Pergamon

Tetrahedron Letters 43 (2002) 3301–3304

TETRAHEDRON
LETTERS

Anodic oxidation of 4-methoxy-1-naphthol

Hesham R. El-Seedi, Shosuke Yamamura and Shigeru Nishiyama*

Department of Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi 3-14-1, Kohoku-ku, Yokohama 223-8522, Japan

Received 28 January 2002; accepted 15 March 2002

Abstract—Anodic oxidation of 4-methoxy-1-naphthol **1** in the presence of nucleophiles provided the corresponding products **8**–**12** and the dimers **13** and **17** were also produced. The reaction mechanism of the oxidation reaction including the [3+2] cycloaddition was investigated. © 2002 Elsevier Science Ltd. All rights reserved.

Anodic oxidation of phenol derivatives is well known to provide a variety of products possessing an aromatic and/or non-aromatic structure.[1] In particular, the latter conversion into cyclohexane derivatives might be comparable to those of the Birch reduction. While a number of investigations have indicated a versatile availability of the phenolic oxidation, only a few have been reported in relation to naphthol derivatives. In particular, reaction of the electrolytically generated active species, which are stabilized with the attached phenyl residue, with olefinic nucleophiles would provide an access to multi-cyclic substances.[2] As part of our extensive electrochemical investigation, study of 4-methoxy-1-naphthol **1** would be included to understand their scope and limitation as substrates in phenolic oxidations.[3]

General procedure for anodic oxidation. Compound **1** (0.33 mmol) was electrolyzed with appropriate alkenic nucleophiles such as isosafrole **2**, 1-methoxy-4-propenylbenzene **3**, dihydrofuran **4** and dihydropyran **5** (5–15 equiv. mol to **1**) [anode: a glassy carbon beaker, cathode: a platinum wire, a divided cell through glass-filters, $n\mathrm{Bu_4NBF_4}$ as supporting salts (240 mg), solvent (25–35 ml)]. The results are summarized in Table 1 and Fig. 1.

Among solvents assessed for the electrolysis employing **2** and **3** as nucleophiles, CH_3CN effected the expected couplings leading to **8**[4] and **9**[2a] (entries 1 and 4), whereas Ac_2O or CH_3CN–Ac_2O provided considerable amounts of undesired quinone **6** or acetate **7**. Accordingly, the following entries employed CH_3CN as a solvent, while such acidic solvents as CH_3CN–AcOH,[2a] Ac_2O,[2b] or CH_3NO_2–AcOH[2c] were used in the case of phenol derivatives. The anodic oxidation commenced with the one-electron oxidation of **1** to give the radical **A**, followed by the second abstraction of an electron to the cation **B** (Scheme 1). Upon capture of the nucleophiles presented, the cation **B** produced such [3+2] cycloaddition products as **8**, **9**, **10**[4] and **11**.[4] This reaction feature was comparable to that of phenol derivatives.[2] Compounds **10** and **11** were obtained in better yields than those derived from 4-methoxyphenol,[2b] owing to the stabilizing effect of the attached phenyl residue of the naphthol molecule. Without such interaction of the nucleophiles, **B** was transformed into the corresponding naphthoquinone **6**.

In entries 7 and 8 using **4** as nucleophile, the *C*-glycosyl product **12**[4] was preferentially produced rather than benzofuran **10**, whereas **10** was obtained in moderate yield under the current-increased CPE conditions (entry 9). The assembly of **12** should adopt an entirely different reaction pathway from that described in Scheme 1, as the sp^2 carbons adjacent to the ring oxygen in dihydrofuran or pyran generally behave as electrophiles, which could not react at the C-2 position. A plausible mechanism is that acidic properties under the reaction conditions produced *O*-glycoside **14**, followed by the O→C glycosyl migration, leading to **15**, which on two-electron oxidation gave **12** (Scheme 2). To ascertain this possibility, **1** was reacted with **4** in the presence of a catalytic amount of TsOH. The reaction required 14 h to give a mixture of **14** (70%) and **15** (30%), while **14** was quantitatively obtained after 1 h, which was a similar reaction time to the anodic oxida-

---

Keywords: anodic oxidation; 4-methoxy-1-naphthol; electroorganic chemistry; cycloaddition.

