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Synthesis of Chromans by Photosensitized Electrochemical Oxidation of Sulfides Mediated by Methylene Blue

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Abstract: *o*-Quinone methides were generated by a photosensitized cleavage of sulfides under neutral conditions using visible light provided by a 100 Watt spot light and methylene blue as a sensitizer. The key step in the oxidative cleavage is the transfer of one electron form the sulfide to the electronically excited visible dye. The resulting phenylthio radical cation undergoes frangmentation, and the correspondign *o*-quinone methides are generated and trapped by varied alkenes to yield chromans.

Keywords: Electrochemical reactions, Chromans, Sulfides, Photochemistry

The electrochemical oxidation of sulfides provides sufficient oxidative cleavage of C-S bonds to generate varied carbocation intermediates which form new C-C or C-hetero atom bonds by the attack of nucleophiles.[1-2] In this direct oxidation system, the selective electron transfer from substrates and the regulation of the chemical reactions of the electrogenerated intermediates are essential. It is particularly difficult to oxidize sulfur compounds without affecting nucleophiles because oxidation potentials of the nucleophiles are often lower than those of sulfur compounds, and the oxidation potentials of the products are also comparable to those of the starting materials. Selective electrooxidation in moderate conditions, *e.g.* at lower potential conditions, could therefore provide a wide variety of applications in which most of the overoxidation of the products and/or the co-existing materials are avoided. Recent research on a photochemically induced electron transfer reaction of the dithio group[3-5] led us to expect that photochemical oxidation by electronically excited photosensitizers followed by their electrochemical regeneration in an inert atmosphere was a promising method for the selective oxidation of sulfur compounds at lower oxidation potentials. The results of our previous research indicated that quinone methides were generated by direct electrooxidation of corresponding sulfides in a solution of lithium perchlorate in nitromethane and that cycloadducts with alkenes were obatained.[6] Our most recent findings now show that a photosensitized electrooxidation of 2-(1-phenylthioalkyl)phenols realizes the oxidative generation of unstable quinone methides at lower electrolytic potentials to complete their cycloaddition with easily oxidizable alkenes in lithium perchlorate / nitromethane.

In a solution of 1.0 M lithium perchlorate in dry nitromethane, a sulfide **1** showed

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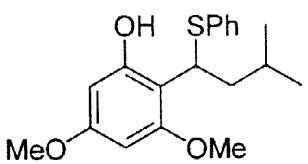
oxidation potential at 1.25 V *vs.* SCE. In the presence of α-phellandrene **8**, the direct oxidation of sulfide **1** on the glassy carbon electrode gave the cycloadduct **12** in 60 % yield with decomposed products of **8**. In the presence of 1/20 mol equiv. of methylene blue (MB) under the irradiation of visible light ($\lambda > 360$ nm) under oxygen atmosphere, messy products and a small amount of the corresponding sulfoxide were obtained. Under Ar atmosphere, MB was soon reduced to decolorize and the reaction did not proceed, but MB was regenerated by anodic oxidation at 0.85 V *vs.* SCE. It was confirmed that diphenyl disulfide and thiophenol generated in the electrolytic reaction mixture and that the thiophenol directly reduced MB to the colorless MB^-. Anodic oxidation was therefore carried out using a PTFE [poly-(tetrafluoro-

Table 1

sulfide	alkene	products	yield(%)
1	**4**	**10**	74
1	**6**	**11**	80
1	**7**	**14**	87
1	**8**	**12**	96
1	**9**	**13**[a)]	80
2	**9**	**15**[b)]	91
2	**5**	**16**	76
3	**4**	**17**	60
3	**6**	**18**	57

a) Four diastereomers were separated (4:4:1:1)
b) Four diastereomers were separated (4:4:1:1)



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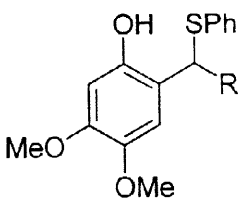
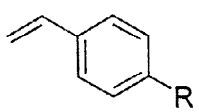
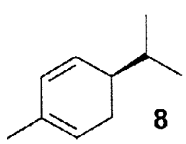


2 R=$CH_2CH(CH_3)_2$
3 R=H



4 R=H
5 R=OMe
6 R=Me



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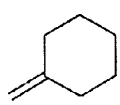

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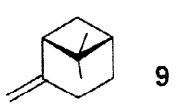

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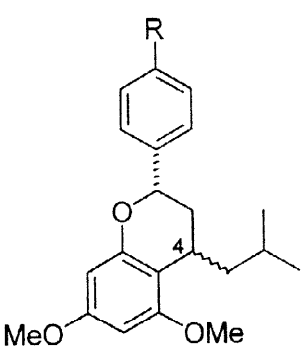
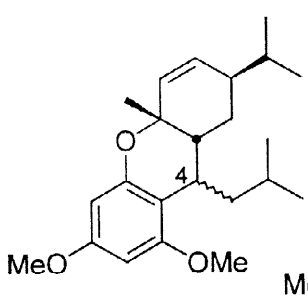
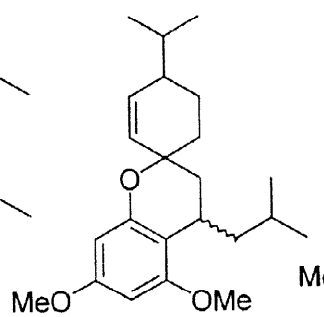


