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Facile Synthesis of Tricyclo[5.4.0.0^{1,5}]undec-9-ene-8,11-diones from Phenols with an Olefin Bearing an Electron-attracting Group at the Side Chain

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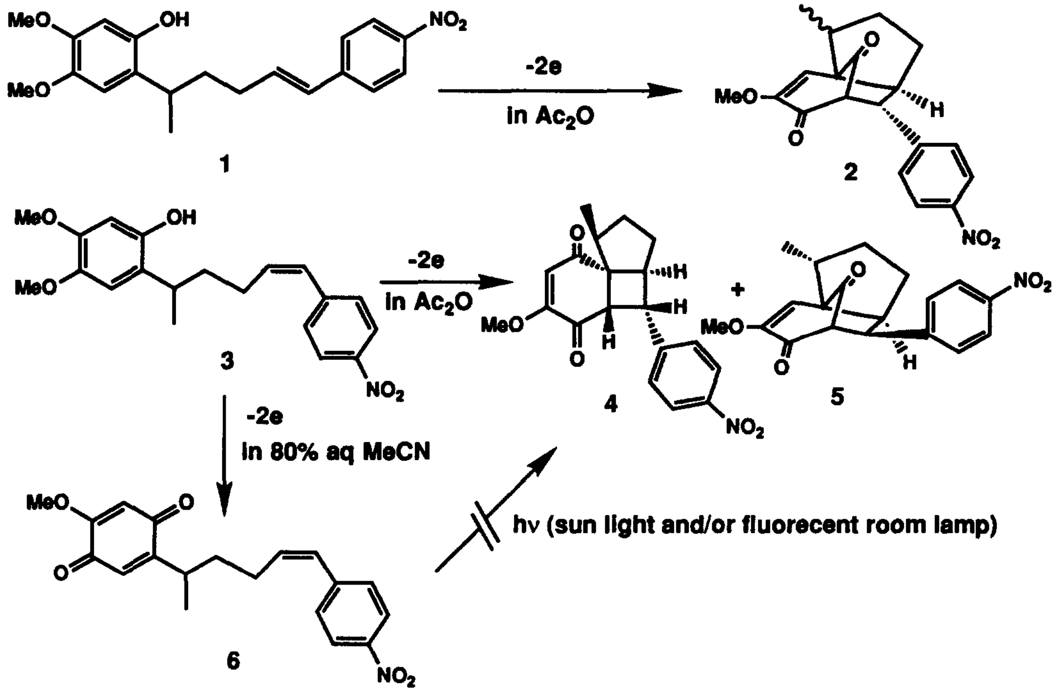
Abstract: 3,4-Dimethoxyphenol with a *trans* *p*-nitrostyryl group at the side chain was electrolyzed in acetic anhydride containing $^{n}Bu_4NBF_4$ to afford a tricyclo[5.3.1.0^{1,5}]undec-9-ene-8,11-dione, while the *cis* isomer was converted into a tricyclo[5.4.0.0^{1,5}]undec-9-ene-8,11-dione as a major product. In the case of several phenols with an α,β-unsaturated ketone or ester grouping, the corresponding tricyclo[5.4.0.0^{1,5}]undec-9-ene-8,11-diones were also obtained in good yields.

From a view point of natural products synthesis, we have demonstrated that electrochemical methodology is quite useful.$^{1)}$ We further carried out anodic oxidation of several phenols bearing a *cis* *p*-nitrostyryl group or an α,β-unsaturated CO group at the side chain affording the corresponding tricyclo[5.4.0.0^{1,5}]undec-9-ene-8,11-diones, as follows.

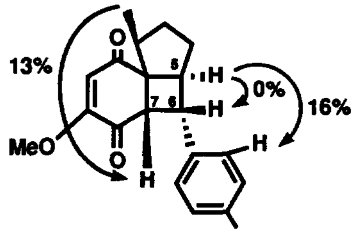
As described in the previous paper,$^{2)}$ several phenols with a *para*-halo (F, Cl, Br) substituted styryl group were electrolyzed to afford the corresponding tricyclo[5.3.1.0^{1,5}]undec-9-ene-8,11-diones in a stereospecific manner. When subjected to anodic oxidation in acetic anhydride containing $^{n}Bu_4NBF_4$ under argon atmosphere, the phenol (**1**)$^{4)}$ with a *trans* *p*-nitrostyryl group at the side chain was converted into the corresponding tricyclic compound (**2**)$^{5)}$ in good yield. In the case of the *cis* isomer (**3**)$^{4)}$, however, an unexpected tricyclo[5.4.0.0^{1,5}]undec-9-ene-8,11-dione (**4**)$^{6)}$ was obtained as a main product (50% yield), wherein the [5+2]cycloaddition product (**5**)$^{6)}$ was formed only in 13% yield. On electrolysis of **3** in 80% aq. MeCN,$^{7)}$ furthermore, the corresponding quinone (**6**)$^{6)}$ was produced in almost quantitative yield, which was stable on exposure to light [sun light and/or fluorescent room lamp (Toshiba Co. Ltd., 40W)], as shown in Scheme 1. This observation is compatible with the following result: when protected from light, anodic oxidation of **3** also afforded both **4** and **5** in almost the same ratio as described above.

