

PURE VACUUM. NOTHING ELSE.



NEW

10⁻³ mbar vacuum range

- + 100% oil-free
- + Chemically resistant
- + No wear parts

VACUU·PURE®

Learn more

www.vacuubrand.com/vacuu-pure

vacuubrand®

Waste-Free Electrochemical Oxidation of Alcohols in Water

Giovanni Palmisano,^{a,c} Rosaria Ciriminna,^a and Mario Pagliaro^{a,b,*}^a Istituto per lo Studio dei Materiali Nanostrutturati, CNR, via U. La Malfa 153, 90146 Palermo, Italy

Fax: (+39)-091-680-9247; e-mail: mario.pagliaro@ismn.cnr.it

^b Institute for Scientific Ethics and Methodology, CNR, via U. La Malfa 153, 90146 Palermo, Italy^c Present address: Dipartimento di Ingegneria Chimica dei Processi e dei Materiali, Università degli Studi, viale delle Scienze, 90128 Palermo, Italy

Received: April 24, 2006; Revised: July 31, 2006; Accepted: August 4, 2006

This article is dedicated to Professor Giuseppe De Rita on the occasion of his 75th birthday

Abstract: We describe a new sol-gel molecular electrode made of a thin layer of organosilica doped with the nitroxyl radical TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) electrodeposited on the surface of an ITO-coated glass and its employment as a selective and versatile oxidation catalyst in the electrochemical conversion of different alcohols to carbonyl compounds. Environmentally friendly water or a water/acetonitrile mixture buffered with bicarbonate is used as solvent. The electrode is highly stable and it can be reused for a prolonged period of time allowing easy separation from the products.

Keywords: alcohols; carbonyl compounds; electrochemistry; green chemistry; oxidation; TEMPO

The design of clean, efficient and simple synthetic routes has become a central issue of chemical research both in industry and in the academy. For example, in chemical oxidations for economic, ecological and legislative reasons the chemical industry will currently not apply toxic transition metals as stoichiometric oxidants and will avoid environmentally unsafe solvents.^[1] Hence, the aerobic oxidation of alcohols to carbonyl compounds – crucial precursors of drugs, dyes and fine chemicals – has become a major goal of contemporary chemical research because older industrial processes made use of toxic heavy metals (notably Cr and Mn salts) in copious amounts generating 15–20 kg of hazardous heavy-metal waste per kg of useful product.^[2]

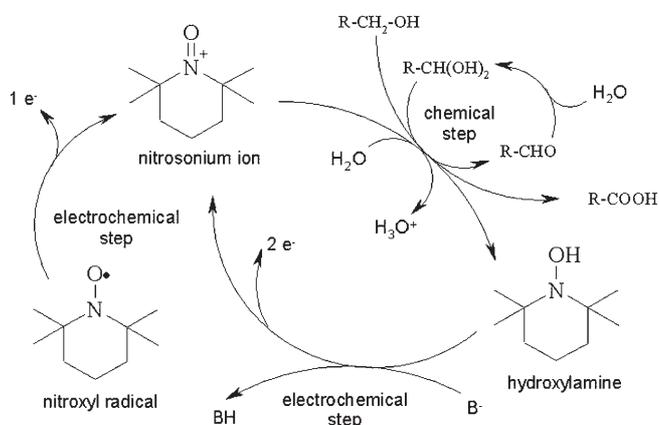
Similarly, avoiding the use of carcinogenic and bioaccumulating chlorinated (or aromatic) hydrocarbon solvents in which these conversions are carried out is also urgent^[3] since solvents have a considerable life cycle impact and continue to be used according to an obsolete resource depletion model typical of tradi-

tional chemical methods.^[4] Accordingly, the use of water as reaction medium is highly desirable as water is a readily available, safe and environmentally friendly solvent which is currently finding a number of surprising applications in synthetic chemistry.^[5]

Research efforts in the field of alcohol oxidation have lately resulted in a number of aerobic heterogeneous metal catalysts of impressive selective activity, mostly based on Ru,^[6] Pd,^[7] and, more recently, bimetallic Pd-Au^[8] catalysts. These metal/O₂ catalytic systems are all atom-efficient,^[9] and yet the ideal goal is to avoid the use of any chemical oxidants preventing all risks associated with the manipulation of O₂ or H₂O₂ in the presence of organic compounds.

