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Photochemical, Electrochemical and Enzymatic Methods for Ether-Bond Cleavage

Andrzej Stolarzewicz,*[a] Zbigniew Grobelny,[a] Wojciech Pisarski,[a] Bożena Łosiewicz,[a] Beata Piekarnik,[a] and Andrzej Swinarew[a]

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The objective of this review is to outline the photochemical, electrochemical, and enzymatic methods that are currently used for ether-bond cleavage. Key results have been extracted from publications covering the past 15 years of research activity in this field.

1. Introduction

In general, it is well accepted that ethers can be cleaved with the use of chemical as well as photochemical, electrochemical, or enzymatic methods. Recently, new data concerning chemical methods have been extensively discussed for various organic compounds.[1,2] It has been reported that ether-bond cleavage proceeds via different mechanisms, for example with electron-transfer reagents such as alkali metals, alkali metal–aromatic radical anions, alkalides (M^-, M^+L salts, where M denotes an alkali metal and L a ligand), and low-valent transition-metal compounds.

The direction of the C–O bond scission in the ether radical anion formed after electron-transfer depends on the kind of ether and the solvent and does not depend on the kind of reagent. The reaction results in the formation of organometallic compounds. In the case of alkalides, these organometallic intermediates then react rapidly with the crown ether to cause its destruction or with a substrate or undergo elimination.

Regioselectivity of C–O bond cleavage has been observed in several systems, and the use of titanocene-based complexes is particularly attractive with respect to the application of intermediate radicals in organic synthesis.

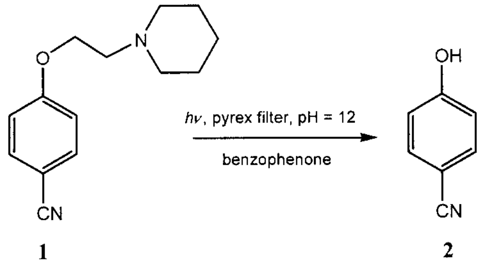
The present work was undertaken in order to report achievements in the field of ether-bond scission, particularly the use of photochemical and electrochemical methods.

2. Photochemical Methods

2.1. Photocleavage of Chain Ethers

Photocleavage reactions involving photoinduced electron-transfer were reviewed by Saeva in 1990.[3] New data on this topic concerning chain ethers are discussed in this part of the article.

The photochemical cleavage of phenyl alkyl ethers, especially 4-substituted-phenyl piperidinoalkyl ethers, has been discussed by Marquet.[4,5] It is known that phenyl ethers substituted by electron-attracting groups do not undergo reductive fragmentation. However, related 4-substituted phenyl ethers linked through a methylene chain to a tertiary amine give either alkyl ether photocleavage when the linker between the redox centers is short (two CH_2 groups, **1**) or reduction when the linker is long (five CH_2 groups). An example is presented in Scheme 1. The product of this reaction (**2**) is obtained with nearly 100% yield. Benzophenone



Scheme 1. Alkyl–oxygen bond photocleavage of 1-piperidino-2-(4-cyanophenoxy)ethane.

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[a] Institute of Materials Science, University of Silesia,
40-007 Katowice, Poland
Fax: +48-32-259-6929,
E-mail: ansto@us.edu.pl

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is used in this experiment as a good energy-transfer sensitizer.

Mechanistic considerations suggest that the photofragmentation operates via charge transfer from the single state (space intramolecular electron transfer) to the excited triplet states and then to the triplet aromatic chromophore, and that a coplanar relative orientation of the alkyl ether bond and the phenyl ring is necessary for this process.

Dneprovskii and Fedosov[6] have reported reactions of sodium thiophenolate with various arylmethyl phenyl ethers

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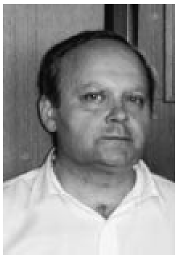
Andrzej Stolarzewicz was born in Żywiec, Poland, in 1941 and received his MSc (1962) degree from the Technical University in Wrocław and PhD (1974) and DSc (1987) degrees from the Silesian Technical University in Gliwice. Between 1968 and 2003 he worked in the Institute of Polymer Chemistry of the Polish Academy of Sciences in Zabrze. His current research interests are focused on the ring-opening polymerization of heterocycles as well as on the synthesis and application of star-shaped polyethers and polyesters.



Zbigniew Grobelny was born in Katowice, Poland, in 1951 and received his MSc (1976) and PhD (1989) and DSc (2004) degrees from the Silesian Technical University in Gliwice. His current research interests are focused on the application of alkalides and other electron-transfer reagents for selective homogeneous organic reactions and for the ring-opening polymerization of heterocycles.

Wojciech A. Pisarski was born in Grudziądz, Poland, in 1965 and received his MSc degree (1993) from Wrocław University and PhD degree (1997) from the Institute of Low Temperature and Structure Research, Polish Academy of Sciences in Wrocław. His current research interests are focused on spectroscopic methods for advanced polymers and inorganic solids as well as luminescent materials doped with rare earth ions.

Bożena Łosiewicz was born in Jaworzno, Poland, in 1972 and received her MSc (1996) and PhD (2002) degrees from the University of Silesia in Katowice. Her current research interests are focused on electrocatalysis, adsorption, absorption and hydrogen evolution, water electrolysis, metal hydrides, reaction kinetics at electrode surfaces, impedance, porous electrodes, electrodeposition of metals, and solid oxide fuel cell electrolytes.

Beata Piekarnik was born in Ruda Śląska, Poland, in 1981 and received her MSc (2005) degree from the University of Silesia in Katowice. Actually she is a PhD student. Her current research interests are focused on the anionic polymerization of oxiranes.

Andrzej Swinarew was born in Świętochłowice, Poland, in 1980 and received his MSc (2005) degree from the University of Silesia in Katowice. Actually he is a PhD student. His current research interests are focused on photoluminescent polymers.

under photochemical stimulation. The composition of the reaction products and the relationship between the reactivity and the structure of the substrates is consistent with a radical anion mechanism. They used a mercury lamp of moderate pressure (DRL-400, 400 W, 35–40 °C) for the photoinitiation and DMSO served as the solvent and found that 4-vinylbenzyl phenyl ether (**3**), 4-phenylbenzyl phenyl ether (**4**), and the 1- and 2-naphthylmethyl phenyl ethers (**5** and **6**, respectively) react with replacement of the phenoxy group. The reactions occur by a radical anion mechanism. For example, the radical anion of **3** is formed after the electron transfer, and this undergoes fragmentation to phenolate anion and 4-vinylbenzyl radical. The reaction of the latter with the thiophenolate anion, followed by electron transfer to the substrate molecule, affords 4-vinylbenzyl phenyl thioether as the main product in 78% yield. Compounds **4**, **5**, and **6** react similarly. These reactions result in 4-phenylbenzyl phenyl thioether (83%), 4-naphthylmethyl phenyl thioether (29%), and 2-naphthylmethyl phenyl thioether (59%), respectively (Scheme 2).

