glycomics. However, use of array technology to understand the intricate role of carbohydrates in cell-signaling will require the immobilization of longer, more complex oligosaccharides. The development of automated methods for the synthesis of oligosaccharides[33, 34] in combination with the development of microcontact printing for the deposition of ligands on the surface of a SAM[35, 36] will make possible the rapid generation of chips containing entire classes of carbohydrates. Interrogation of these surfaces by systematic exposure to fluorescently labeled proteins, including bacterial and viral toxins, will ultimately lead to a better understanding of the role of carbohydrates in numerous signaling processes.

[1] R. A. Dwek, *Chem. Rev.* **1996**, *96*, 683.
[2] K. A. Karlsson, *Curr. Opin. Struct. Biol.* **1995**, *5*, 622.
[3] S. Hakomori, Y. Zhang, *Chem. Biol.* **1997**, *4*, 97.
[4] S. P. Fodor, J. L. Read, M. C. Pirrung, L. Stryer, A. T. Lu, D. Solas, *Science* **1991**, *251*, 767.
[5] M. Schena, D. Shalon, R. W. Davis, P. O. Brown, *Science* **1995**, *270*, 467.
[6] A. Schulze, J. Downward, *Nat. Cell Biol.* **2001**, *3*, E190.
[7] H. Zhu, J. F. Klemic, S. Chang, P. Bertone, A. Casamayor, K. G. Klemic, D. Smith, M. Gerstein, M. A. Reed, M. Snyder, *Nat. Genet.* **2000**, *26*, 283.
[8] P. Arenkov, A. Kukhtin, A. Gemmell, S. Voloshchuk, V. Chupeeva, A. Mirzabekov, *Anal. Biochem.* **2000**, *278*, 123.
[9] H. Zhu, M. Snyder, *Curr. Opin. Chem. Biol.* **2001**, *5*, 40.
[10] M. Wilchek, E. A. Bayer, *Anal. Biochem.* **1988**, *171*, 1.
[11] A. Ulman, *Chem. Rev.* **1996**, *96*, 1533.
[12] M. C. Shao, *Anal. Biochem.* **1992**, *205*, 77.
[13] Y. Shinohara, H. Sota, M. Gotoh, M. Hasebe, M. Tosu, J. Nakao, Y. Hasegawa, M. Shiga, *Anal. Chem.* **1996**, *68*, 2573.
[14] R. J. Green, R. A. Frazier, K. M. Shakesheff, M. C. Davies, C. J. Roberts, S. J. B. Tendler, *Biomaterials* **2000**, *21*, 1823.
[15] C. Leteux, R. A. Childs, W. Chai, M. S. Stoll, H. Kogelberg, T. Feizi, *Glycobiology* **1998**, *8*, 227.
[16] C. Leteux, M. S. Stoll, R. A. Childs, W. Chai, M. Vorozhaikina, T. Feizi, *J. Immunol. Methods* **1999**, *227*, 109.
[17] K. D. McReynolds, M. J. Hadd, J. Gervay-Hague, *Bioconjugate Chem.* **1999**, *10*, 1021.
[18] M. Hernaiz, J. Liu, R. D. Rosenberg, R. J. Linhardt, *Biochem. Biophys. Res. Commun.* **2000**, *276*, 292.
[19] M. C. Fritz, G. Hahner, N. D. Spencer, *Langmuir* **1996**, *12*, 6074.
[20] D. J. Revell, J. R. Knight, D. J. Blyth, A. H. Haines, D. A. Russell, *Langmuir* **1998**, *14*, 4517.
[21] H. Hoffmann, U. Mayer, H. Brunner, A. Krischanitz, *Vib. Spectrosc.* **1995**, *8*, 151.
[22] B. T. Houseman, M. Mrksich, *Angew. Chem.* **1999**, *111*, 876; *Angew. Chem. Int. Ed.* **1999**, *38*, 782.
[23] N. Horan, L. Yan, H. Isobe, G. M. Whitesides, D. Kahne, *Proc. Natl. Acad. Sci. USA* **1999**, *96*, 11782.
[24] M. N. Yousaf, E. Chan, M. Mrksich, *Angew. Chem.* **2000**, *112*, 2019; *Angew. Chem. Int. Ed.* **2000**, *39*, 1943.
[25] E. Chan, M. N. Yousaf, M. Mrksich, *J. Phys. Chem. A* **2000**, *104*, 9315.
[26] M. N. Yousaf, M. Mrksich, *J. Am. Chem. Soc.* **1999**, *121*, 4286.
[27] B. T. Houseman, J. H. Huh, S. J. Kron, M. Mrksich, *Nat. Biotechnol.* **2002**, *20*, 270.
[28] B. T. Houseman, M. Mrksich, *Chem. Biol.* **2002**, *9*, 443.
[29] D. Wang, S. Liu, B. J. Trummer, C. Deng, A. Wang, *Nat. Biotechnol.* **2002**, *20*, 275.
[30] M. Mrksich, *Chem. Soc. Rev.* **2000**, *29*, 267.
[31] M. N. Yousaf, B. T. Houseman, M. Mrksich, *Angew. Chem.* **2001**, *113*, 1127; *Angew. Chem. Int. Ed.* **2001**, *40*, 1093.
[32] M. N. Yousaf, B. T. Houseman, M. Mrksich, *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 5992.
[33] O. J. Plante, E. R. Palmacci, P. H. Seeberger, *Science* **2001**, *291*, 1523.
[34] P. Sears, C. H. Wong, *Science* **2001**, *291*, 2344.
[35] M. Mrksich, G. M. Whitesides, *Annu. Rev. Biophys. Biomol. Struct.* **1996**, *25*, 55.
[36] J. Lahiri, E. Ostuni, G. M. Whitesides, *Langmuir* **1999**, *15*, 2055.