10 R=H 4α-H:4β-H (2:5)
11 R=Me 4α-H:4β-H (4:5)



12 4α-H:4β-H(1:1)



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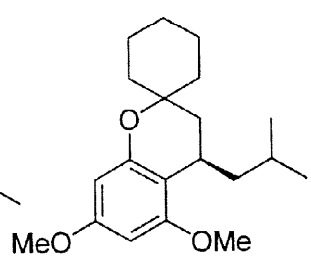

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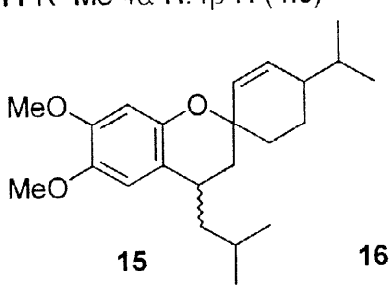

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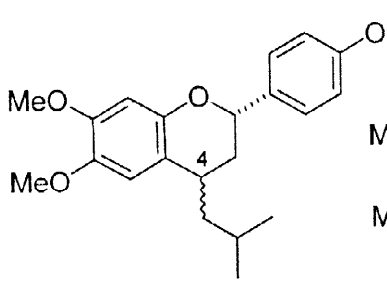
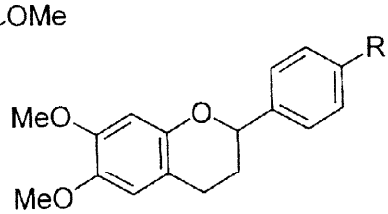


16 4α-H:4β-H (1:2)



17 R=H
18 R=Me

ethylene)]-fiber-coated glassy carbon anode[7] and a Pt cathode under Ar atmosphere, and the reaction mixture containing 1/20 mol equiv. of MB was simultaneously irradiated by the visible light (Fig.1). After the reaction completed (*ca.* 1.2 F), products were separated by silica-gel column chromatograpy.**

Table 1 shows the result of chroman synthesis by photosensitized electrooxidation. Although the oxidation potentials of the sulfides were 1.2 to 1.4 V *vs.* SCE, they could be