$$\mathrm{ArOPh} + \mathrm{PhSNa} \xrightarrow[\mathrm{DMSO}]{h\nu} \underset{\mathbf{3-6}}{\mathrm{ArSPh}} + \mathrm{PhONa}$$

Ar:	
4-vinylbenzyl	**3**
4-phenylbenzyl	**4**
4-naphthylmethyl	**5**
2-naphthylmethyl	**6**

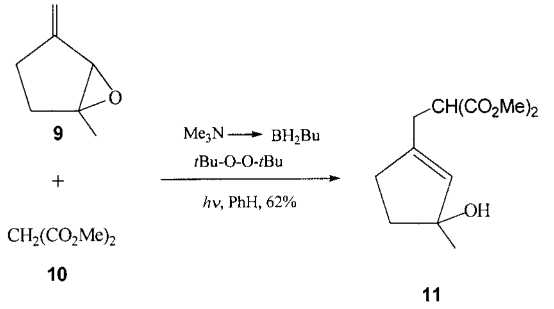
Scheme 2. Reactions of aryl phenyl ethers with sodium thiophenolate under photochemical stimulation.

The reaction rate increases in the order **3** < **4** < **5** < **6**, and the reaction fails to occur when a cyano group is attached to the benzyl position or with (1- and 2-methoxymethyl)naphthalenes.

Reactions of oxiranylcarbinyl radicals generated from α-hydroxyoxiranes, α-vinyloxiranes, and α-ketooxiranes have been reviewed by Li.[7] The ring opening of the former can proceed by either C–O bond cleavage to give an alkoxy radical or by C–C bond cleavage to afford an enol ether radical depending on the nature of substituent. An unpaired electron is located on the carbon atom bonded to the oxygen atom in the enol ether radical ($R^2C^{\cdot}HOCH{=}CHR^1$; R^2 = vinyl, aryl, or acyl). Ring opening of thw oxiranylcarbinyl radical depends on the nature of the substituent R^2 but not on R^1; C–O bond cleavage predominates when thid substituent is a simple alkyl group or hydrogen.

A phenylthiyl radical transforms acetoxyalkenyl oxirane **7** into acetoxyalkenyl cyclopentanol **8** (Scheme 3),[8,9] whereas addition of the phenylthiyl radical to an oxiranesilyl ether occurs smoothly and is followed by ether-bond cleavage to afford the ketone under photochemical conditions.[9–11]

In another method, the atom-transfer cyclization of iodooxirane leads to iodocyclopentanol under photoirradiation.[12] However, oxiranes are also transformed into alcohols by C–O bond cleavage. For example, allylic alcohol **11** is obtained photochemically from the reaction of vinyl oxirane **9** with dimethyl malonate **10** in the presence of an aminoborane catalyst and di-*tert*-butyl peroxide (Scheme 4).[13]

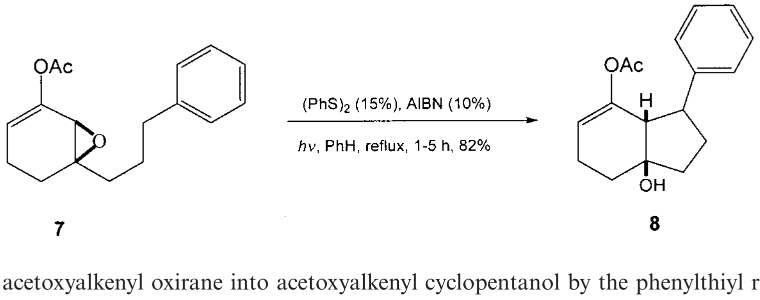


Scheme 4. Photochemically induced reaction of vinyl oxirane with dimethyl malonate.

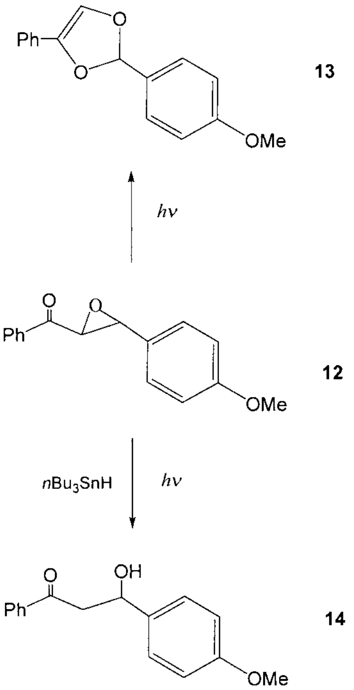
The C–O bond cleavage predominates for ketooxiranes with aryl substituents. Scheme 5 shows that although the photolysis of ketooxirane **12** leads to 1,3-dioxolane **13** due to C–C bond cleavage, its irradiation in the presence of tributyltin hydride as the reducing agent gives β-hydroxy ketone **14** followed by C–O bond scission.[14,15]

Wiest[16] has presented a contrary idea, i.e. oxirane formation by ring closure. 4-Nitrobenzenesulfenate, derived from cinnamyl alcohol and 4-nitrobenzenesulfenyl chloride, undergoes a homolytic C–O bond cleavage under photolysis conditions to give 4-nitrobenzenethiyl radical and cinnamyloxy radical. The oxiranylbenzyl radical derived from cyclization of the latter subsequently couples with thiyl radical to give the oxirane.

The Claisen-type photorearrangement of allyl aryl ethers or benzyl aryl ethers involves an intramolecular radical process that gives migration products at the *ortho* and *para* positions of phenol.[17,18] It is worth noting that the thermal Claisen rearrangement results only in *ortho*-substituted phenol.



Scheme 3. Transformation of acetoxyalkenyl oxirane into acetoxyalkenyl cyclopentanol by the phenylthiyl radical.



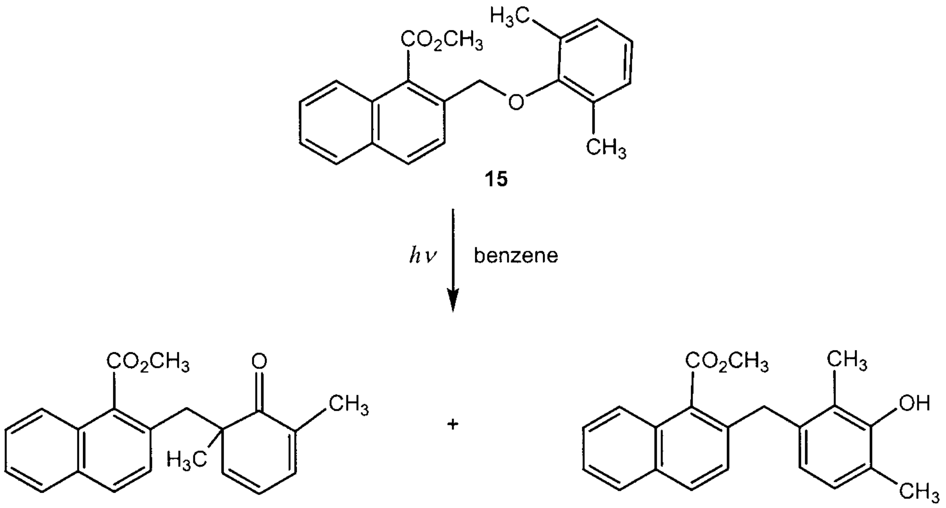
Scheme 5. The influence of tributyltin hydride on the photolysis of ketooxirane.