Direct Electrochemical Aziridination of Alkenes under Metal-Free Conditions

Gerhard Hilt*

The generally accepted advantage of electrochemical conversions is the mass-free electron transfer between the electrode and the substrate, thereby eliminating the need for the waste disposal of a used redox reagent.[1] Since many chemical redox reagents are produced by electrochemical pathways, it would be an advantage to use the electrochemical power directly for the conversion of the starting materials in redox reactions. From this viewpoint, and because of increasing environmental problems, electrochemical methods will become more and more attractive in the future. Many classes of substrates could be successfully converted directly at the electrode under electrochemical conditions and the intermediates generated by electron transfer could be employed in synthetically useful follow-up reactions. Among these electrochemical conversions, applications on an industrial scale[2] and for the production of fine chemicals and laboratory-scale chemicals exist.[3]

The synthetic value of small, strained, and therefore highly reactive, ring systems is well established, and among these epoxides and aziridines are of great interest.[4] Indeed, the asymmetric synthesis of epoxides from allylic alcohols[5] was honored by the award of the Nobel prize to Sharpless in 2001.[20] Hydroperoxides are used as oxidants as an easily handled source of oxygen, even on a large scale.[5, 6]

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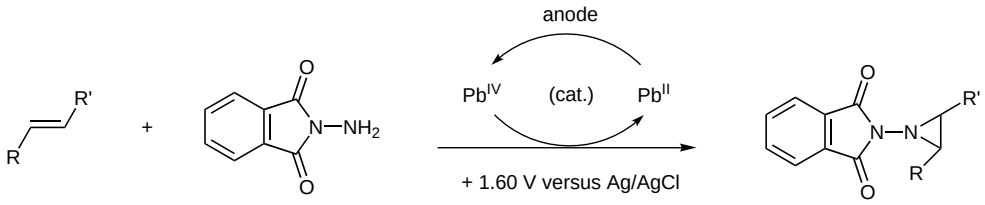
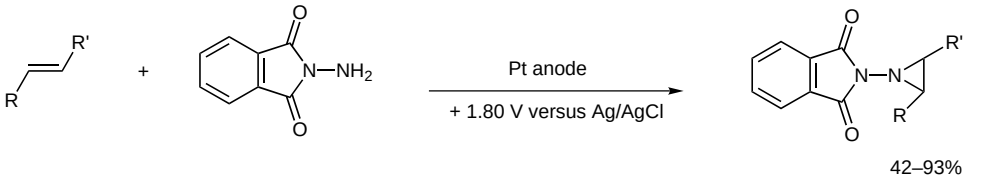
Similar amination reagents are not described for the analogous aziridination process, so that other methods for the activation of the nitrogen atom in aziridination reagents must be used.[7] Thus, chemical methods for the activation of nitrogen are applied, such as reactions with stabilized, oxidized nitrogen-containing compounds (for example, hypervalent compounds such as RI=NR′),[8] as well as photochemical-initiated metal-catalyzed aziridinations starting from azides.[8a] Furthermore, acceptor-stabilized hydrazine derivatives can be oxidized in situ by lead(IV) reagents,[9] as well as *N*-acetoxyhydrazine derivatives, which are preformed from the hydrazine derivative upon oxidation with lead(IV) reagents.[10] The disadvantage of these methods is the stoichiometric use and the accompanying problems of the disposal of the spent reagents.



