCl–NaBr–TEMPO in alkaline media, the active oxidation species is presumably oxoammonium ion **20** generated from TEMPO under the action of hypohalites. In the catalytic cycle, this cation undergoes redox transformations similar to those shown in Scheme 1. Cation **20** brings about the oxidation of the polysaccharide primary alcohol groups

Scheme 7



20

21

21

20

$$2\,Br^- + 2\,NaOCl \longrightarrow 2\,OBr^- + 2\,NaCl,$$

$$RCO_2H + NaOH \longrightarrow RCO_2Na + H_2O.$$

Overall reaction:

$$RCH_2OH + 2\,NaOCl + NaOH \longrightarrow RCO_2Na + 2\,H_2O + 2\,NaCl,$$

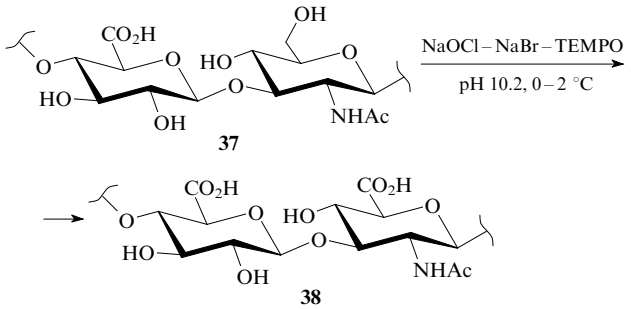
R is the polysaccharide residue.

to the carboxyl groups and is reduced to hydroxylamine **21**. The oxidation of the latter with hypohalites recovered the oxoammonium cation **20** (Scheme 7).[25, 103]

As follows from Scheme 7, the formation of 1 mole of carboxylic acid requires consumption of 2 moles of oxoammonium cation **20**, while the regeneration of the latter from TEMPOH (**21**) consumes 2 moles of hypohalite. To maintain pH of the reaction mixture at the required level, it is necessary to neutralize the carboxylic acid formed by adding 1 mole of an alkali (see Scheme 7).

The consumption of NaOH for maintaining pH of the medium at a given level can serve as a control of the degree of conversion of the CH_2OH groups into the carboxylic groups in studies of the oxidation kinetics.[68, 103, 107–109] However, for the oxidation of starch,[103] cellulose[107] and chitosan,[108] it was noticed that the consumption of NaOH exceeded the content of the COOH groups in the reaction products, which was explained[103] by the formation of sodium salt of aldehyde hydrate **36**. The intra- or intermolecular reactions of the aldehyde and alcohol groups produce hemiacetals.[103] The subsequent oxidation of aldehyde hydrate **36** and hemiacetals under the action of oxoammonium cation **20** afforded the sodium salt of the acid and TEMPOH (**21**). The oxidation of the latter with a hypohalite returned oxoammonium cation **20** into the cycle (Scheme 8).

The oxidation of hyaluronic acid (**37**) with an excess of NaOCl (3–6 equiv.) in the N_2 atmosphere in the presence of TEMPO and various salts (NaBr, Na_2SO_4 and NaCl) proceeded with an induction period (up to 30 min), which is believed to be required for the transformation of the TEMPO radical to the oxoammonium cation **20**. The oxidized hyaluronic acid contained ~80% of new structural units of *N*-acetylglucosaminuronic acid and its molecular mass was halved.[109] The oxidation of hyalururonic acid (**37**) in air at the initial pH ~13, which was established after the single-step addition of 1.8 M NaOCl to the mixture **37**–NaBr–TEMPO, resulted in the exhaustive conversion of acid **37** to acid **38** called carboxyhyaluronic acid.[60]