In place of metal catalysts mentioned above, stable di-tertiary alkyl nitroxyl radicals such as 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO) are increasingly finding use in industry as oxidation catalysts due to their high selectivity and pronounced versatility (Scheme 1).^[10]

In these catalytic oxidations the active species is the cyclic nitrosonium ion generated *in situ* by an auxiliary oxidant. However, the species can be generated



Scheme 1. Electrochemical oxidation of primary alcohol mediated by TEMPO.

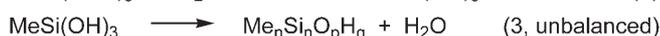
also electrochemically by applying a small electric potential (0.7 V vs. Ag/AgCl) to a solution of nitroxyl radicals. Hence, recently a number of different alcohols were oxidised in good yield and selectivity either to carbonyl compounds (in organic solvent mixed with 5% water) or to carboxylic acids in H₂O.^[11]

Similarly, the electrochemical oxidation of several alcohols can be heterogeneously carried out either (in organic solvent) using a graphite electrode coated with a thin poly(acrylic acid) (PAA) layer grafted with 4-amino-TEMPO;^[12] or (in water) using silica-entrapped TEMPO coupled to catalytic Br⁺ anodically regenerated from bromide.^[13]

Now, we report the preparation of a molecular electrode able to afford high yields of commercially valued carbonyl compounds in water with complete selectivity and marked stability as shown by repeated use of the same electrode in consecutive reaction runs. Indeed, only one and the same electrode was used in all the experiments discussed in the following.

The electrode is made of a thin film of sol-gel organosilica doped with nitroxyl radicals deposited on the surface of an indium-tin oxide (ITO) electrode according to a recent method^[14] that exploits the pH increase at the electrode surface by reduction of protons near such a surface [Eq. (1)].

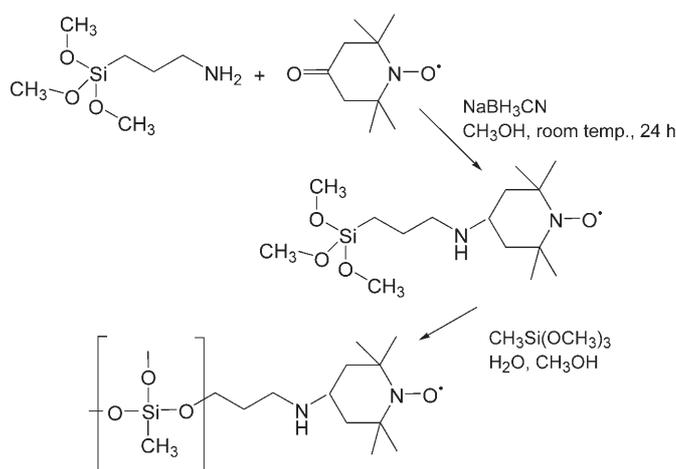
Such proton consumption in the proximity of the electrode's surface catalyses the sol-gel polycondensation of an organosilane such as methyltrimethoxysilane [MTMS, Eq. (2)] and thus ensures the electrodeposition of a thin layer of organosilica [Eq. (3)]:



Carrying out this organosilica electrodeposition in the presence of aminopropyl(trimethoxy)silane derivatised with the TEMPO moiety (*via* reductive amination with 4-oxo-TEMPO), a thin film of TEMPO-entrapped ORMOSIL (organically modified silicate) is obtained (Scheme 2 and Figure 1) which shows extraordinary performance in terms of both selective activity and stability.

Voltammetry experiments recorded in a single cell (Figure 2) comparing the electrode thereby obtained (TEMPO@DE) with the CV of the bare ITO electrode (Figure 3) clearly show the powerful electrochemical activity imparted to the electrodeposited electrode by the entrapped radical (the negative sign of current at positive potential is due to the instrument's software).