Mizuno[19] has reported a novel photorearrangement of 2-naphthylmethyl-2,6-disubstituted phenyl ethers that gives stable cyclohexa-2,4-dienone derivatives by C–O bond cleavage. Irradiation of a benzene solution of the substrate under argon is conducted with a mercury lamp (>280 nm). The photorearrangement of 2-[(2,6-dimethylphenoxy)-methyl]-1-methoxycarbonylnaphthalene (**15**) gives 2,6-dimethyl-6-(1-methoxycarbonyl-2-naphthylmethyl)cyclohexa-2,4-dienone (**16**) and 2,6-dimethyl-3-(1-methoxycarbonyl-2-naphthylmethyl)phenol (**17**) as the main reaction products (Scheme 6). It is assumed that homolytic cleavage of the C–O bond occurs in this case to give two radicals as intermediates, i.e. naphthylmethyl and phenoxy ones.

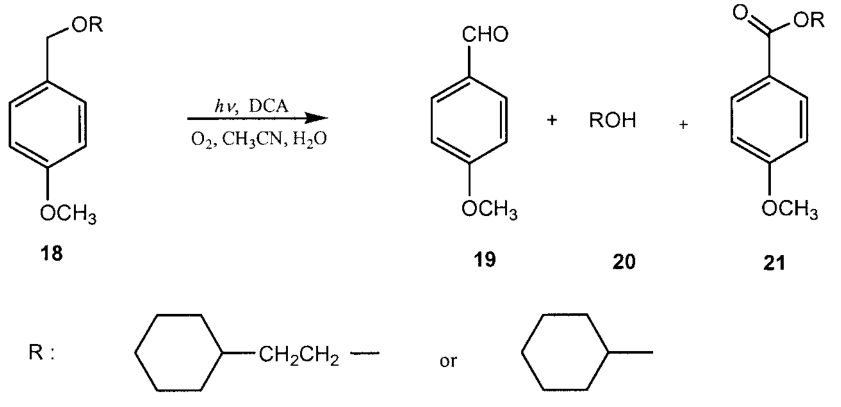
In the cases of compounds having only one *ortho*-methyl group on the phenyl ring, the naphthylmethyl radical rearranges to the *ortho* and *para* positions followed by aromatization. The intramolecular charge-transfer nature of the exciplexes causes the efficient photocleavage of the C–O bond.

Sensitizers covalently linked to the surface of silica beads have been selected for investigations of photochemical reactions since 1981.[20–25] 9,10-Dicyanoanthracene (DCA) has been used as an electron-accepting sensitizer in various systems under homogeneous and heterogeneous conditions, such as for the photocleavage of anisyl ether.[26] That reaction was then selected as a test reaction for different experiments.[27] For example, irradiation of a homogeneous mixture containing hexyl or ethylhexyl anisyl ether **18** and DCA, in CH_3CN/H_2O with air bubbling, leads to the formation of aldehyde **19**, alcohol **20**, and ester **21** (Scheme 7). A mechanism based on a stepwise two-electron transfer, with the formation of an anisyl ether radical cation and then a benzylic ether radical as intermediates, has been proposed for this process. Initially, the first electron is transferred from the anisyl ether to DCA upon photoirradiation of the reaction mixture to give a radical anion, which transfers a proton to a water molecule to give a radical. Transfer of the second electron from this radical to an acceptor is necessary to form the benzylic ether cation, which is the expected precursor of the hemiacetal leading to an aldehyde and alcohol. The transfer of the second electron is not photoinduced.

$BrCCl_3$ has also been tested as an electron acceptor in attempts to selectively orient the reaction towards the cleavage. The ratio between aldehyde, alcohol, and ester changes when the photoreaction is performed in the presence of $BrCCl_3$ and oxygen in acetonitrile/water solvent. In the absence of oxygen the ester is not formed.



Scheme 6. The photorearrangement of aryl naphthylmethyl ethers.



Scheme 7. Photoreactions of anisyl ethers.

Similar results were observed for a heterogeneous system with DCA linked covalently to silica beads. However, an ester as the next reaction product is detected when the process occurs in the presence of oxygen and CH_3CN/H_2O instead of $BrCCl_3$.

In some compounds the ether bond has been found to be stable. Such a result is obtained, for example, for the photodegradation of 4,4′-dibromodiphenyl ether in aqueous and organic solvent systems,[28] whose photochemically induced reduction occurs only by C–Br bond cleavage. The exclusive and sequential reductive debromination results in the formation of the parent diphenyl ether system. No evidence of other degradation products resulting from aryl–oxygen bond cleavage or alternative pathways was observed.

Diaryl ethers have also been studied. Hageman[29] has investigated the ether-bond cleavage of diphenyl ether, 1,4-diphenoxybenzene, and methyl- or methoxy diaryl ethers irradiated by UV light from a high-pressure mercury lamp. The cleavage occurs by H-abstraction from the solvent to yield phenols and benzene derivatives and a photo-Claisen-type rearrangement to yield 2- and 4-hydroxybiphenyl derivatives. Diphenyl ether is converted into *o*-phenyl phenol, *p*-phenyl phenol, and a small amount of phenol by UV light in several solvents. *p,p′*-Ditolyl ether is similarly converted into 2-(*p*-tolyl)-4-methylphenol and *p*-cresol, thus indicating that the photochemical rearrangement proceeds by C–O bond cleavage and recombination of the radical fragments. These reactions are reported as intramolecular ones that occur via an excited singlet state or a short-lived triplet.[30] Other substituted diphenyl ethers have been studied under 300-nm irradiation.[31] One of the reaction pathways involves the cleavage of the ether linkage to yield phenols.

The behavior of the herbicide oxyfluorfen [2-chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene] has been investigated by Bufo.[32] Photochemical reactions were carried out with a high-pressure mercury arc and a solar simulator. The results indicated that the first excited singlet state can undergo both homolytic and heterolytic cleavage of the ether bond in the side-chain of oxyfluorfen, which obviously influences the herbicidal activity upon exposure to light.

2.2. Photopolymerization with Ring Opening

Photoinitiated cationic ring-opening polymerization has been applied to a wide variety of monomers (Scheme 8).[33] The polymerization occurs efficiently in the presence of certain onium salts such as diaryliodonium and triarylsulfonium.[33–36] The choice of the salt depends on the wavelength of light to be used as well as on the reactivity of the monomer or oligomer. Electron-beam and γ-radiation have also been employed for the polymerization. However, in the absence of photoinitiators the polymerization does not take place even on prolonged irradiation at high doses (>10 Mrad).