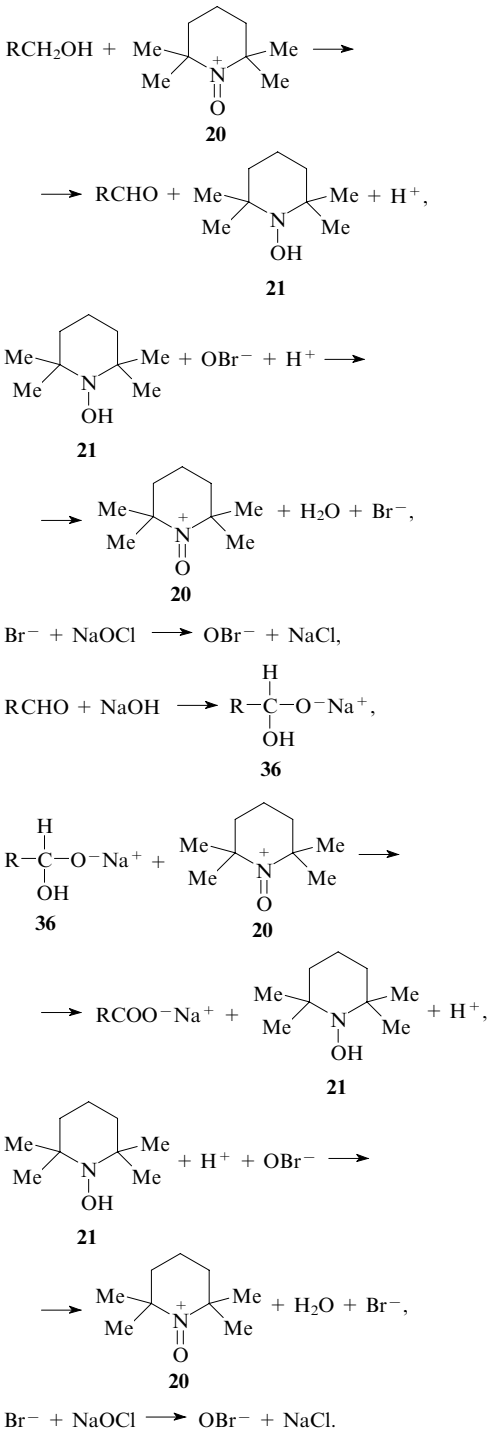


37

38

In was noted that consumption of NaOCl determined by spectrophotometry[110] at 292 nm (ClO^-, ε_{292} = 350 litre mol^{-1} cm^{-1}) and the amount of NaOH required to maintain pH of the reaction mixture at 10.2 were half that required for stoichiometry of the overall process shown in Scheme 8. Hence, atmospheric oxygen was involved in the oxidation of hyaluronic acid **37** in the step of oxidation of a transient aldehyde according to the radical autoxidation scheme.[111] The possible involvement of radicals in the oxidation process in the presence of TEMPO followed from chemiluminescence detected in the initial moment of the reaction and the formation of hybrid macromolecules in the oxidation of a mixture of hyaluronic acid and heparin.[60]

Scheme 8



Overall reaction:

$$RCH_2OH + 2\,NaOCl + NaOH \longrightarrow RCO_2Na + 2\,H_2O + 2\,NaCl,$$

R is the polysaccharide residue.

As compared with the natural hyaluronic acid, carboxyhyaluronic acid (**38**) was more easily soluble in water, exhibited stronger affinity to dyes, *e.g.*, Methylene Blue,[112] its zinc salt manifested antibacterial effect against *Escherichia coli* and *Staphylococcus aureus*.[113] In carbodiimide-assisted coupling of acid **38** with amines, the reactivity of COOH groups in the modified unit was shown to be higher than in the D-glucuronic acid unit. In contrast to the natural hyaluronic acid, carboxyhyaluronic acid (**38**) and its conjugates with amines exhibited the unusually high *in vitro* stability with respect to the enzyme testicular hyaluronidase.[60,114] This feature is important in the development of drugs of prolonged action.

Unlike oxidation of hyaluronic acid, the oxidation of dermatan sulfate (**39**) with a twofold excess of NaOCl under the same conditions afforded a product that contained only 25% of modified *N*-acetylgalactosaminuronic acid units and 15% of units of the corresponding aldehyde in its hydrated form per saccharide unit.[60] The aldehyde group was identified by NMR spectroscopy: in the ^{13}C NMR spectrum, a signal was observed in the region of δ 87.8 characteristic of the $CH(OH)_2$ group.[115] The increase in the NaOCl concentration up to its threefold excess resulted in product **40**, which corresponded to the exhaustive oxidation of the CH_2OH groups, the galactosamine residue being converted to units with aldehyde hydrate and COOH groups in the equimolar ratio. Carboxydermatan sulfate with ~100% content of *N*-acetylylgalactosaminuronic acid units was obtained in the presence of a sixfold excess of NaOCl (Scheme 9).[60]

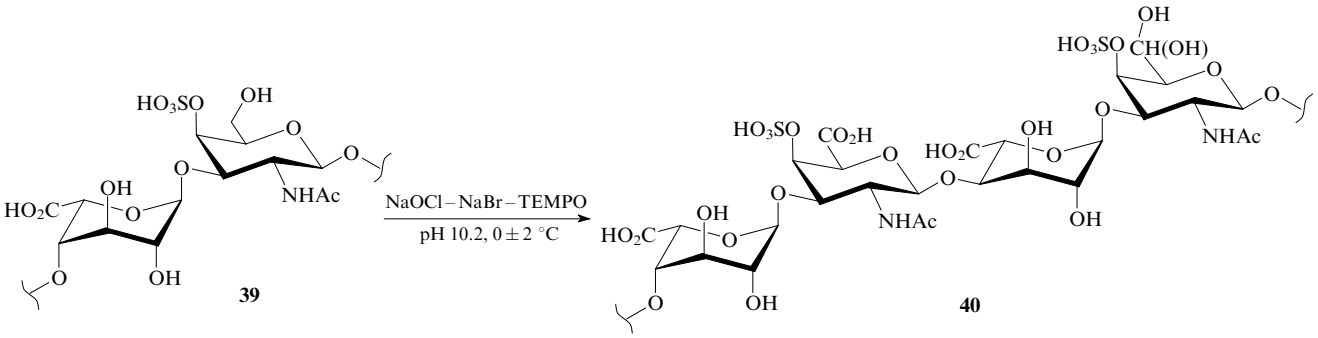
The oxidation of a neutral polysaccharide scleroglucan (**41**), produced by microorganisms of the genus *Sclerotium*, in the system NaOCl–NaBr–TEMPO afforded anionic polyelectrolyte **42**. Its conformation in aqueous solutions was studied as a function of the degree of oxidation of the primary alcohol groups. At the degree of conversion less than 40%, the oxidized scleroglucan (like the original polymer) represented a triple helix; at higher conversions, the polysaccharides behaved as random coils (Scheme 10).[116]

The oxidation of maltodextrin with the NaOCl–NaBr–TEMPO reagent in a strongly acidic basic medium (pH $\geqslant$ 11) occurred selectively (98%) to afford a carboxyl-containing compound in a high yield. In a nearly neutral medium, scission of vicinal diols in the pyranose ring occurred, which was evidenced by the formation of oxalic acid.[117]