The scope of the method is illustrated by the range of primary, secondary, allylic and benzylic alcohols that are oxidised in high conversion and selectivity (Table 1) to form either their corresponding aldehydes or ketones. All oxidative runs were carried out



Scheme 2. Synthesis of the TEMPO@DE electrode.



Figure 1. TEMPO@DE is obtained by electrodeposition of a thin layer of organosilica doped with TEMPO upon application of -1.1 V (vs. Ag/AgCl) for 15 min to a solution of suitable organosilanes (left). The electrocatalytic film thereby obtained selectively converts benzyl alcohol dissolved in 0.2M NaHCO₃ to pure benzaldehyde by simply applying a 1.4 V voltage (right).

setting the voltage (relative to the reference electrode) at 1.4 V and in the presence of 0.2M hydrogen carbonate acting both as the electrolyte and as the base needed for proton abstraction (Scheme 1). A typical CV had the shape shown in Figure 4.

For control, under the same reaction conditions no oxidation of benzyl alcohol occurred both at a bare ITO electrode and at an ORMOSIL-modified ITO electrode without entrapped TEMPO even after 200 h. On the other hand, when the protocol was applied to benzyl alcohol using TEMPO@DE, after 180 h reaction was complete (Figure 5) and all the benzaldehyde formed – which partly separated from solution due to its low water solubility (0.1 gL⁻¹ at 20°C) – was recovered from the reaction mixture by

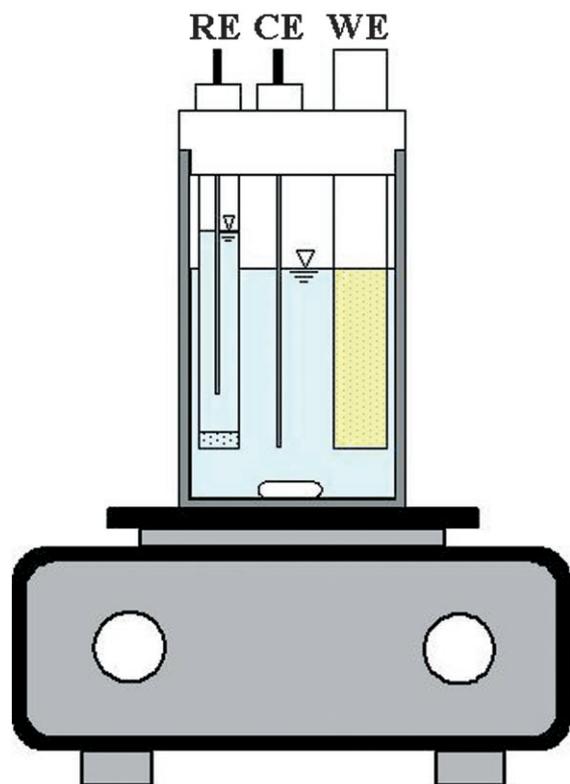


Figure 2. Scheme of the oxidation cell. TEMPO@DE is the working electrode (WE) while the reference electrode (RE) is made of Ag/AgCl and the counter electrode (CE) is a platinum thin wire.

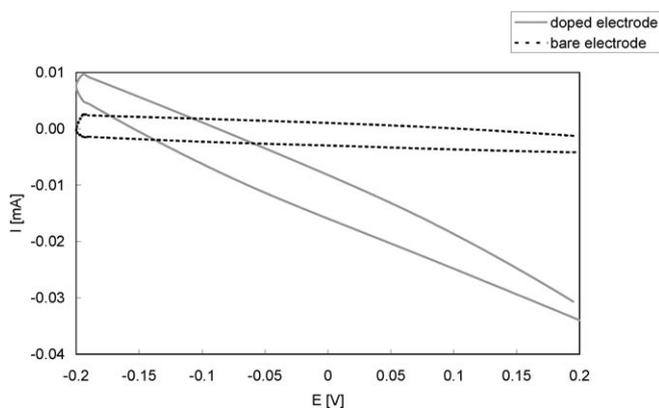


Figure 3. Cyclic voltammetry of bare ITO and sol-gel doped electrodes in 0.2 M KNO_3 .

final extraction with ethyl acetate. No traces of benzoic acid were detected (by GC) throughout the reaction using a highly sensitive FID detector connected to a column for separation of carbonyl compounds and organic acids.