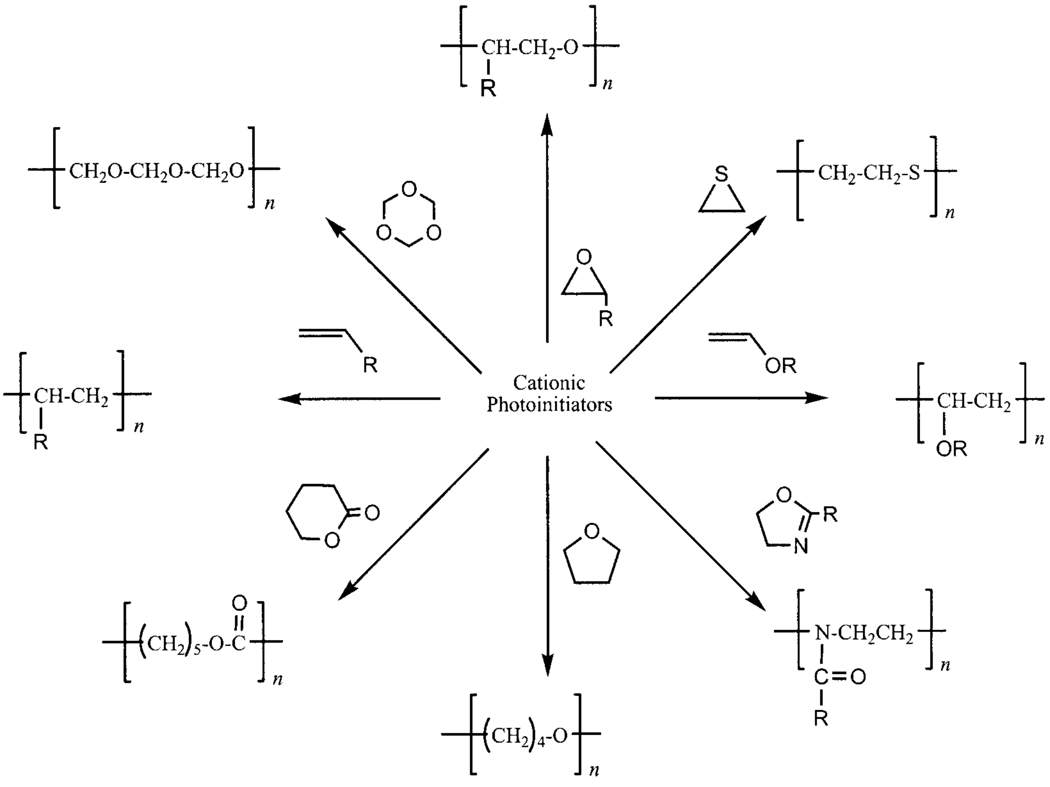
The mechanism of the radical[37–39] and cationic polymerization[40,41] of 2-substituted-4-methylene-1,3-dioxolanes has been discussed thoroughly by Davidson.[42] The results of the polymerization with a photogenerated acid show that the ring opening occurs concurrently with a disappearance of the unsaturation of the vinyl ether group. 2-Phenyl-4-methylene-1,3-dioxolane (**22**) gives exclusively ring-opened polymer (Scheme 9) whereas with 2-methyl-2-phenyl-4-methylene-1,3-dioxolane a polymer is also produced by elimination of acetophenone.

2,2′-Diphenyl-4-methylene-1,3-dioxolane (**25**) undergoes elimination to form a polyketone and benzophenone (Scheme 10). The photoinitiated free-radical reaction of 2-phenyl-4-ethylene-1,3-dioxolane with thiols leads to a 1,2-addition product with little or no ring opening.

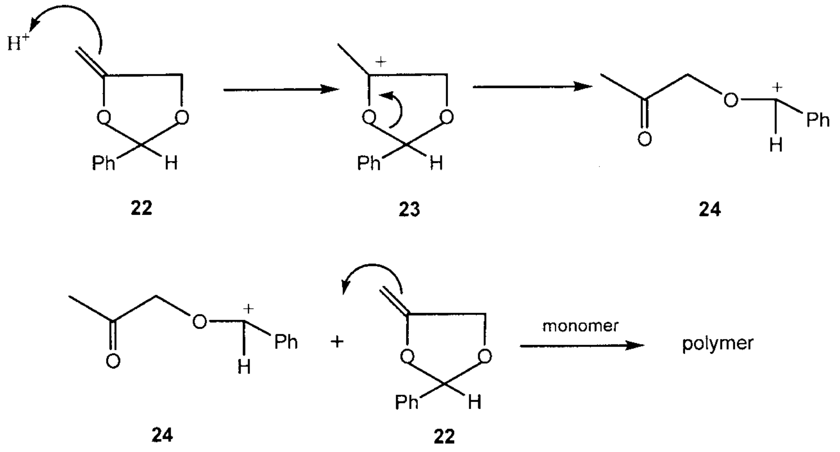
The cationic polymerization of an unsaturated cyclic ether, i.e. 2,3-dihydro-4*H*-pyran (**30**), occurs mainly at the carbon–carbon double bonds and also partly by ring-opening reactions (Scheme 11).[43]

The same mechanism of propagation involving both C=C bonds and ring opening is assumed for the photopolymerization of 2,3-dihydro-4*H*-pyran with diphenyliodonium hexafluorophosphate ($Ph_2I^+PF_6^-$) upon irradiation at 310 nm.[44] The polymerization of another unsaturated cyclic ether, 2,3-dihydrofuran, with triphenylsulfonium hexafluorophosphate ($Ph_3S^+PF_6^-$) has a living character and the propagation involves only C=C bonds.

Interestingly, 2,5-dihydrofuran does not polymerize under any conditions,[45] whereas the cationic polymerization



Scheme 8. Photoinitiated cationic polymerization of vinyl and cyclic monomers.



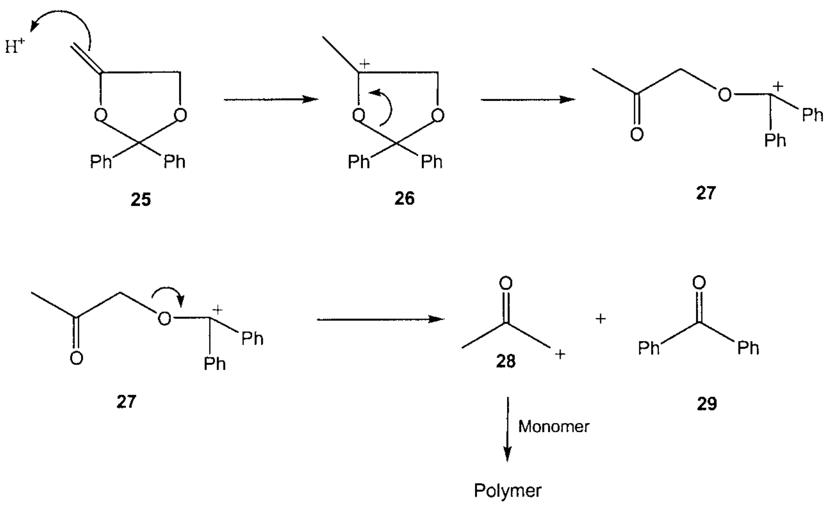
Scheme 9. Polymerization of 2-phenyl-4-methylene-1,3-dioxolane with photogenerated acid.