Cyclodextrins, *i.e.*, cyclic oligosaccharides containing 6, 7 and 8 α-(1→4)-bound glucose residues, can form complexes with different hydrophobic molecules including pharmacophores, thereby increasing their solubility in water. The application field of the ability of cyclodextrins to form complexes can be substantially extended by converting their primary alcohol groups into carboxyl ones. The oxidation of β-cyclodextrin (**43**) with the NaOCl–NaBr–TEMPO system afforded mono- (**44**) and dicarboxycyclodextrins (**45**–**47**), their structures were established by 2D NMR spectroscopy (Scheme 11).[118]

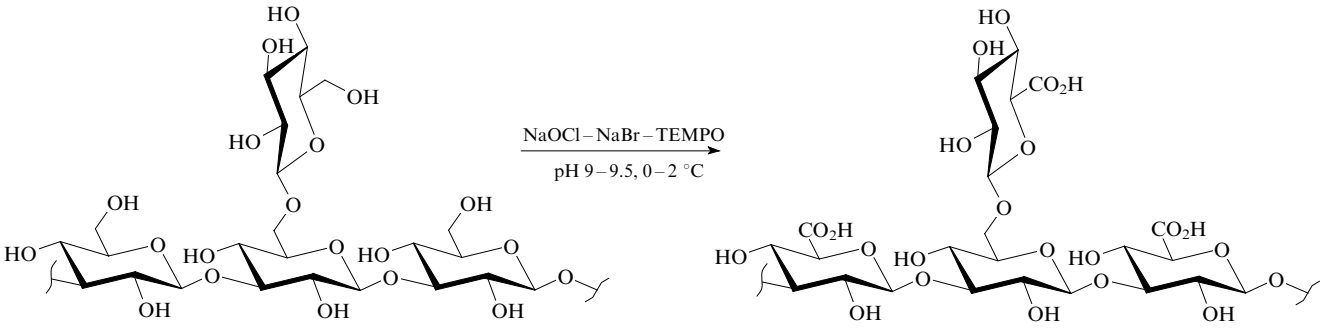
Oxidation of mannans from pathogenic yeasts of the genus *Candida* with the NaOCl–NaBr–TEMPO system was studied with special attention to preservation of the antigenic properties important for the development of vaccines.[119] Oxidized mannans of *Amorphophallus konjak* tubors and guar gum were subjected to epimerization under the action of recombinant mannuronan-C(5)-epimerase to afford analogues of alginic acid containing 12%–15% of α-L-guluronate residues; the oxidized carob tree gum was resistant to the enzyme action.[120]

Scheme 9



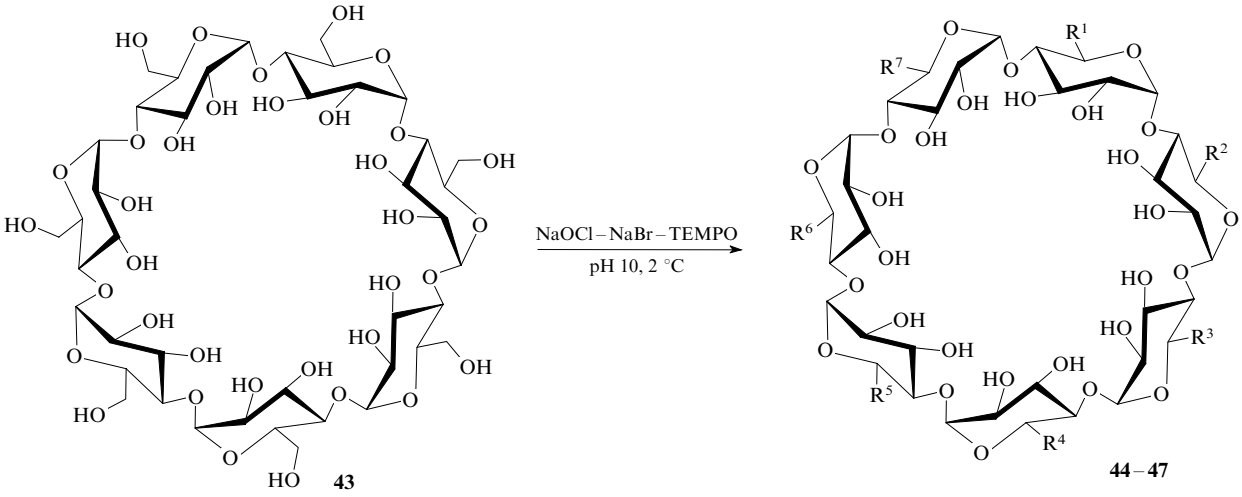
39 40

Scheme 10



41 42

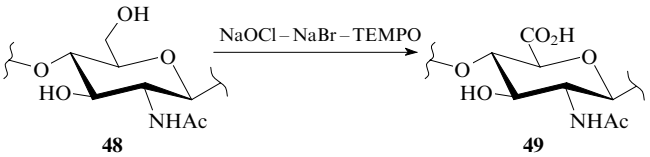
Scheme 11



43 44–47

$R^1 = CO_2Na$: $R^2 = R^3 = R^4 = R^5 = R^6 = R^7 = CH_2OH$ (**44**); $R^2 = CO_2Na$: $R^3 = R^4 = R^5 = R^6 = R^7 = CH_2OH$ (**45**);
$R^3 = CO_2Na$: $R^2 = R^4 = R^5 = R^6 = R^7 = CH_2OH$ (**46**); $R^4 = CO_2Na$: $R^2 = R^3 = R^5 = R^6 = R^7 = CH_2OH$ (**47**).