* Corresponding author. Tel./fax: +81-45-566-1717; e-mail: nisiyama@chem.keio.ac.jp

PII: S0040-4039(02)00544-0

Table 1. The anodic oxidation of **1** with or without nucleophiles and the corresponding products

Entry	Additives	mA/mV	Solvents	Products (%)										
				6	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**16**	**17**
1	**2**	10 250–550	CH_3CN			95								
2		10 350–750	Ac_2O		50	48								
3		10 340–780	CH_3CN-Ac_2O (1/1)	55		36								
4	**3**	10 300–610	CH_3CN				96							
5		10 320–690	Ac_2O		50		44							
6		10 380–720	CH_3CN-Ac_2O (1/1)	68			28							
7	**4**	5 300–570	CH_3CN							79				
8		15 180–650	CH_3CN							70	17			
9		80–3[a] 1500	CH_3CN[b]	17				39			11	25		
10	**5**	15 150–650	CH_3CN						45[c]				32	
11	–	13 220–600	CH_3CN	52							45			
12		50–3[a] 1500	CH_3CN[b]	11							22			58

[a] Electrolysis was performed under the CPE (constant potential electrolysis) conditions, whereas CCE (constant current electrolysis) conditions were employed for others.

[b] A 15 ml amount of solvent was used, whereas 25–35 ml amounts were for others.

[c] Compound **1** was recovered in 20% yield.

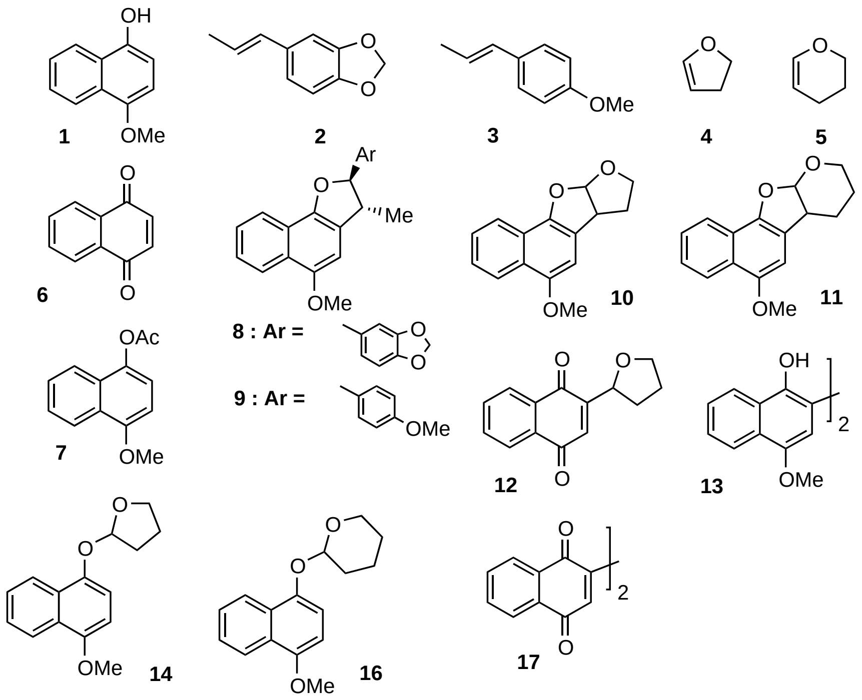
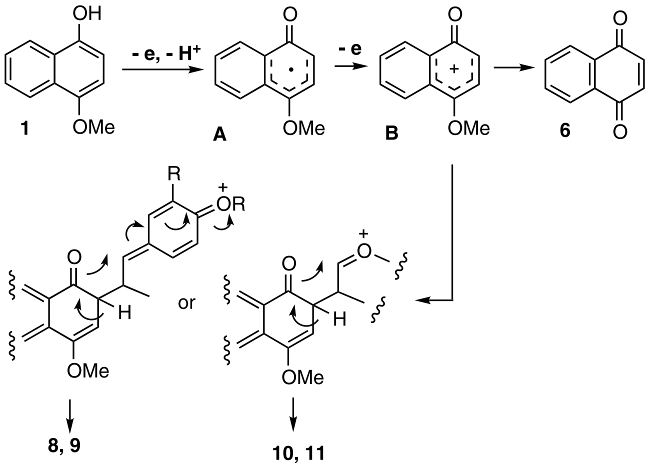
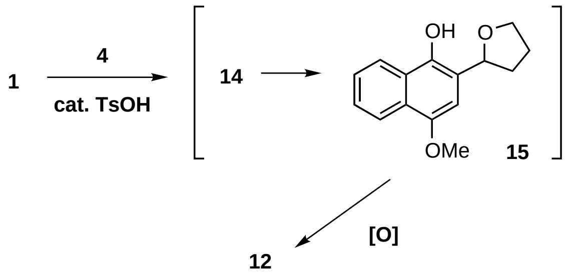


Figure 1.