of 2,3-dihydro-4*H*-pyran derivatives is easy and has been used for the synthesis of biodegradable polymers.[46,47]

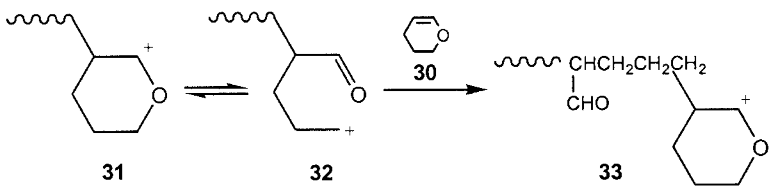
Crivello[48] has found that the photopolymerization of multifunctional oxiranes is accelerated by polyols, which act as chain-transfer reagents. The use of a diol or triol leads to a crosslinked system, whereas a monoalcohol leads to dead ends in the polymer network.[49]

The photoinitiated ring-opening polymerization of cyclohexene oxide, a representative monomer to commercial epoxides, has been studied by Yagci,[50] who showed that poly(ε-caprolactone) polyols influence the polymerization rate – block copolymer of ε-caprolactone and cyclohexene oxide is formed in their presence. The mechanism proposed by Penczek and Kubisa[51,52] for the cationic polymerization of oxiranes with hydroxy-containing compounds is accepted for this process.

Recently, Hartwig[53] has examined the effect of different diols on the photochemically and thermally induced cationic polymerization of 3,4-oxiranecyclohexylmethyl-3′,4′-oxiranecyclohexane carboxylate, i.e. a dioxirane monomer. In the presence of a 1,2-diol-based polyether the polymerization is retarded as compared to the pure dioxirane. The



Scheme 10. Polymerization of 2,2′-diphenyl-4-methylene-1,3-dioxolane with photogenerated acid.



Scheme 11. Propagation step in the cationic polymerization of 2,3-dihydro-4*H*-pyran.

same phenomenon is observed after the addition of a small amount of 12-crown-4. The polymerization is enhanced by a 1,4-diol-based polyether or a low molar mass 1,2-diol.

2.3. Photodegradation of Polyethers

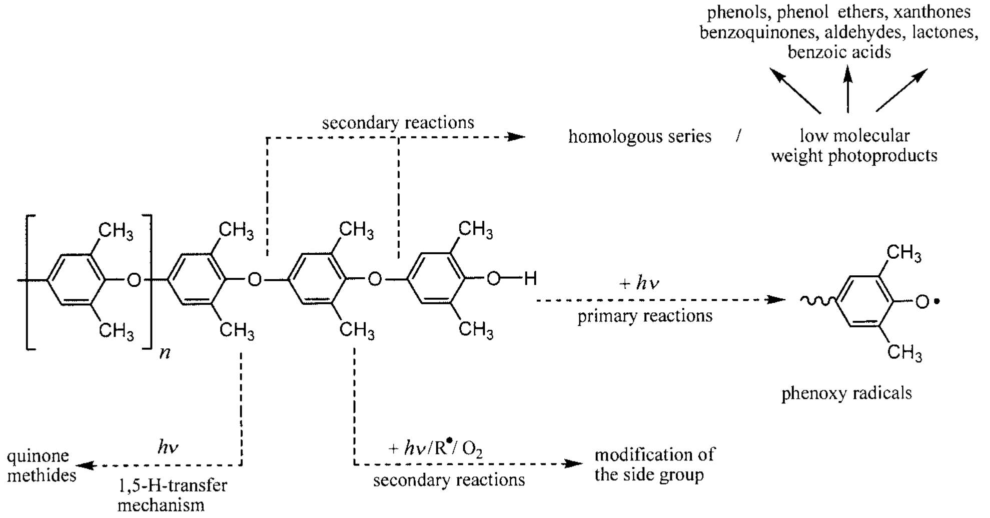
The photodegradation of one of the poly(phenylene ether)s, i.e. poly(2,6-dimethyl-1,4-phenylene oxide), has been studied particularly thoroughly because of its widespread use in commercial applications, especially in blends with various polymers. A drawback of this polymer is its yellowing upon contact with air and light.[54,55] Two mechanisms for this process have been presented in the literature. According to one of them the primary radicals are formed by photoinduced ether-bond cleavage during the photodegradation.[55]

New facts concerning that problem have been presented by Schneider.[56–58] The samples were illuminated in air with the output of a 200-W Hg/Xe arc lamp. Intense lines at 264, 295, and 301 nm due to excitation of the polymer are observed in the emission spectrum. In the second series of experiments a 1000-W Xe arc lamp was used. This produces a continuous emission spectrum whose color temperature is in the range of that of the sun. The authors concluded that the homolytic cleavage of the hydroxyl end-group is the primary photochemical process occurring after irradiation of the polymer (Scheme 12). This step was found to be independent of the excitation wavelength. The phenoxyl radicals formed at the end-standing monomeric unit can initiate several secondary reactions, which lead to the scission of a nearby ether bond. This results in a homologous series of low molar mass photoproducts, among which are chromophores like xanthones, lactones, and benzoquinones, which are responsible for the yellowing.

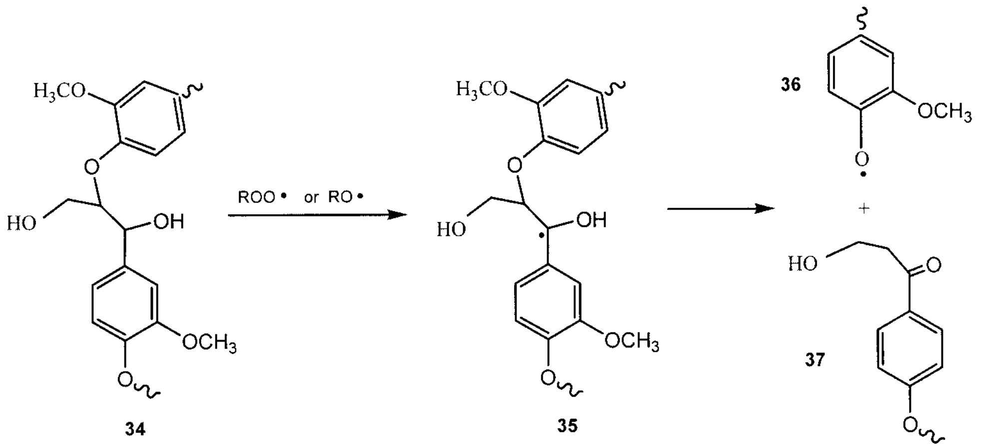
Lignin is a natural polymer built from phenylpropane units linked together by different bonds, mostly by ether ones. β-Aryl ether (β-*O*-4), α-aryl ether (α-*O*-4), and diphenyl ether (4-*O*-5) are the most common types of these linkages. The behavior of lignin has usually been studied with model compounds, whose photochemically induced degradation has been reviewed by Lanzalunga.[59] It has been reported that several reactions occur upon ether-bond cleavage after direct photoirradiation. One of these models is α-(2′,4′,6′-trimethylphenoxy)-3,4-dimethoxytoluene whose photoirradiation leads to the formation of products deriving from homolytic α-C–O bond cleavage.