TEMPO-mediated oxidation of water-insoluble chitin (**48**) afforded water-soluble chitouronic acid (**49**) containing *N*-acetylglucosaminuronic acid residues.[121]

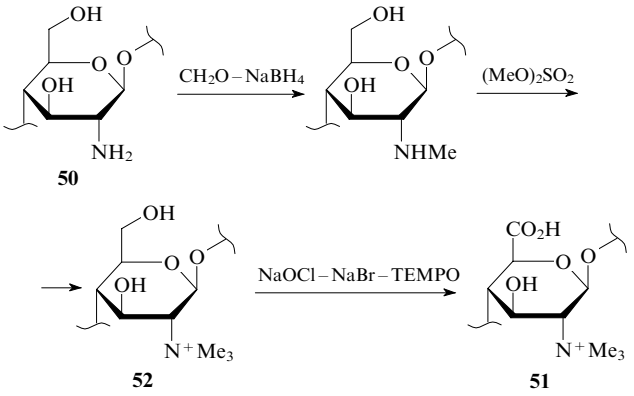


48 49

Chitouronic acid (**49**) absorbs water to form gels like hyaluronic acid and carboxymethylchitosan and forms salts with metals and polyelectrolyte complexes with chitosan.[122] Films of chitouronic acid (or of its sodium salt) exhibited high permeability with respect to oxygen.[123] Based on partially oxidized chitin containing aldehyde and carboxyl groups, nanocrystals measuring 340×8 nm were obtained by sonication.[124]

Oxidation of chitosan (**50**) by the NaOCl–NaBr–TEMPO system results in its virtually complete degradation[108] or cross-linking.[125] Selective oxidation required the

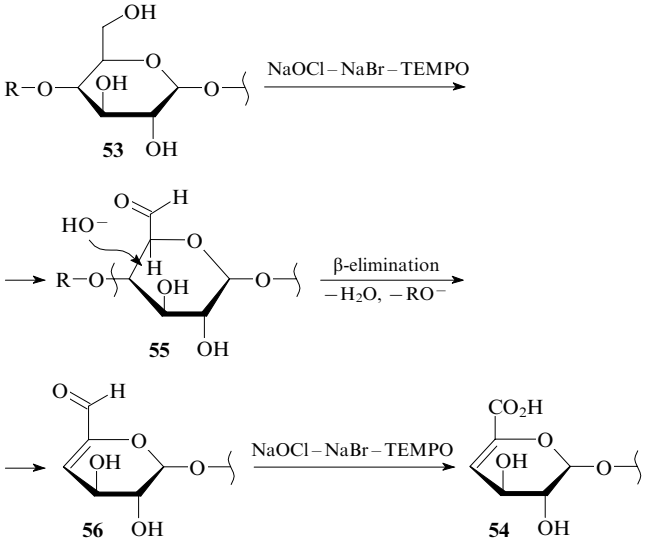
amino groups to be preliminarily protected. The use of *N*-acetyl or *N*-phthaloyl derivatives was to no avail. A suitable candidate for the synthesis of *N*,*N*,*N*-trimethylcarboxychitosan (**51**) was *N*,*N*,*N*-trimethyl derivative **52** prepared by a two-step transformation of chitosan (**50**).[108]



For the maximum water solubility of oxidized chitosan, 25% of its primary alcohol groups should be converted into carboxylic. At higher conversion, the solubility decreased, which was due to the formation of an intramolecular salt that involved carboxyl and amino groups.[126]

A large number of studies were devoted to the TEMPO-mediated oxidation of cellulose (**53**). Without any preliminary treatment, water-insoluble natural cellulose could be oxidized with the TEMPO – NaOCl – NaBr reagent only with a low conversion of primary alcohol groups to aldehyde and carboxyl groups (0.3 and 0.7 mmol g^{-1}, respectively [127]). This was associated with the fact that the oxidation occurred only on the surface of cellulose fibres that possess a high degree of crystallinity due to the presence of intra- and intermolecular hydrogen bonds.[127 – 130]

The water-soluble fraction (< 20%) of oxidized cellulose was low-molecular and contained hexenuronic acids **54** formed as a result of β-elimination of the carbohydrate chain from aldehydes **55** followed by the oxidation of enals **56**.[130]



R is a polysaccharide residue.

The partially oxidized cellulose (the degree of conversion of CH_2OH groups of 5% – 10%) was hydrolyzed more easily with 82.5% phosphoric acid,[131] it is conveniently used in the preparation of paper,[132] nanofibres,[133, 134] and also in further modification of the COOH groups by the reactions with various amines (benzylamine, hexylamine, dodecylamine, *etc.*).[135]

The oxidizability of the natural cellulose could be enhanced by long-term (12 – 24 h) mechanical treatment in a ball mill. Based on mechanically activated cellulose with the amorphous structure, polyuronic acids were synthesized in high yields but with a substantial loss of the molecular mass.[136]

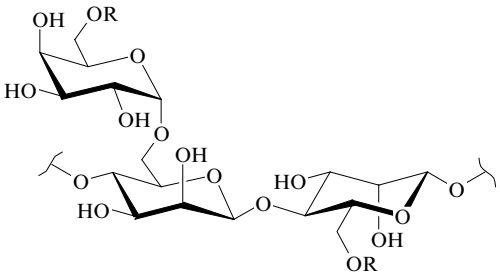
The oxidation of mercerized and regenerated cellulose (cellulose II) afforded 6-carboxycellulose (cellouronic acid) with the uniform chemical structure in almost quantitative yields.[107, 121, 128, 137] The partially oxidized product synthesized by mild TEMPO-mediated oxidation of cellulose II that contained carboxyl, aldehyde and hemiacetal groups was used for reinforcing paper at its lamination with polyvinylamine.[138]