A brief analysis shows the potential applications of this new technology. Benzaldehyde is industrially obtained by as a by-product in the oxidation of toluene directed towards the production of phenol or directly by the catalytic aerobic oxidation of toluene.^[15] On

Table 1. Conversion of primary and secondary alcohols.^[a]

Substrate	Product	Time [h]	Conversion [%]	Selectivity
1-phenylethanol	acetophenone	12	98	99
benzyl alcohol	benzaldehyde	180	88	99
geraniol ^[b]	citral	100	85	99
cinnamyl alcohol	cinnamaldehyde	90	87	99

^[a] Conditions: 0.5 mmol alcohol, TEMPO@DE (1 cm²), water (10 mL), NaHCO_3 (0.2 M), $V=1.4$ V vs. Ag/AgCl. Conversion and selectivity determined by GC.

^[b] Reaction in $\text{H}_2\text{O}/\text{CH}_3\text{CN}$ (7:3).

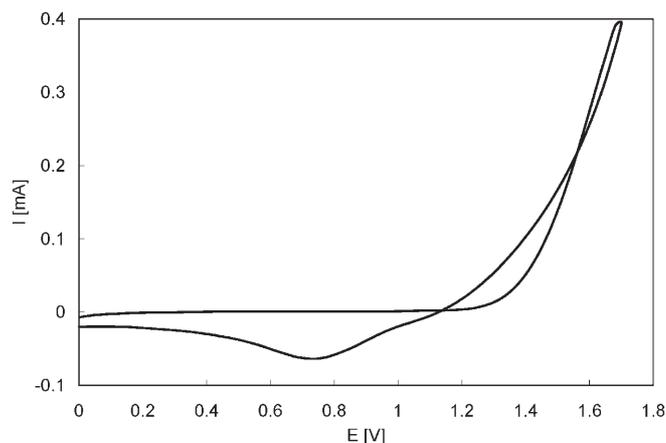


Figure 4. Cyclic voltammetry of sol-gel doped electrode TEMPO@DE in 0.2 M NaHCO_3 and 0.05 M 1-phenylethanol at voltage between 0 and 1.7 V (vs. Ag/AgCl).

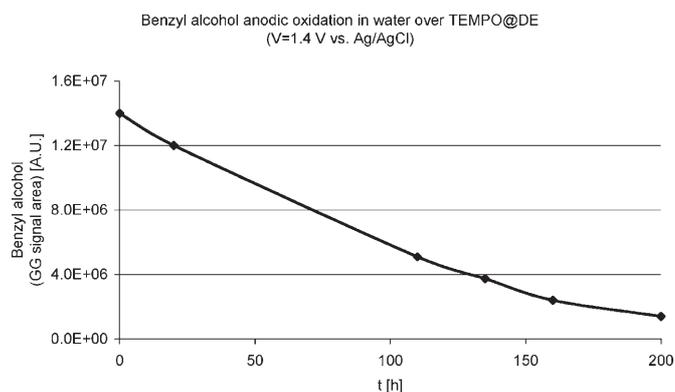


Figure 5. Benzyl alcohol oxidation in water mediated by the electrode TEMPO@DE ($V=1.4$ V vs. Ag/AgCl).