The photodegradation of nonacetylated lignin has been studied by Argyropoulos[60] and Ragauskas.[61] The loss of aliphatic hydroxy groups during irradiation is observed and this effect is attributed to photoinitiated side-chain oxidation. In the case of acetylated lignin this loss of hydroxy groups can occur, in part, by free-radical ketyl oxidation of β-*O*-aryl ethers (Scheme 13).[62]

Ragauskas[63] has described the chemistry of acetylated and nonacetylated lignins, whose photobehavior shows substantially decreased reactivity during irradiation. The extent



Scheme 12. Primary (photoinduced) and secondary reactions occurring during the photodegradation of poly(2,6-dimethyl-1,4-phenylene oxide).

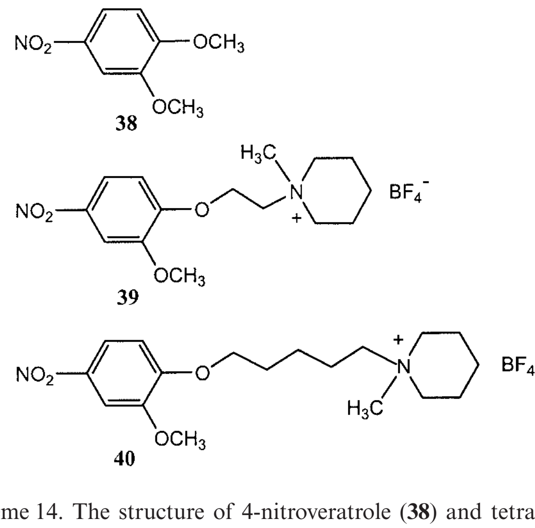


Scheme 13. Free-radical ketyl oxidation of lignin.

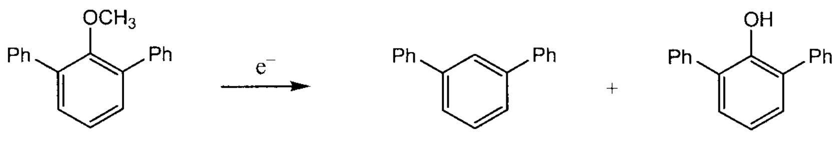
of lignin acetylation prior to photolysis has been shown to be a very important parameter in controlling the overall photoreactivity of the acetylated materials.

3. Electrochemical Methods

Marquet[5] has reported that an electrochemical method can be applied to confirm the mechanism of a photochemical process, namely the cleavage of some phenyl alkyl ethers. The problemwas solved by preparative electrolyses of 4-nitroveratrole (**38**) as well as the tetrafluoroborates of *N*-[2-(2-methoxy-4-nitrophenoxy)ethyl]-*N*-methylpiperidinium (**39**) and *N*-[5-(2-methoxy-4-nitrophenoxy)pentyl]-*N*-methylpiperidinium (**40**), i.e. *N*-methyl quaternary salts of 4-nitrophenyl piperidinoalkyl ethers, in DMF (Scheme 14). The applied potential (–1.2 V vs. SCE) was selected in such a way as to allow only the first reduction to happen.



Scheme 14. The structure of 4-nitroveratrole (**38**) and tetrafluoroborates **39** and **40** used for the preparative electrolysis.



41 **42** **43**

Scheme 15. Electrochemical cleavage of methyl 2,6-diphenyl ether.

Compounds **38** and **40** were found to be stable under the reaction conditions but **39** underwent reductive cleavage to give phenol in 39% yield. After the first reduction of **38** and **40** the negative charge should be concentrated on the nitro group, which makes any further reduction difficult. However, in the case of **39** a topologically controlled coulombic interaction (TCCI) effect reduces the electron density on the nitro group and the second reduction occurs more easily. The TCCI effect as a new tool in the study of photochemical and electrochemical cleavage of phenyl alkyl ethers is discussed in more detailed in ref.[5]

Marquet and Melloni[64] have studied the electrochemically promoted cleavage of alkyl 2,6-diphenylphenyl ethers (Scheme 15) and have shown that the preparative electrolysis of 2,6-diphenylanisole (**41**) in THF solution at controlled potential (–2.6 V vs. SCE) gives only a trace of *m*-diphenyl **42** (dealkoxylation). No 2,6-diphenylphenol (dealkylation) is produced, whereas the electrolysis in DMF affords a 29% yield of 2,6-diphenylphenol (dealkylation). Thus, the use of a solvent with better cation-solvating properties, which should favor the presence of solvent-separated ionic pairs, allows the intervention of the mechanistic pathway leading to dealkylation, although with a low Faradaic yield. On the other hand, the reaction of *N*-[2-(2,6-diphenylphenoxy)ethyl]-*N*-methylpiperidinium tetrafluoroborate in THF and DMF gives 2,6-diphenylphenol in very good yields (88% and 91%, respectively). No dealkoxylation product is detected.

On the basis of these and other experiments it has been concluded that both directions of the fragmentation, i.e. alkyl–oxygen and aryl–oxygen bond scission, have to involve an intramolecular π^*-σ^* electron-transfer step, or at least a large component of π^*-σ^* electron-transfer in the transition state.

Two fragmentation processes are thermodynamically allowed for alkyl aryl ethers. The alkyl–O bond cleavage corresponds to a "homolytic" cleavage that does not regioconserve the spin density and should therefore show an intrinsic kinetic barrier. The thermodynamically less favorable aryl–O bond cleavage corresponds to a "heterolytic" process and no extra kinetic barrier should exist in this case. This situation is reflected in the behavior of alkyl nitrophenyl ether radical anions, which are inert toward any fragmentation.[65–67]

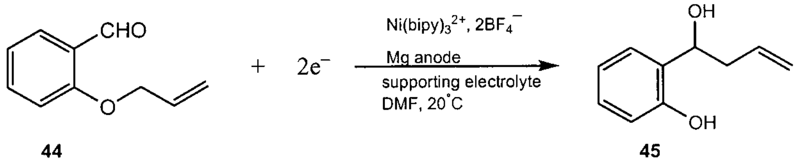
It is worth noting that cleavage of the alkyl–oxygen bond of alkyl aryl ethers with formation of phenols (dealkylation) is most often observed when alkali metals are used, whereas the aryl–oxygen one is achieved only in particular cases, especially in the presence of potassium and in solvents of low or very low polarity.[68–71] Similarly, potassium anions cleave exclusively the allyl–oxygen or benzyl–oxygen bond in some glycidyl ethers to give organopotassium compounds as intermediate reaction products.[72,73]

The classical methods of allyl ether deprotection generally proceed through double-bond isomerization to enol ethers by potassium *tert*-butoxide[74] or rhenium complexes followed by acidic hydrolysis.[75,76] In the case of the electrochemical procedure a mechanism involving the allyl–oxygen cleavage with formation of a π-allylnickel intermediate has been suggested.[77]

Duñach[76] has described the first example of an intramolecular allylation of carbonyl compounds in a series of electrochemical reactions involving the cleavage and transfer of the allyl group in a nickel-catalyzed process. A series of substituted *o*-(allyloxy)benzaldehydes and *o*-(allyloxy)acetophenones were selected for that study. The reaction of unsubstituted *o*-(allyloxy)benzaldehyde (**44**) is presented in Scheme 16.