Of eleven types of nitroxide radicals (**1** – **6**, **8**, **9**, **13** – **15**) used in the cellulose oxidation with the aim of producing its form completely soluble in water, namely, cellouronic acid, the highest selectivity was achieved with (**1**), 4-acetamido-TEMPO (**2**), 4-carboxy-TEMPO (**3**) and 4-phosphonooxy-TEMPO (**9**).[139] To reduce the degree of degradation in the oxidation of cellulose II, different radical scavengers were used.[104] All oxidation products were characterized by the bimodal molecular-mass distribution. Cellouronic acid with the maximum molecular mass was synthesized in the presence of crotonic acid but its degradation failed to be totally avoided. At the same time, a fraction was isolated with the molecular mass higher than that of the original material due to the cross-linking typical of radical processes.[104, 139]

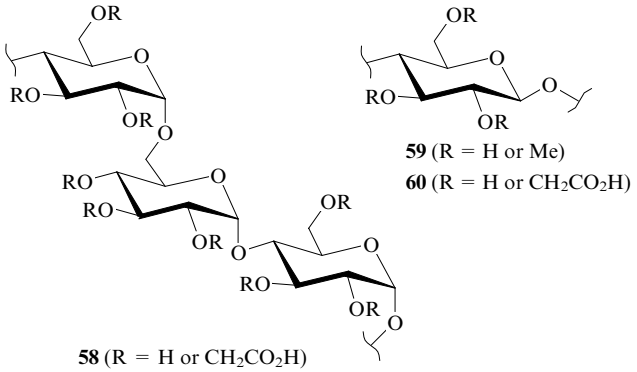
A film of cellouronic acid with the reduced permeability to oxygen, comparable with the permeability of poly(vinyl alcohol),[123] decomposed under the action of soil microorganisms, enzymes of the hydrolase type [140] and glucuronyl lyase from the *Trichoderma* strain GL2 (Ref. 141) to afford unsaturated oligocellouronates. After cross-linking with divinyl sulfone, diglycidyl ether and other diepoxides, the cellouronic acid-based products are promising as superabsorbents, complexation agents, crystallization inhibitors and antiflocculating agents.[132]

Cellulose III prepared by treating native cellulose with liquid or gaseous ammonia (and also with amines, diamines or polyamines) underwent TEMPO-mediated oxidation more easily than native cellulose or cellulose II.[142, 143] Cellulose acetate (degree of acetylation ~ 0.5) [144] and carboxycellulose prepared by processing of agave biomass [145] were oxidized by the NaOCl – NaBr – TEMPO system under sufficiently mild conditions (pH $\sim$ 10, 0 – 4 °C). This was accompanied by selective oxidation of unprotected primary alcohol groups to form the corresponding cellouronic acids. Due to the mild oxidation conditions, the degree of acetylation of the product remained unchanged.

TEMPO-mediated oxidation was used in the determination of the degree of substitution with respect to the primary alcohol groups in modified polysaccharides, namely, hydroxypropylguaran (**57**), carboxymethylpullulan (**58**), methyl- (**59**) and carboxymethylcellulose (**60**). The degree of substitution was calculated from the difference in the COOH group content determined by oxidation of unmodified and the corresponding modified polysaccharides.[146]



57 (R = H or $CH_2CH(OH)Me$)



59 (R = H or Me)
60 (R = H or CH_2CO_2H)

58 (R = H or CH_2CO_2H)

* * *

The material on the oxidation of polysaccharides catalyzed by nitroxide radicals presented in this review is indicative of the wide prospects of this approach, which allows one to selectively synthesize carboxylic acids, carbonyl compounds and modified polysaccharides with the increased content of the carboxyl and carbonyl groups. These carboxylated polysaccharides acquire new practically important properties, which extends the possibilities of their conjugation with different biologically active compounds and opens up a way to new drugs of targeted delivery and prolonged action.