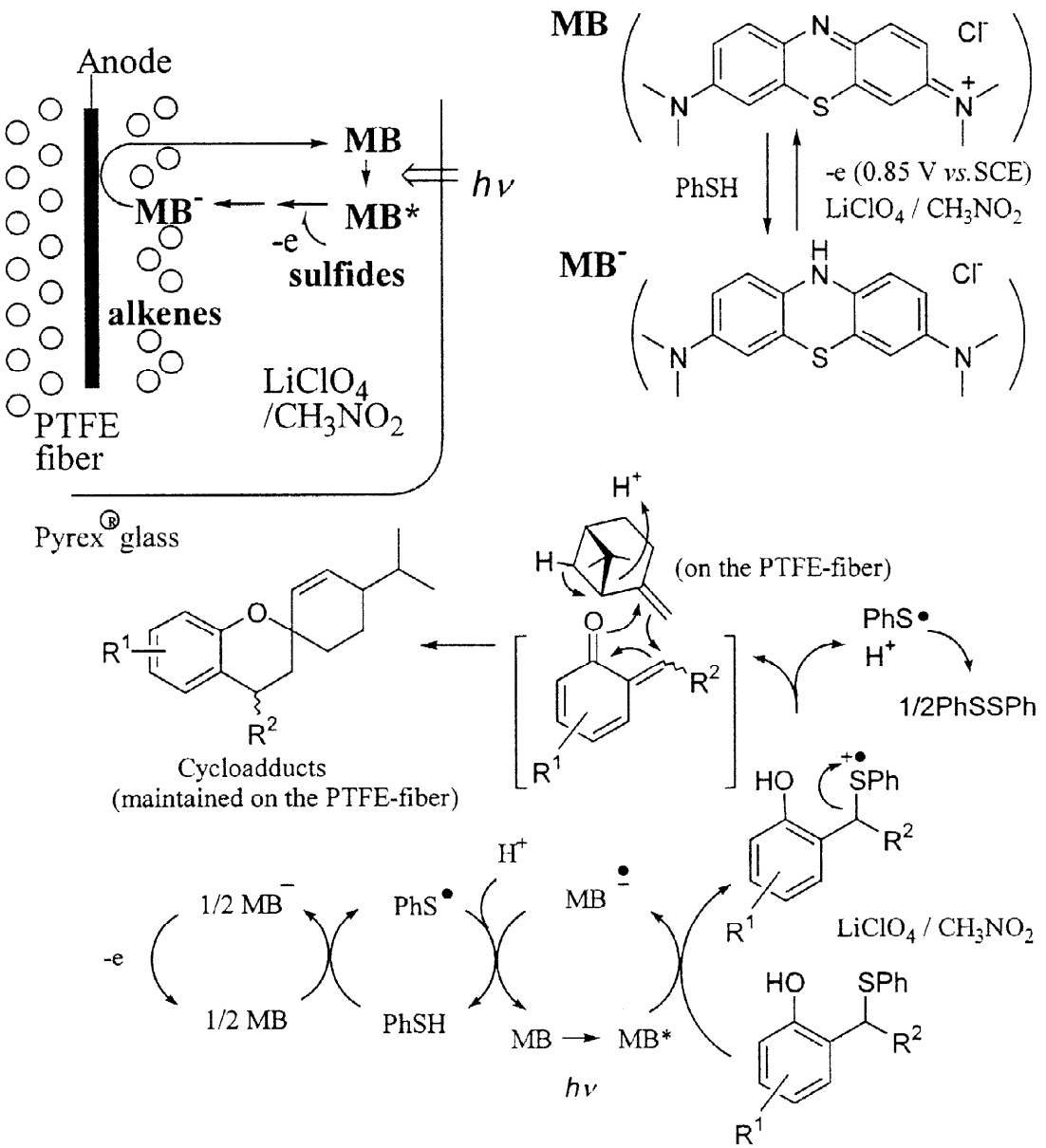


Fig. 1 Photoelectrochemical reaction system of sulfides using PTFE-fiber coated anode in lithium perchlorate / nitromethane and proposed reaction mechanism of cyclo-addition between alkenes and photoelectrochemically generated quinone methides

oxidized at lower potentials by using excited MB as a redox mediator. Although the direct anodic oxidation of **1** by the PTFE-fiber-coated electrode in the presence of **4** or **8** gave cycloadduct **10** or **12** in only 10 % or 71% yield, respectively, the photoelectrochemical system gave varied cycloadducts in higher yields even in the presence of easily oxidizable alkenes which possessed diene or styrene moiety. The cycloaddition reaction with β-pinene gave rearranged spirochromans **13** and **15** which have euglobal IIb skeleton isolated from *Eucalyptus globulus* (Fig. 1).[8]

The reaction scarcely proceeded in the dark, so it should be completed by the one electron transfer from sulfides to the photochemically excited methylene blue (MB^*) followed by the generation of the radical anion ($MB^{\cdot}$). The fragmented phenylthio radical is proposed to be reduced to corresponding anion by accepting one electron from the $MB^{\cdot}$.[5] In this reaction system, the photochemically generated thiols convert the MB to the reduced form(MB^-), which could be electrochemically oxidized to regenerate the MB. In this reaction system requires that MB be irradiated just on the inside surface of Pyrex glassware to be excited and oxidize the dissolved sulfides. Most of the hydrophobic alkenes absorbed on the PTFE-fiber were avoided to be oxidized by the MB*. Furthermore, the electrolytic current was not quenched, which often occurs by the oxidative decomposition of alkenes on the electrodes.

Oxidation and subsequent cycloaddition were successfully completed at the lower oxidation potential, which should provide selective oxidation and efficient electron transfer on the electrode. We believe that the reaction system could be applied for various kinds of electrooxidation of sulfides.

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References

[1] Yoshiyama T, Fuchigami T, *Chem. Lett.*, **1992**,1995-8
[2] Fuchigami T, Fujita T, *J. Org. Chem.*, **1994**, *59*, 7190-2
[3] Kamata M, Kato Y, Hasagawa E, *Tetrahedron Lett.*, **1991**, *32*, 4349-52
[4] Garcia H, Iborra S, Miranda MA, Primo,J. *New J. Chem.*, **1989**, *13*, 805-6
[5] Epling GA, Wang Q, *Tetrahedron Lett.*, **1992**, 33, 5905-12
[6] Chiba K, Sonoyama J, Tada M, *J.Chem.Soc.,Chem.Commun.*, **1995**, 1381-2
[7] Chiba K. Jinno M, Kuramoto R, Tada M, *Tetrahedron Lett.*,**1998**, 5527-30
[8] Kozuka M, Sawada T, Kasahara F, Mizuta E, Amano T, Komiya T, Goto M, *Chem. Pharm. Bull.*, **1982**, *30*, 1952-63

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** **General procedure** Compound **1** (166 mg, 0.5 mmol) was dissolved in 10 ml of $MeNO_2$ containing dry $LiClO_4$ (1.06 g) as supporting electrolyte, methylene blue (0.025 mmol) as photosensitizer, and **8** (136 mg, 1.0 mmol). Anode for the macro electrolysis was prepared by binding up a glassy carbon plate (60 mm x 20 mm) with PTFE strings (composed of the PTFE-fibers 20 μm x 1 m, 2.0 g , Flon Industry) to completely cover the surface of the anode. Electrooxidation was carried out at a constant potential (0.85 *vs.* SCE), using the PTFE-coated anode and a platinum plate (10 mm x 10 mm) as a cathode, respectively, without separating the two electrodes under Ar. The reaction mixture was simultaneously irradiated by the halogen lamp (100 Watt, distant 15 cm from the reaction flask) at ambient temperature. After the reaction completed (ca. 1.2 F), compound **12** was isolated (96%).