Scheme 1. Indirect lead-mediated electrochemical azirdination of alkenes.



Scheme 2. Direct electrochemical aziridination of alkenes.

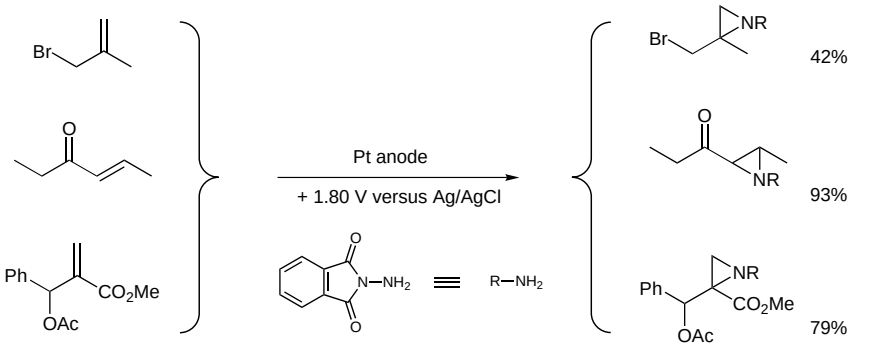
A sustainable electrochemical method for the aziridination of alkenes with catalytic amounts of lead compounds, and electrochemical regeneration of the spent Pb^{IV} species, would be a reasonable improvement, thus avoiding the stoichiometric use of toxic heavy metal oxidizing agents. Of even greater interest would be an aziridination method that would reduce the amount of toxic reagents to a minimum or avoid any of these reagents at all. Siu and Yudin recently published an electrochemical method for a lead-mediated indirect electrochemical oxidation as well as for a direct electrochemical heavy-metal-free aziridination of alkenes using *N*-aminophthalimide as a nitrogen source (see Scheme 1).[11] In the latter method the *N*-aminophthalimide is directly oxidized at the anode to generate a reactive species which reacts with a variety of alkenes to form the corresponding aziridines.

The restriction that even catalytic amounts of lead represent an ecological hazard could be overcome by using appropriate electrochemical conditions. Electroanalytical measurements revealed that the redox potentials for the Pb^{II}/Pb^{IV} couple ($E = +1.60$ V versus Ag/AgCl, platinum working electrode) were in the same region as the oxidation potential of the hydrazine derivative ($E =$ $+1.35$ V and $+1.68$ V versus Ag/AgCl; two irreversible one-electron oxidations). On the other hand, the oxidation of the mainly acceptor-substituted alkenes take place at higher potentials, so that the direct electrochemical oxidation of the hydrazine derivative under potentiostatic conditions was possible, which renders the use of lead as a redox-mediator obsolete (Scheme 2).