References

1. *Degradable Polymers: Principles and Applications* (Ed. G Scott) (Dordrecht; London: Kluwer Academic, 2002)
2. *Food Polysaccharides and Their Applications* (Ed A M Stephan) (New York: Marcel Dekker, 1995)
3. *Polysaccharides: Structural Diversity and Functional Versatility*. (Ed. S Dumitriu) (New York: Marcel Dekker, 1998)
4. P P Shorygin, E V Khait *Zh. Obshch. Khim.* **7** 188 (1937)
5. E C Yackel, W O Kenyon *J. Am. Chem. Soc.* **64** 121 (1942)
6. M P Pavlyuchenko, I N Ermolenko, F I Kaputskii *Zh. Prikl. Khim.* 1385 (1960) [a]
7. S M Butrim, T D Bil'dyukevich, N S Butrim, T L Yurkshtovich *Khim. Prirod. Soedin.* 251 (2007) [b]
8. T J Painter *Carbohydr. Res.* **55** 95 (1977)
9. A E J de Nooy, M Pagliaro, H van Bekkum, A C Besemer *Carbohydr. Res.* **304** 117 (1997)
10. I R Mullagaliev, N N Kabal'nova, G G Galiaskarova, E I Pokalo, V V Shereshovets, Yu B Monakov *Zh. Prikl. Khim.* 1709 (1997) [a]
11. I M Borisov, E N Shirokova, R Kh Mudarisova, R R Muslukhov, Yu S Zimin, S A Medvedeva, G A Tolstikov, Yu B Monakov *Izv. Akad. Nauk, Ser. Khim.* 305 (2004) [c]
12. E N Shirokova, Candidate Thesis in Chemical Sciences, Institute of Organic Chemistry, Urals Research Centre of the Russian Academy of Sciences, Ufa, 2003
13. L A Badykova, Candidate Thesis in Chemical Sciences, Institute of Organic Chemistry, Urals Research Centre of the Russian Academy of Sciences, Ufa, 2007
14. L A Edye, G V Meehan, G N Richards *J. Carbohydr. Chem.* **13** 273 (1994)
15. G O Aspinall, A Nicolson *J. Chem. Soc.* 2503 (1960)
16. D L Verraest, J A Peters, H van Bekkum *Carbohydr. Res.* **306** 197 (1998)
17. Z A Rogovin *Khimiya Tsellyulozy* (The Chemistry of Cellulose) (Moscow: Khimiya, 1972)
18. R L Whistler, R Schweiger *J. Am. Chem. Soc.* **80** 5701 (1958)
19. A C Besemer, H van Bekkum *Starch/Stirke* **46** 95 (1994)
20. A C Besemer, H van Bekkum *Starch/Stirke* **46** 101 (1994)
21. A R Kuramshina, Candidate Thesis in Chemical Sciences, Institute of Organic Chemistry, Urals Research Centre of the Russian Academy of Sciences, Ufa, 2007
22. M Pagliaro *Carbohydr. Res.* **308** 311 (1998)
23. A E J De Nooy, A C Besemer, H van Bekkum *Synthesis* 1153 (1996)
24. W Adam, C S Saha-Moller, P A Ganeshpure *Chem. Rev.* **101** 3499 (2001)
25. P L Bragd, H van Bekkum, A C Besemer *Top. Catal.* **27** 49 (2004)
26. *Nitroksil'nye Radikaly: Sintez, Khimiya, Prilozheniya* (Nitroxide Radicals: Synthesis, Chemistry, Applications) (Eds E G Rozantsev, R I Zhdanov) (Moscow: Nauka, 1987)
27. E G Rozantsev *Iminoksil'nye Radikaly* (Iminoxyl Radicals) (Moscow: Khimiya, 1970)
28. A L Buchachenko, A M Vasserman *Stabil'nye Radikaly* (Stable Radicals) (Moscow: Khimiya, 1973)
29. E G Rozantsev, V Sholle *Organicheskaya Khimiya Svobodnykh Radikalov* (Organic Chemistry of Free Radicals) (Moscow: Khimiya, 1979)
30. E G Rozantsev, V D Sholle *Usp. Khim.* **40** 417 (1971) [*Russ. Chem. Rev.* **40** 223 (1971)]
31. J F W Keana *Chem. Rev.* **78** 37 (1978)
32. J M Bobbitt, M C L Flores *Heterocycles* **27** 509 (1988)
33. R L Zhang, S Goldstein, A Samuni *Free Radical Biol. Med.* **26** 1245 (1999)
34. S Goldstein, A Samuni *J. Phys. Chem. A* **111** 1066 (2007)
35. P J Wright, A M English *J. Am. Chem. Soc.* **125** 8655 (2003)
36. M Ferrari, S Colacicchi, G Gualtieri, M T Santini, A Sotgiu *Biochem. Biophys. Res. Commun.* **166** 168 (1990)
37. M Yu Zaremskii, E G Drozdova, E S Garina, M B Lachinov, V B Golubev *Vysokomol. Soedin., Ser. B* **48** 1925 (2006) [d]
38. Å Lagunas, A Mairata i Payeras, C Jimeno, M A Pericàs *Org. Lett.* **7** 3033 (2005)
39. M F Semmelhack, C R Schmid *J. Am. Chem. Soc.* **105** 6732 (1983)
40. D H Hunter, D H R Barton, W J Motherwell *Tetrahedron Lett.* **25** 603 (1984)
41. T Miyazawa, T Endo, M Okawara *J. Polym. Sci. A: Polym. Chem.* **23** 1527 (1985)
42. T Miyazawa, T Endo *J. Mol. Catal.* **49** L31 (1988)
43. M Gilhespy, M Lok, X Baucherel *Chem. Commun.* 1085 (2005)
44. P Ferreira, E Phillips, D Rippon, S C Tsang, W Hayes *J. Org. Chem.* **69** 6851 (2004)
45. G Pozzi, M Cavazzini, S Quici, M Benaglia, G Dell'Anna *Org. Lett.* **6** 441 (2004)
46. A Schätz, R N Grass, W J Stark, O Reiser *Chem. – Eur. J.* **14** 8262 (2008)
47. WO 02058844 (2002)
48. L Liu, L-Y Ji, Y-Y Wei *Monatsh. Chem.* **139** 901 (2008)
49. B P Mason, A R Bogdan, A Goswami, D T McQuade *Org. Lett.* **9** 3449 (2007)
50. A Gheorghe, T Chinnusamy, E Cuevas-Yañez, P Hilgers, O Reiser *Org. Lett.* **10** 4171 (2008)
51. V A Golubev, E G Rozantsev, M B Neiman *Izv. Akad. Nauk SSSR, Ser. Khim.* 1927 (1965) [c]
52. C M Paleos, P Dais *J. Chem. Soc., Chem. Commun.* 345 (1977)
53. V A Golubev, V D Sen', I V Kulyk, A L Aleksandrov *Izv. Akad. Nauk SSSR, Ser. Khim.* 2235 (1975) [c]