Scheme 1.



Scheme 2.

tions (all of the entries in Table 1 were completed within ca. 2 h). The acquisition of **12** in high yields (entries 7 and 8) indicated that the electrolytic conditions had a comparable acidity to those of Lewis acids,[5] which effected efficient migration under mild conditions (ex.[5b] 0°C to room temp., 1–4 h).[6] It is still unclear at this stage why only **4** afforded such migration, which was not observed in the case of **5**.

In addition, the dimeric derivatives **13** and **17**[7] were obtained (entries 8, 9, 11 and 12): the radical dimerization of **A** produced **13**, which experienced further oxidation, leading to **17**. The dimers were effectively produced, when the reaction without nucleophiles was undertaken in high concentrations (entry 12). Relatively mild anodic oxidation condition and the stabilizing factor of the phenyl residue enabled the isolation of **13**,[7] which was not obtained by the usual chemical oxidations.[8]

In conclusion, anodic oxidation of 4-methoxy-1-naphthol was undertaken. The cation **B**, electrolytically generated, reacted with nucleophiles to give the corresponding benzofuran derivatives, **8**–**11**. Upon using **4**, the *C*-glycoside **12** was characteristically obtained. The appropriate control of the oxidation conditions effectively produced the dimers **13** and **17** possessing different oxidation stages.

Further investigation of naphthols possessing additional substituents, which open up a possibility to construct synthetic intermediates of naturally occurring complicated molecules, is under way.

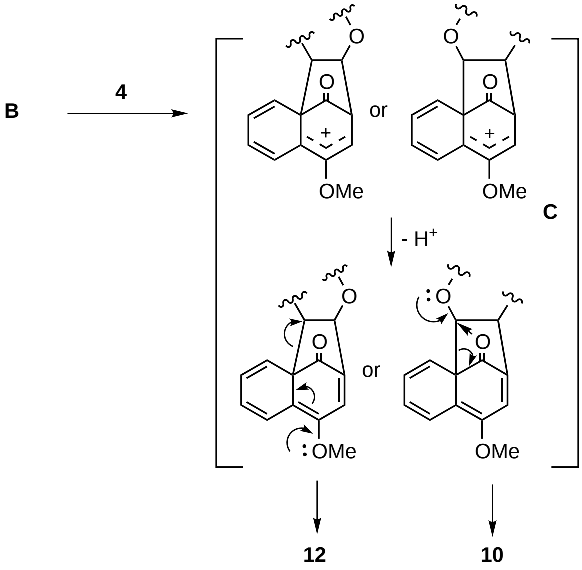
Acknowledgements

The authors are very grateful to the Japan Society for the Promotion of Science for a fellowship to H.R.E. and generous financial support from Tokubetsu Kenkyuin Shorei-hi (Grant in Aid for Scientific Research P 00168).