The electrochemical reactions were conducted under potential-controlled conditions in a divided electrochemical cell with a silver wire as a quasi-reference electrode,[12] which minimizes the disadvantages that sometimes accompany the use of a conventional reference electrode. Further operative simplifications, such as an undivided cell (conversions in a quasi-divided cell can be envisioned)[13] or electrolysis under galvanostatic conditions might be possible, so that researchers not equipped for specialist electrochemistry could use this simple and clean methodology for the synthesis of aziridines in the future. The synthetic utility of the reaction could be enhanced further if the cathodic deprotection (to generate the free aziridine) could also be realized under electrochemical conditions.[14]

However, the synthetic value of the electrochemical aziridination was demonstrated when unfunctionalized, acceptor-substituted and highly functionalized alkenes were aziridinated in good to excellent yields. Some selected examples of the direct electrochemical aziridination are shown in Scheme 3. The methodology described above for the functionalization of alkenes under electrochemical conditions represents an interesting reaction with potential for further developments.

An asymmetric version of the reaction cannot be realized by direct electrochemical reaction of the hydrazine derivative at the electrode. However, the use of chiral transition-metal catalysts (such as chiral titanium complexes) can be envisioned, so that an electrochemically initiated and transition-metal-catalyzed asymmetric variant could be realized. Further developments towards an electrochemical removal of the



Scheme 3. Preparative direct electrochemical aziridination of functionalized alkenes.

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phthalimide group as well as the use of primary amines as a nitrogen source would also be of great interest.

Among the most recent interesting developments, which include a) paired electrolysis on industrial scale,[15] b) electrochemical regeneration of azadicarboxylic esters,[16] c) electroenzymatic reaction in flow-through reactors,[17] d) electrocatalytic coupling reactions,[18] and e) selective electrochemical fluorinations,[19] the electrochemical aziridination can be seen as a further highlight in electroorganic synthesis.

[1] E. Steckhan, T. Arns, W. R. Heineman, G. Hilt, D. Hoormann, J. Jörissen, L. Kröner, B. Lewall, H. Pütter, *Chemosphere* **2001**, *43*, 63 – 73; P. M. Bersier, L. Carlsson, J. Bersier, *Top. Curr. Chem.* **1994**, *170*, 113 – 229.

[2] H. Pütter in *Organic Electrochemistry*, 4th ed. (Eds.: H. Lund, O. Hammerich), Marcel Dekker, New York, **2001**, pp. 1259 – 1307. For example, substituted benzaldehydes are anodically generated from substituted toluene derivatives (BASF; >1000 t/a), functionalized (per)fluorinated compounds are synthesized from the corresponding functionalized hydrocarbons (several companies) and nitro compounds are cathodically reduced to amino or azoxy compounds.

[3] *Organic Electrochemistry*, 4th ed. (Eds.: H. Lund, O. Hammerich), Marcel Dekker, New York, **2001**; J. Grimshaw *Electrochemical Reactions and Mechanisms in Organic Chemistry*, Elsevier, Amsterdam, **2000**.

[4] S. S. Murphree, A. Padwa, *Prog. Heterocycl. Chem.* **2001**, *13*, 52 – 70; B. Zwanenburg, P. ten Holte, *Top. Curr. Chem.* **2001**, *216*, 93 – 124; W. McCoull, F. A. Davis, *Synthesis* **2000**, 1347 – 1365; F. Brown, *Vaccine* **2001**, *20*, 322 – 327.

[5] a) T. Katsuki, K. B. Sharpless, *J. Am. Chem. Soc.* **1980**, *102*, 5974 – 5976; b) T. Katsuki, V. S. Martin, *Org. React.* **1996**, *48*, 1 – 299.

[6] For industrial-scale Katsuki – Sharpless epoxidations, see W. P. Shum, M. J. Cannarsa in *Chirality in Industry II* (Eds.: A. N. Collins, G. N. Sheldrake, J. Crosby), Wiley, New York, **1997**, pp. 363 – 380.

[7] a) R. S. Atkinson, *Tetrahedron* **1999**, *55*, 1519 – 1559; b) E. N. Jacobsen in *Comprehensive Asymmetric Catalysis* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, chap. 17, pp. 607 – 618.