54. V A Golubev, V N Borislavskii, A L Aleksandrov *Izv. Akad. Nauk SSSR, Ser. Khim.* 2025 (1977) [c]
55. J A Cella, J A Kelley, E F Kenehan *J. Org. Chem.* **40** 1860 (1975)
56. V A Golubev, Yu N Kozlov, A N Petrov, A P Purmal', O A Travina *Khim. Fiz.* **4** 838 (1985) [e]
57. A N Petrov, Yu N Kozlov, A P Purmal', A M Uskov *Zh. Fiz. Khim.* **58** 2109 (1984) [f]
58. D G B Boocock, R Darcy, E F Ullman *J. Am. Chem. Soc.* **90** 5945 (1968)
59. T Endo, T Miyazawa, S Shiihashi, M Okawara *J. Am. Chem. Soc.* **106** 3877 (1984)
60. E A Khaibrakhmanova, Candidate Thesis in Chemical Sciences, Institute of Inorganic Chemistry, Russian Academy of Sciences, Ufa, 2008
61. Neth. P. 1000396 (1995)
62. A Heeres, H A van Doren, K F Gotlieb, I P Bleeker *Carbohydr. Res.* **299** 221 (1997)
63. L M Slaughter, J P Collman, T A Eberspacher, J I Brauman *Inorg. Chem.* **43** 5198 (2004)
64. N Jiang, A J Ragauskas *J. Org. Chem.* **71** 7087 (2006)
65. G Yang, J Ma, W Wang, J Zhao, X Lin, L Zhou, X Gao *Catal. Lett.* **112** 83 (2006)
66. N Wang, R Liu, J Chen, X Liang *Chem. Commun.* 5322 (2005)
67. F Lin, W Peng, W Xu, X Han, B Yu *Carbohydr. Res.* **339** 1219 (2004)
68. A E J de Nooy, A C Besemer, H van Bekkum *Carbohydr. Res.* **269** 89 (1995)
69. M M Zhao, J Li, E Mano, Z J Song, D M Tschaen *Org. Synth.* **81** 195 (2005)
70. J Einhorn, C Einhorn, F Ratajczak, J -P Pierre *J. Org. Chem.* **61** 7452 (1996)
71. T Miyazawa, T Endo *J. Mol. Catal.* **31** 217 (1985)
72. X-F Zhao, C Zhang *Synthesis* 551 (2007)
73. F-E Chen, Y-Y Kuang, H-F Dai, L Lu, M Huo *Synthesis* 2629 (2003)
74. R A Miller, R S Hoerrner *Org. Lett.* **5** 285 (2003)
75. R-H Liu, X-M Liang, C-Y Dong, X-Q Hu *J. Am. Chem. Soc.* **126** 4112 (2004)
76. R-H Liu, C-Y Dong, X-M Liang, X-J Wang, X-Q Hu *J. Org. Chem.* **70** 729 (2005)
77. A Cecchetto, F Fontana, F Minisci, F Recupero *Tetrahedron Lett.* **42** 6651 (2001)
78. W A Herrman, J P Zoller, R W Fischer *J. Organomet. Chem.* **579** 404 (1999)
79. Z-Q Liu, X Shang, L Chai, Q Sheng *Catal. Lett.* **123** 317 (2008)
80. Y Xie, W Mo, D Xu, Z Shen, N Sun, B Hu, X Hu *J. Org. Chem.* **72** 4288 (2007)
81. M Fabbrini, C Galli, P Gentili, D Macchitella *Tetrahedron Lett.* **42** 7551 (2001)
82. WO 0050463 (2000)
83. Yu N Ogibin, M N Elinson, G I Nikishin *Usp. Khim.* **78** 99 (2009) [*Russ. Chem. Rev.* **78** 89 (2009)]
84. R Barhdadi, C Comminges, A P Doherty, J Y Nédélec, S O'Tool, M Troupel *J. Appl. Electrochem.* **37** 723 (2007)
85. C Comminges, R Barhdadi, A P Doherty, S O'Tool, M Troupel *J. Phys. Chem. A* **112** 7848 (2008)
86. Z Ma, J M Bobbitt *J. Org. Chem.* **56** 6110 (1991)
87. P L Anelli, C Biffi, F Montanari, S Quici *J. Org. Chem.* **52** 2559 (1987)
88. M F Semmelhack, C R Schmid, D A Cortés *Tetrahedron Lett.* **27** 1119 (1986)
89. W F Bailey, J M Bobbitt, K B Wiberg *J. Org. Chem.* **72** 4504 (2007)
90. M B Smith, J March, in *March's Advanced Organic Chemistry* (Hoboken, NJ: Wiley, 2007) p. 362
91. A Dijksman, A Marino-Gonzalez, A Marata i Payeras, I W C E Arends, R A Sheldon *J. Am. Chem. Soc.* **123** 6826 (2001)
92. R A Sheldon, I W C E Arends, G-J ten Brink, A Dijksman *Acc. Chem. Res.* **35** 774 (2002)
93. A Dijksman, I W C E Arends, R A Sheldon *Org. Biomol. Chem.* **1** 3232 (2003)
94. P Gamez, I W C E Arends, R A Sheldon, J Reedijk *Adv. Synth. Catal.* **346** 805 (2004)
95. D Geißlmeier, W G Jary, H Falk *Monatsh. Chem.* **136** 1591 (2005)
96. N Jiang, A J Ragauskas *Org. Lett.* **7** 3689 (2005)
97. N J Davis, S L Flitsch *Tetrahedron Lett.* **34** 1181 (1993)
98. A E J de Nooy, A C Besemer, H van Bekkum *Tetrahedron* **51** 8023 (1995)
99. T Takeda, J G Miller, S C Fry *Planta* **227** 893 (2008)
100. US P. 7109325 (2004)
101. US P. 6875861 (2005)
102. US P. 6540876 (2003)
103. Y Kato, R Matsuo, A Isogai *Carbohydr. Polym.* **51** 69 (2003)
104. I Shibata, A Isogai *Cellulose* **10** 151 (2003)
105. A E J de Nooy, A C Besemer, H van Bekkum, J A P P van Dijk, J A M Smith *Macromolecules* **29** 6541 (1996)
106. P L Bragd, A C Besemer, H van Bekkum *J. Mol. Catal.* **170** 35 (2001)
107. B Sun, C J Gu, J H Ma, B R Liang *Cellulose* **12** 59 (2005)
108. N Bordenave, S Grelier, V Coma *Biomacromolecules* **9** 2377 (2008)
109. B Jiang, E Drouet, M Milas, M Rinaudo *Carbohydr. Res.* **327** 455 (2000)
110. J C Morris *J. Phys. Chem.* **70** 3798 (1966)
111. D C Nonhebel, J C Walton *Free-Radical Chemistry: Structure and Mechanism* (Cambridge: Cambridge University Press, 1974)
112. V Crescenzi, A Francescangeli, D Renier, D Bellini *Macromolecules* **34** 6367 (2000)
113. V Crescenzi, A Francescangeli *J. Bioact. Compat. Polym.* **18** 229 (2003)
114. I Yu Ponedel'kina, V N Odinokov, E A Saitgalina, U M Dzhemilev *Dokl. Akad. Nauk* **417** 557 (2007) [g]
115. W A Bubb *Concepts Magn. Reson. Part A* **19** 1 (2003)
116. A E J de Nooy, V Rori, G Masci, M Dentini, V Crescenzi *Carbohydr. Res.* **324** 116 (2000)
117. J-F Thaburet, N Merbouh, M Ibert, F Marsais, G Queguiner *Carbohydr. Res.* **330** 21 (2001)
118. C Fraschini, M R Vignon *Carbohydr. Res.* **328** 585 (2000)
119. R Durana, I Lacik, E Paulovicova, S Bystricky *Carbohydr. Polym.* **63** 72 (2006)
120. V Crescenzi, M Hartmann, A E J de Nooy, V Rori, G Masci, G Skjak-Bræk *Biomacromolecules* **1** 360 (2000)
121. A Isogai, Y Kato *Cellulose* **5** 153 (1998)
122. R A A Muzzarelli, C Muzzarelli, A Cosani, M Terbojevich *Carbohydr. Polym.* **39** 361 (1999)
123. Y Kato, J Kaminaga, R Matsuo, A Isogai *J. Polym. Environ.* **13** 261 (2005)
124. Y Fan, T Saito, A Isogai *Biomacromolecules* **9** 192 (2008)
125. K Yu Murinov, N N Kabal'nova, Yu B Monakov, in *Panorama Sovremennoi Khimii Rossii. Sovremennyi Organicheskii Sintez (Sbornik Obzornykh Statei)* [Survey of Modern Chemistry of Russia. State-of-the-art Organic Synthesis (Collection of Reviews)] (Moscow: Khimiya, 2003) p. 496
126. S H Yoo, J S Lee, S Y Park, Y S Kim, P S Chang, H G Lee *Int. J. Biol. Macromol.* **35** 27 (2005)
127. T Saito, A Isogai *Biomacromolecules* **5** 1983 (2004)
128. C Tahiri, M Vignon *Cellulose* **7** 177 (2000)
129. Y Habibi, H Chanzy, M R Vignon *Cellulose* **13** 679 (2006)
130. T Saito, M Yanagisawa, A Isogai *Cellulose* **12** 305 (2005)
131. S Hirosawa, K Minato, F Nakatsubo *J. Wood Sci.* **47** 141 (2001)
132. US P. 6635755 (2003)
133. T Saito, Y Nishiyama, J-L Putaux, M Vignon, A Isogai *Biomacromolecules* **7** 1687 (2006)
134. T Saito, S Kimura, Y Nishiyama, A Isogai *Biomacromolecules* **8** 2485 (2007)
135. E Lasseuguette *Cellulose* **15** 571 (2008)
136. T Isogai, M Yanagisawa, A Isogai *Cellulose* **16** 117 (2009)
137. Eur. P. 1215217 (2002)
138. J-L Di Flavio, R Pelton, M Leduc, S Champ, M Essig, T Frechen *Cellulose* **14** 257 (2007)
139. I Shibata, A Isogai *Cellulose* **10** 335 (2003)