References

1. (a) Shizuri, Y; Shigemori, H.; Suyama, K.; Nakamura, K.; Okuno, Y.; Ohkubo, M.; Yamamura, S. In *Studies in Natural Products Chemistry*; Att-ur-Rahman, Ed.; Elsevier Science, 1991; pp. 159–173; (b) Yamamura, S; Nishiyama, S. *Synlett* **2002**, 533–543.
2. Related investigations employing phenol derivatives: (a) Gates, B. D.; Dalidowicz, P.; Tebben, A.; Wang, S.; Swenton, J. S. *J. Org. Chem.* **1992**, *57*, 2135–2143; (b) Shizuri, Y.; Nakamura, K.; Yamamura, S. *J. Chem. Soc., Chem. Commun.* **1985**, 530–531; (c) Chiba, K.; Fukuda, M.; Kim, S.; Kitano, Y.; Tada, M. *J. Org. Chem.* **1999**, *64*, 7654–7656.
3. Anodic oxidation of other naphthols, has been unsuccessful until now, owing to high oxidation potentials and/or production of complicated mixtures.
4. Compound **8**: IR (film) 3068, 1596 cm^{-1}; δ_H ($CDCl_3$) 1.47 (3H, d, $J=6.8$ Hz), 3.54 (1H, dq, $J=8$, 6.8 Hz), 3.95 (3H, s), 5.19 (1H, d, $J=8$ Hz), 5.94 (2H, s), 6.60 (1H, s), 6.77 (1H, d, $J=8$ Hz), 6.90 (1H, dd, $J=2$, 8 Hz), 6.94 (1H, d, $J=2$ Hz), 7.43 (2H, complex), 7.91 (1H, dd, $J=1.5$, 7.2 Hz) and 8.17 (1H, dd, $J=1.5$, 7.2 Hz). δ_C ($CDCl_3$) 18.8, 47.1, 55.6, 92.2, 99.7, 100.7, 106.3, 107.8, 119.3, 120.7, 121.1, 122.3, 122.7, 124.7, 125.3, 125.7, 135.1, 147.2, 147.5, 147.7 and 150.1. Compound **10**: δ_H ($CDCl_3$) 1.56 (1H, m), 1.65 (1H, m), 1.91 (1H, m), 2.12 (1H, m), 3.49 (1H, dt, $J=1.5$, 6.4 Hz), 3.78 (2H, complex), 3.89 (3H, s), 6.11 (1H, d, $J=6.8$ Hz), 6.68 (1H, s), 7.47 (2H, ddd, $J=1.5$, 4.8, 6.8 Hz), 7.96 (1H, d, $J=8.0$ Hz) and 8.20 (1H, d, $J=8.0$ Hz). Compound **11**: δ_H ($CDCl_3$) 1.56 (1H, m), 1.65 (1H, m), 1.91 (1H, m), 2.12 (1H, m), 3.49 (1H, dt, $J=1.5$, 6.4 Hz), 3.78 (2H, complex), 3.98 (3H, s), 6.11 (1H, d, $J=6.8$ Hz), 6.68 (1H, s), 7.47 (2H, dq, $J=1.5$, 6.8 Hz), 7.96 (1H, d, $J=7.8$ Hz) and 8.20 (1H, d, $J=8.8$ Hz). Compound **12**: IR (film) 1663 and 1593 cm^{-1}; δ_H ($CDCl_3$) 1.70 (1H, m), 1.98 (2H, complex), 2.52 (1H, m), 3.92 (1H, dq, $J=6.8$, 7.3 Hz), 4.04 (1H, dq, $J=5.9$, 7.3 Hz), 4.98 (1H, t, $J=8.3$ Hz), 7.01 (1H, s), 7.72 (2H, ddd, $J=2.0$, 4.9, 7.3 Hz) and 8.06 (2H, ddd, $J=2.0$, 2.4, 4.9 Hz). Compound **13**: δ_H ($CDCl_3$) 3.98 (6H, s), 6.71 (2H, s), 7.57 (4H, m), 8.18 (2H, dd, $J=2.4$, 7.3 Hz) and 8.28 (2H, dd, $J=2.4$, 7.3).
5. (a) Suzuki, K.; Matsumoto, T.; Hosoya, T. *J. Synth. Org. Chem. Jpn.* **1995**, *53*, 1045–1054; (b) Kometani, T.; Kondo, H.; Fujimori, Y. *Synthesis* **1988**, 1005–1007.

6. Compound **14** was not observed by monitoring the reaction (entry 7) every 10 min. Probably, the migration and the following oxidation might be so fast as to catch neither **14** nor **15**. In addition, upon the same anodic oxidation (reaction time = 1 h) of **14** in the presence of **4**, a trace amount of **12** was obtained along with **6** (58%), **13** (31%) and **17** (4%). Although the O→C migration might be reasonable, an alternative mechanism involving cationic [5+2] cycloaddition could not be excluded to explain the high-yield formation of **12**: the intermediate by the cationic [5+2] cycloaddition of **4** might be the bicyclo[3.2.1]-type derivative **C**, which was observed in the case of phenol derivatives.[1,2a] The following rearrangement afforded the glycosyl product **12** with abstraction of the methoxy group, as well as **10** (Scheme 3).



Scheme 3.

7. Such a dimer was not electrochemically produced from 4-methoxyphenol. The Lewis acid-promoted synthesis see, (a) Sartori, G.; Maggi, R.; Bigi, F.; Arienti, A.; Casnati, G.; Bocelli, G.; Mori, G. *Tetrahedron* **1992**, *48*, 9483–9494; (b) Sartori, G.; Maggi, R.; Bigi, F.; Arienti, A.; Casnati, G. *Tetrahedron Lett.* **1992**, *33*, 2207–2210.
8. During preparation of the manuscript, the oxidation of **1** under rather strong AgO–40% HNO_3 conditions was published to provide naphthoquinone **6** and/or dimer **17**: Tanoue, Y.; Sakata, K.; Hashimoto, M.; Morishita, S.; Hamada, M.; Kai, N.; Nagai, T. *Tetrahedron* **2002**, *58*, 99–104 and references cited therein.