Good yields of allylation are generally obtained in electrolyses with a single-compartment cell. A magnesium anode is the best for aryl aldehydes, whereas a zinc anode gives better results with ketone derivatives. The allylation involving the intramolecular transfer of substituted allyl units favors the regioselective formation of the branched isomer.

The ability of Pd^0 complexes to form π-allylpalladium(II) compounds has been combined with the use of a reducing agent for the Pd-catalyzed deprotection of allyl ethers.[78] It was found[79] that Pd complexes associated with nitrogen ligands, e.g. with 2,2′-bipyridine or pyridine-oxazoline, can

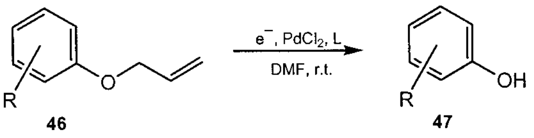


44 **45**

Scheme 16. Electrochemical intramolecular allylation of 2-allyloxybenzaldehyde.

catalyze the electrochemical cleavage of the carbon–oxygen bond of 2-allyloxy-1-bromobenzene to afford 2-bromophenol under mild conditions.

This method has been extended to the Pd-catalyzed deprotection of allyl aryl ethers **44** using an electrochemical procedure (Scheme 17).[80] The yield of the C–O bond cleavage ranges from 73 to 99% for various ether derivatives.



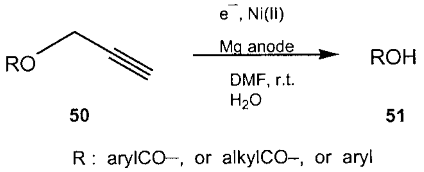
R: Cl, CN, CO_2CH_3

Scheme 17. Electrochemical ether-bond cleavage of allyl ethers catalyzed by a Pd^{II} precursor.

In contrast to these results, the Pd-catalyzed electroreduction of 2-allyloxybenzaldehyde (**44**) in the presence of 2,2′-bipyridine affords 2-hydroxybenzaldehyde (**48**; 55% yield), 2-(1′-hydroxy-3′-butenyl)phenol (**45**; 25%), and a small amount of bis-allylated compound **49** (2%; Scheme 18).[80] The C–O cleavage is followed by the partial allylation of the carbonyl moiety to give, after hydrolysis, the corresponding homoallylic alcohol (phenol). The use of chiral pyridine-oxazoline ligands instead of bipyridine in order to examine the asymmetric process gives the same products, although with different yields.

The idea of using nitrogen ligands in an electrochemical process has also been applied to propargyl compounds. Only a few examples dealing with the related C–O bond cleavage in propargylic derivatives have been reported previously. They include the use of low-valent titanium[81] and palladium-catalyzed reductive cleavage of propargylic esters mediated by Bu_3SnH[82] or by SmI_2.[83,84]

A Ni^{II}-catalyzed electrochemical one-pot procedure has recently been described to obtain carboxylic acids or phenol derivatives in good yields from propargyl esters or ethers (Scheme 19).[85] This method is based on the application of a single-compartment cell fitted with a sacrificial magnesium anode.[86] The reaction proceeds through electrosynthesis combined with the catalysis by Ni^{II}-bipyridine complexes under mild conditions.

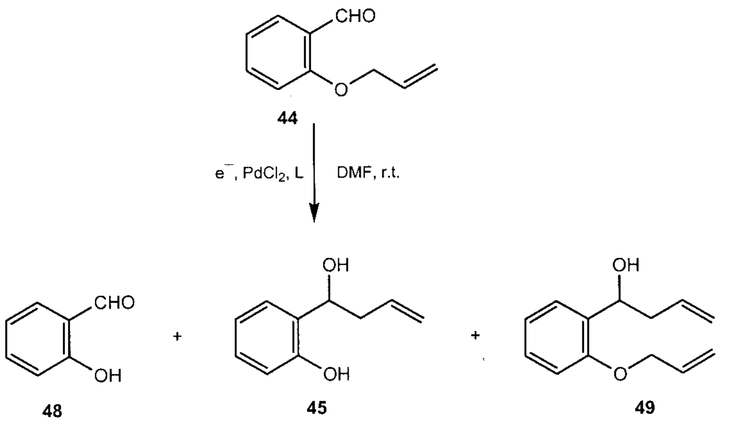


Scheme 19. Ni^{II}-catalyzed electroreductive cleavage of propargyl esters and ethers.

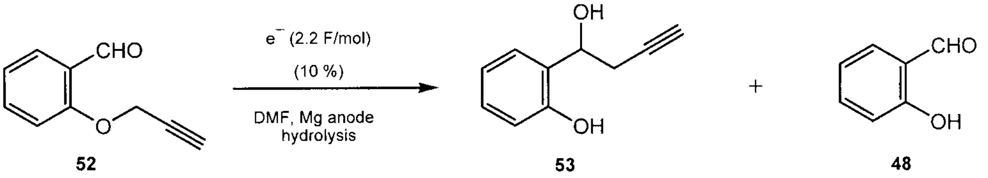
Electrochemical propargylation of carbonyl compounds has been reported in another work by Duñach.[87] A similar allylation of carbonyl derivatives has been described in both intermolecular[88–90] and intramolecular versions[76] to afford homoallylic alcohols. The electrochemical method for carbonyl propargylation has been examined for *o*-substituted aryl aldehydes.[87] The electrolysis was carried out in DMF at ambient temperature with the Ni^{II} complex $[Ni(2,2'\text{-bipyridine})_3][BF_4]_2$ as the catalyst. 2-Propargyloxy benzaldehyde (**52**) was used as a model compound for the study of intramolecular transfer of the propargyl group to a carbonyl one (Scheme 20). The electroreduction leads to its complete conversion and formation of 2-(1-hydroxybut-3-ynyl)phenol (**53**; 51% yield) and 2-hydroxybenzaldehyde (**48**; 49%). The cleavage of the C–O bond occurs quantitatively, and the aldehyde group is not reduced in this process.