140. Y Kato, N Habu, J Yamaguchi, Y Kobayashi, I Shibata, A Isogai, M Samejima *Cellulose* **9** 75 (2002)
141. C Delattre, Ph Michaud, R Elboutachfaiti *Cellulose* **13** 63 (2006)
142. D Da Silva Perez, S Montanari, M R Vignon *Biomacromolecules* **4** 1417 (2003)
143. Y Habibi, M R Vignon *Cellulose* **15** 177 (2008)
144. S Gomez-Bujedo, E Fleury, M R Vignon *Biomacromolecules* **5** 565 (2004)
145. M C Vieira, T Heinze, R Antonio-Cruz, A M Mendoza-Martinez *Cellulose* **9** 203 (2002)
146. B Ding, Y Ye, J Cheng, K Wang, J Luo, B Jiang *Carbohydr. Res.* **343** 3112 (2008)

[a] — *Russ. J. Appl. Chem. (Engl. Transl.)*
[b] — *Chem. Nat. Compd.(Engl. Transl.)*
[c] — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*
[d] — *Polym. Sci. (Engl. Transl.)*
[e] — *Russ. J. Phys. Chem., B (Engl. Transl.)*
[f] — *Russ. J. Phys. Chem., A (Engl. Transl.)*
[g] — *Dokl. Biochem. Biophys. (Engl. Transl.)*