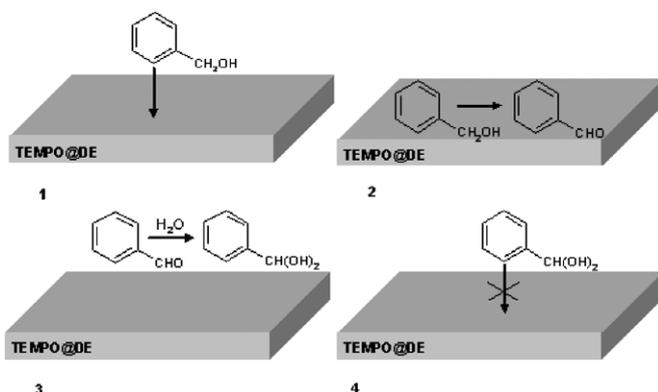
the other hand, its production by the method described herein starting from benzyl alcohol^[16] might be desirable for the fragrance and pharmaceutical industries where this aromatic aldehyde is employed in large amounts as an intermediate in the manufacture of flavours, perfumery chemicals and pharmaceuticals.

The use of water instead than organic solvent and the absence of transition metals and traditional chemical oxidants would indeed afford a product of unprecedented purity.

Despite being highly desirable, electroorganic syntheses traditionally have been limited by the low selectivity typical of the electrochemical reactivity of most conductive surfaces (metals or semi-metals) where reactions take place.^[17] Indeed, a few synthetic electrochemical processes are carried out on an industrial scale including the 340,000 t/year production of adiponitrile^[18] [it is of relevance to this report that the success of this process was also due to the use of water as reaction solvent and to the relatively low voltage (3.8 V) employed]; and the production (without mediator) of aryl aldehydes on a 5000 t/year scale from toluenes.^[19]

On the other hand, functionalised sol-gel electrodes have a rich and varied electrochemistry due to their vast accessible inner porosity that allows the oxidant and reducing reactant molecules to diffuse through the material and eventually to the surface of a conducting electrode that can be modified and tailored to selectively target specific applications.^[20] For instance, a major advantage of the sol-gel technique herein described is the ability to prepare electrodes with the desired surface hydrophilicity-lipophilicity balance (HLB) in order to render them suitable for the oxidation of alcohols in water and prevent overoxidation to acids.

Hence, whereas in water solution with TEMPO, benzyl alcohol is anodically oxidised to benzoic acid,^[11] the use of the hydrophobic sol-gel molecular electrode TEMPO@DE affords uniquely benzaldehyde. We make the hypothesis that such a selectivity is due to the HLB of the organosilica surface which prevents diffusion of the hydrated aldehyde molecules (*gem*-diol) to the hydrophobic surface of the electrode (Scheme 3). Indeed, supporting this hypothesis,



Scheme 3. Alcohols are oxidised at the inner surface of TEMPO@DE (**1** → **2**) but not so the hydrophilic hydrated aldehydes (**3** → **4**) which cannot enter the pores due to the HLB of the material (see text).

the surface of a similar, markedly alkylated ORMOSIL not only is highly hydrophobic but also shows a pronounced low degree of *hydrophilicity* due to depletion of silanol groups at the organosilica matrix surface.^[21]

Finally, in contrast with the immobilisation of nitroxyl radicals by surface derivatisation of an organic polymer resulting in a material whose stability was not reported,^[12] sol-gel encapsulation in the inner porosity of the ORMOSIL film protects the radicals from chemical degradation which is due to intermolecular quenching of the radicals tethered at the surface.^[22] As a result, we were able to use the same catalytic electrode in tens of experiments with different substrates without any treatment between consecutive oxidative runs besides sonication with ultrasound in distilled water.

Clearly, reaction rates that are here limited by the electrode's low area for the experiments described in this report, need to be improved by using larger electrodes. Moreover, far less amounts of water can be successfully employed which here was prevented by the limited versatility of the reaction cell employed. Finally, we are currently investigating the reason why encapsulation of the TEMPO moiety within a thin layer of methylsilica results in an alteration of the electrochemistry of the dopant TEMPO molecule which in solution has an oxidation potential at about 0.7 V (vs. Ag/AgCl) and upon entrapment shows a relatively high current occurring already at 0.2 V (Figure 3).

However, considering both the ease and reproducibility of electrochemical TEMPO-mediated oxidations^[23] and of the sol-gel electrodeposition process for the preparation of organosilica films,^[14] the findings described in this report may open the route to the commercial electrochemical oxidation of alcohols in the fine chemicals industry, especially in the case of small scale reactions.