[8] For selected examples, see a) Z. Li, R. W. Quan, E. N. Jacobsen, *J. Am. Chem. Soc.* **1995**, *117*, 5889 – 5890; b) D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson, D. M. Barnes, *J. Am. Chem. Soc.* **1993**, *115*, 5328 – 5329; c) Z. Li, K. R. Conser, E. N. Jacobsen, *J. Am. Chem. Soc.* **1993**, *115*, 5326 – 5327; d) D. A. Evans, M. M. Faul, M. T. Bilodeau, *J. Org. Chem.* **1991**, *56*, 6744 – 6746; e) H.-J. Jeon, S. T. Nguyen, *Chem. Commun.* **2001**, 235 – 236.

[9] For selected examples, see K.-S. Yang, K. Chen, *J. Org. Chem.* **2001**, *66*, 1676 – 1679; T. K. Chakraborty, A. Ghosh, *Indian J. Chem. Sect. B* **2001**, *40*, 895 – 897; J. T. Kapron, B. D. Santasiero, J. C. Vederas, *Chem. Commun.* **1993**, 1074 – 1076, and references therein.

[10] For selected examples, see R. S. Atkinson, C. K. Meades, *Tetrahedron Lett.* **2000**, *41*, 7769 – 7772; R. S. Atkinson, S. Ulukanli, P. J. Williams, *J. Chem. Soc. Perkin Trans. 1* **1999**, 2121 – 2128; R. S. Atkinson, T. A. Claxton, I. S. T. Lochrie, S. Ulukanli, *Tetrahedron Lett.* **1998**, *39*, 5113 – 5116; R. S. Atkinson, A. P. Ayscough, W. T. Gattrell, T. M. Raynham, *J. Chem. Soc. Perkin Trans. 1* **1998**, 2783 – 2793; R. S. Atkinson, E. Barker, S. Ulukanli, *J. Chem. Soc. Perkin Trans. 1* **1998**, 583 – 589; R. S. Atkinson, P. M. Coogan, C. L. Clive, *Chem. Commun.* **1993**, 1215 – 1216.

[11] T. Siu, A. K. Yudin, *J. Am. Chem. Soc.* **2002**, *124*, 530 – 531.

[12] For quasi-reference electrodes, see D. T. Sawyer, A. Subkowiak, J. L. Roberts, *Electrochemistry for Chemists*, 2nd ed., Wiley, New York, **1995**, p. 197.

[13] For quasi-divided cells (working electrode area $\gg$ counter electrode area), see K. Danielmeier, K. Schierle, E. Steckhan, *Tetrahedron* **1996**, *52*, 9743 – 9754.

[14] For cathodic hydrazine cleavage, see L. Horner, M. Jordan, *Liebigs Ann. Chem.* **1978**, 1505 – 1517.

[15] For paired electrosynthesis on an industrial scale, see ref. [1]; H. Pütter, H. Hannebaum (BASF AG), Ger. Offen. DE 19618854, **1997** [*Chem. Abstr.* **1997**, *127*, P338559y].

[16] C. Merk, M. Brudermüller, H. Pütter (BASF AG), Ger. Offen. DE 10063195 **2002**.

[17] E. Steckhan, S Lütz, C. Wandrey, A. Liese (Forschungszentrum Jülich), PCT Int. Appl., WO 0236794, **2002** [*Chem. Abstr.* **2002**, *136*, 354244].

[18] For a leading reference, see S. Condon, D. Dupre, G. Falgayrac, J.-Y. Nedelec, *Eur. J. Org. Chem.* **2002**, 105 – 111; M. Durandetti, J.-Y. Nedelec, J. Perichon, *Org. Lett.* **2001**, *3*, 2073 – 2076.

[19] For a leading reference, see M. Hasegawa, H. Ishii, T. Fuchigami, *Tetrahedron Lett.* **2002**, *43*, 1503 – 1505; M. R. Shaaban, T. Fuchigami, *Tetrahedron Lett.* **2002**, *43*, 273 – 276.

[20] Nobel Lecture: K. B. Sharpless, *Angew. Chem.* **2002**, *114*, 2126 – 2135; *Angew. Chem. Int. Ed.* **2002**, *41*, 2024 – 2032.

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