The presence of the nickel complex is essential for the coupling reaction. In its absence the electrolysis of **52** leads to the recovery of 90% of the starting material without the propargyl group transfer. The nickel(II) is reduced in the electrochemical process to nickel(0) at –1.2 V vs. SCE; Ni^0 is presumably the active catalytic species effecting the C–O bond cleavage and the further carbonyl addition.

The use of allyl and cinnamyl ethers as protecting groups for alcohols and the methods for their removal have been described in several papers.[91–93] Recently, some conduritol derivatives protected as allyl and cinnamyl ethers have been subjected to electrochemical reduction at a mercury cath-



Scheme 18. Pd^{II}-catalyzed electroreduction of 2-allyloxybenzaldehyde.

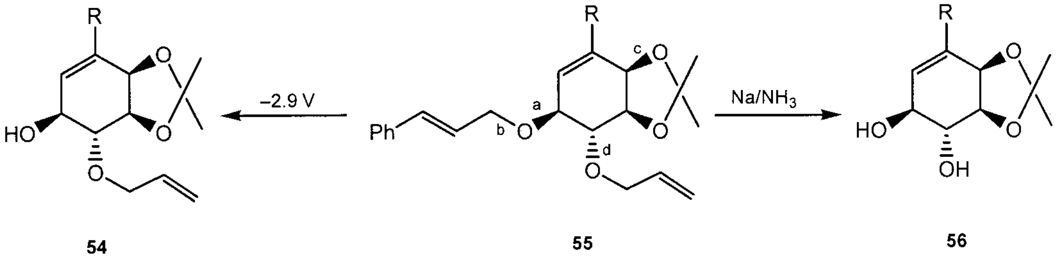


Scheme 20. Electroreduction of 2-(propargyloxy)benzaldehyde.

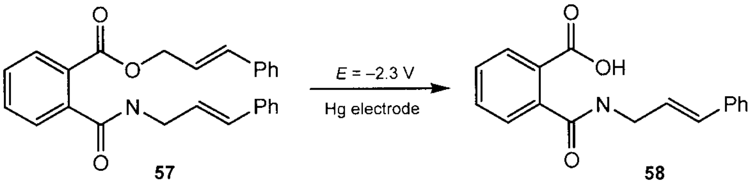
ode, resulting in a selective removal of the cinnamyl group under extremely mild conditions.[94]

The conduritol derivative containing endocyclic and exocyclic cinnamyl units in addition to endocyclic and exocylic allyl groups was chosen as an example for the study. The dissolving metal reduction of two exocyclic groups occurs without selectivity, whereas the electrochemical reduction at –2.9 V cleaves only the *exo* cinnamyl ether (Scheme 21).

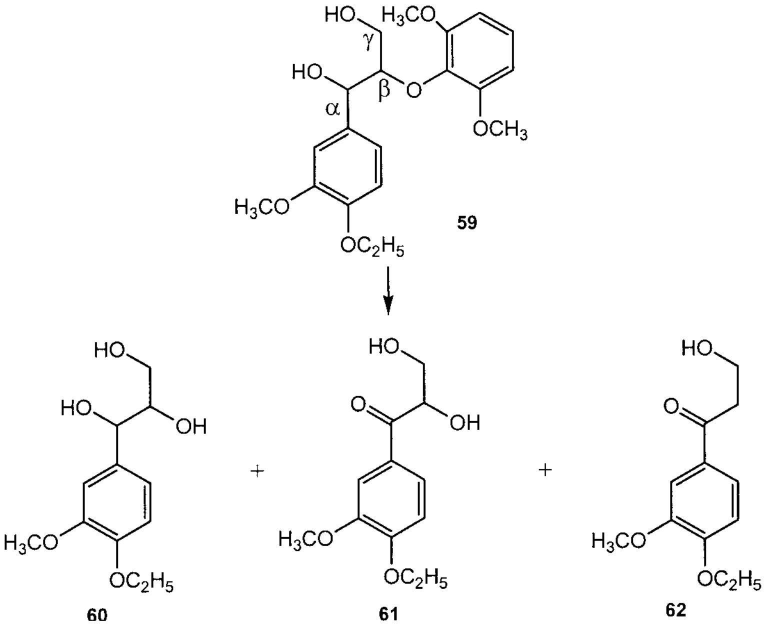
It should be also stressed that electrochemical methods of removal offer advantages over chemical or photochemical methods. Firstly, the electrochemical configuration of the alcohol may be retained, which does not take place



Scheme 21. Electrochemical and dissolving metal reduction of cinnamyl-allyl ether.



Scheme 22. Selective electrochemical reduction of an ester-amide.



Scheme 23. Degradation of nonphenolic beta-*O*-4-lignin model dimer by *Trametes versicolor* laccase.

when other methods performed under oxidizing conditions are employed. Secondly, it is a selective process not only with respect to allyl groups but also with respect to other cinnamyl units, where the reductively generated anion would be more basic, i.e. localized at the secondary cyclic carbon atom. Details concerning various reactions and products in cinnamyl–allyl systems are presented in ref.[94] Finally, alkylative methods of removal offer no selectivity in differentiating between allylic and cinnamyl carbons.

Electrochemical deprotection of the cinnamyl moiety from ethers, esters, and carbamates has been studied by Hudlicky[95] with the focus on O- vs. N-selectivity as well as the selectivity for allyl or benzyl systems. One example is shown in Scheme 22. The electrochemical reduction of ester-amide **57** produces only acid **58** (in 71% yield). Generally, oxygen deprotection is found to occur selectively over nitrogen deprotection except for carbonate/carbamate competition.

4. Enzymatic Methods

Laccase has been applied for biological degradation of phenolic lignin model compounds since 1968.[96,97] However, this enzyme alone can not oxidize the nonphenolic lignin moieties that are decisive for the degradation. This problem has been solved by the addition of 1-hydroxybenzotriazole.[98]

It has been reported[99,100] that *Trametes versicolor* laccase catalyzes the β-ether cleavage, Cα–Cβ cleavage, and aromatic ring cleavage of 2-(2,6-dimethoxyphenoxy)-1-(4-ethoxy-3-methoxyphenyl)-1,3-dihydroxypropane (**59**), a nonphenolic β-*O*-4 lignin model dimer, in the presence of 1-hydroxybenzotriazole. The detailed degradation mechanism for these pathways has been studied by Kawai.[101] It is assumed that the formation of glycerol proceeds by the β-ether cleavage via the aryl cation radical. The α-keto and β-deoxy derivatives are obtained in this case as the final reaction products **60**–**62** (Scheme 23).

5. Conclusions

Photochemical and electrochemical processes involving C–O bond cleavage seem to be very attractive for organic synthesis as they occur under mild or even extremely mild conditions. In several cases they are regioselective, whereas no selectivity can be expected when traditional methods are used.

These methods have already found many commercial applications due to their rapidity, low energy requirements, and, particularly, because the reactions can be carried out in bulk, thereby eliminating the need for solvents. For example, photopolymerization is suitable for the production of thin films[33] or for the curing of adhesives, printing inks, coatings, and electronic packing materials.[102] Enzymatic methods enable the study of the biodegradation of substances in nature.

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