Experimental Section

All chemicals were purchased from Aldrich and used without further purification. Ultrapure water (Milli-Q Millipore System) was used in all the experiments. Cyclic voltammetry and amperometric curves were performed by using a CH Instruments (Austin, TX) potentiostat CHI630B Electrochemical Workstation. A standard three-electrode cell was used for the experiments. The volume of the reaction vessel was 10 mL and an Ag/AgCl electrode in 3M KCl was used as reference electrode. The counter electrode was a platinum wire ($d=0.5$ mm) whereas the working electrodes were indium-tin oxide (ITO) plates obtained from Delta Technologies (Stillwater, MN) with a coated surface area of 0.36 cm². The ITO-coated glasses were washed prior to film deposition with water, 80% (v/v) ethanol and water after which they were dried at room temperature for 2 h.

General Procedure for the Preparation of the Doped Electrode

The organosilane precursor solution (solution A) was obtained adding 5 mL of 3-aminopropyl(trimethoxy)silane to a solution of 1.32 g of 4-oxo-TEMPO (4-oxo-2,2,6,6-tetramethylpiperidine-1-oxyl) and 221.2 mg of NaBH₃CN (95%) in MeOH (18 mL) in a reaction flask kept closed under a nitrogen atmosphere which results in the required compound as described elsewhere.^[24] The resulting mixture was stirred for 48 h, after which the excess of sodium cyanoborohydride was quenched with 7M HCl (50 μ L).

The solution for the electrodeposition of sol-gel film consisted of 0.612 mL of MeTMS (methyltrimethoxysilane), 0.612 mL of solution A, 5 mL of ethanol and 5 mL of a solution buffered at pH 4 (Fisherbrand) and 0.4M in KNO₃. Upon stirring this solution for 1 h at room temperature to promote hydrolysis in the presence of the ITO electrode, a constant negative potential of -1.1 V vs. Ag/AgCl was applied to the solution for 15 min under fast stirring. The resulting coated electrode was washed with water and absolute ethanol and then dried at room temperature for 6 h.

General Procedure for the Oxidation of Alcohols

Cyclic voltammetry experiments were recorded in 0.2M KNO₃ at potentials between ± 0.2 V vs. Ag/AgCl without stirring. The oxidation of alcohols (0.5 mmol) was carried out in 10 mL of buffered water (0.2M in NaHCO₃) although for alcohols with low water solubility (geraniol, for instance) a CH₃CN/H₂O solution 30:70 (v/v) was employed. Initial substrate concentration was 0.05M. For all the substrates the selected potential was 1.4 V and the electrolysis was carried out under fast stirring (900 rpm). Substrate and product concentrations were assessed by a Shimadzu GC-17 A gas chromatograph equipped with a Supelcowax 10 capillary column (30 m, 0.25 mm ID) by the internal standard method (with previously calculated response factors) using 10 μ L decane as internal standard.

Acknowledgements

We thank the Quality College del CNR and Fox Petroli (Pesaro, Italy) for financial support.

References

- [1] The potential waste coproduced with active pharmaceutical ingredients (APIs) is in the range of 500 million to 2 billion kg per year. Even at a nominal disposal cost of \$1 per kg, the potential savings just in waste avoidance are significant faced to the pharmaceutical industry annual sales (almost \$500 billion in 2003): B. W. Cue, *Chem. Eng. News* **2005**, 83 (39), 46.
- [2] R. A. Sheldon, I. W. C. E. Arends, G. J. ten Brink, A. Dijkstra, *Acc. Chem. Res.* **2002**, 35, 774.
- [3] J. M. DeSimone, *Science* **2002**, 297, 799.
- [4] S. J. Broadwater, S. L. Roth, K. E. Price, M. Kobašlija, D. Tyler McQuade, *Org. Biomol. Chem.* **2005**, 3, 2899.
- [5] For carrying out reactions in aqueous suspension: S. Narayan, J. Muldoon, M. G. Finn, V. V. Fokin, H. C. Kolb, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2005**, 44, 3275.
- [6] For a recent review, see: S. Campestrini, R. Ciriminna, M. Pagliaro, *Chem. Soc. Rev.* **2005**, 347, 825.
- [7] G. J. ten Brink, I. W. C. E. Arends, R. A. Sheldon, *Science* **2000**, 287, 1636.
- [8] D. I. Enache, J. K. Edwards, P. Landon, B. Solsona-Espriu, A. F. Carley, A. A. Herzing, M. Watanabe, C. J. Kiely, D. W. Knight, G. J. Hutchings, *Science* **2006**, 311, 362.
- [9] B. M. Trost, *Angew. Chem. Int. Ed.* **1995**, 34, 259.
- [10] A. E. J. de Nooy, A. C. Besemer, H. van Bekkum, *Synthesis* **1996**, 1153. TEMPO-mediated industrial oxidations are for instance carried out by DSM using polyoxometalate/O₂ as primary oxidant: R. Ben-Daniel, P. Alsters, R. Neumann, *J. Org. Chem.* **2001**, 66, 8650.
- [11] D. Liaigre, T. Breton, E. M. Belgsir, *Electrochem. Commun.* **2005**, 7, 312.
- [12] a) Y. Kashiwagi, H. Ono, T. Osa, *Chem. Lett.* **1993**, 257; the method was recently extended to oxidative synthesis yields of enantiopure lactones from optically active diols by grafting of an optically active cyclic nitroxyl radical: b) Y. Kashiwagi, F. Kurashima, S. Chiba, J. Anzai, T. Osa, J. M. Bobbitt, *Chem. Commun.* **2003**, 114.
- [13] H. Tanaka, Y. Kawakami, K. Goto, M. Kuroboshi, *Tetrahedron Lett.* **2001**, 42, 445.
- [14] R. Shacham, D. Avnir, D. Mandler, *Adv. Mater.* **1999**, 11, 384.
- [15] a) R. V. Chaudhari, V. H. Rane, A. A. Deshmukh, S. S. Divekar, *US Patent Application* 20050215827, **2005**; b) F. Wang, J. Xu, X. Li, J. Gao, L. Zhou, R. Ohnishi, *Adv. Synth. Catal.* **2005**, 347, 1987.
- [16] Yet, as one referee rightly remarks, benzyl alcohol that is here proposed as the starting material for the production of benzaldehyde is still almost universally manufactured from toluene by chlorination/hydrolysis, with the usual environmental problems of traditional chemical processes that are being addressed by chemical research inspired by the "green chemistry" principles.
- [17] *Organic Electrochemistry*, Vol. 8 in the series: *Encyclopedia of Electrochemistry*, (Eds.: A. Bard, M. Stratmann), Wiley-VCH, Weinheim, **2004**.
- [18] H. Lund, *J. Electrochem. Soc.*, **2002**, 149, 21.
- [19] H. Pütter, in: *Organic Electrochemistry*, (Eds.: H. Lund, O. Hammerich), 4th edn., Marcel Dekker, New York, **2001**.
- [20] A. Walcarius, D. Mandler, J. A. Cox, M. Collinson, O. Lev, *J. Mater. Chem.* **2005**, 15, 3663.
- [21] A. Fidalgo, R. Ciriminna, L. M. Ilharco, M. Pagliaro, *Chem. Mater.* **2005**, 17, 6686.
- [22] T. Fey, H. Fischer, S. Bachmann, K. Albert, C. Bolm, *J. Org. Chem.* **2001**, 66, 8254.
- [23] Partly immobilized TEMPO in similar oxidations was described in: E. M. Belgsir, H. J. Schäfer, *Electrochem. Commun.* **2001**, 3, 32. In these oxidations, hydrogen carbonate buffer electrolyte can be completely removed by a cation-exchange resin membrane: M. Schämman, H. J. Schäfer, *Eur. J. Org. Chem.* **2003**, 351.
- [24] R. Ciriminna, J. Blum, D. Avnir, M. Pagliaro, *Chem. Commun.* **2000**, 1441.