The stereostructure of **4** was unambiguously determined by its spectral data, particularly NOE experiments as seen in [A], wherein the *p*-nitrophenyl group at C_6-position must be in an α-configuration indicating that the four-membered ring may be formed in a stepwise manner, although the formation process has not always been clarified.

Furthermore, anodic oxidation of several phenols (**7-14**)$^{4)}$ with an α,β-unsaturated ketone or ester grouping at the side chain was carried out under essentially the same condition as described in both **1** and **3** to afford the corresponding tricyclo[5.4.0.0^{1,5}]undec-9-ene-8,11-diones (**12-16**)$^{6)}$ in good yields, as seen in Scheme 2. The stereostructure of **12** was unambiguously determined by an X-ray crystallographic analysis,$^{8)}$ as shown in Figure 1. The stereostructures of the other compounds (**13-16**) were also elucidated by the spectral data, particularly ^{1}H and ^{13}C NMR spectra with the aid of NOE experiments. In the case of both **10** and **11**, it is noted that the Me group at C_2-position is in a β-configuration as seen in [**B**] and [C], respectively. And the corresponding α-isomer has not been detected.



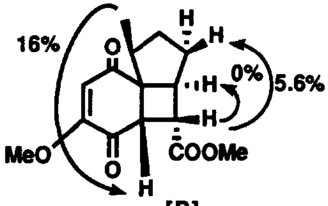
Scheme 1.



[A]

$J_{C5\text{-}H,\ C6\text{-}H} = 4.9Hz$

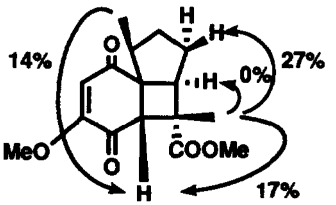
$J_{C6\text{-}H,\ C7\text{-}H} = 11.7Hz$



[B]

$J_{C5\text{-}H,\ C6\text{-}H} = 4.3Hz$

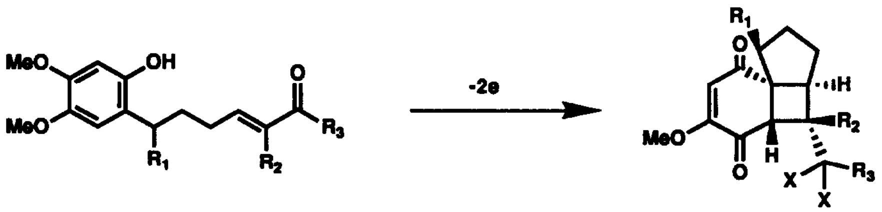
$J_{C6\text{-}H,\ C7\text{-}H} = 10.9Hz$



[C]

In order to clarify the formation process of these tricyclic compounds (**12-16**), anodic oxidation of **10** was carried out again under essentially the same condition as described above except for protecting from light (sun light and fluorescent room lamp) to give only the corresponding quinone (**17**).[6] On exposure to light (fluorescent room lamp) **17** was converted into **15** in quantitative yield, as seen in Scheme 3.

On electrolysis of **10**, as shown in Scheme 3, the resulting phenoxy cation was converted into the quinone (**17**) instead of a [5+2]cycloaddition product, because of an electron-deficient double bond. **17** was then subjected to intramolecular [2+2]cycloaddition to give the tricyclic compound (**15**). Synthetic study on bioactive sesqui- and diterpenes is in progress using these tricyclo[5.4.0.0^{1,5}]undec-9-ene-8,11-diones.



7 (R_1=H, R_2=Me, R_3=Me)	12 (X,X=O 61%)
8 (R_1=H, R_2=H, R_3=H)	13 (X=OAc 30%)
9 (R_1=H, R_2=H, R_3=OMe)	14 (X,X=O 80%)
10 (R_1=Me, R_2=H, R_3=OMe)	15 (X,X=O 79%)
11 (R_1=Me, R_2=Me, R_3=OMe)	16 (X,X=O 77%)

Scheme 2.

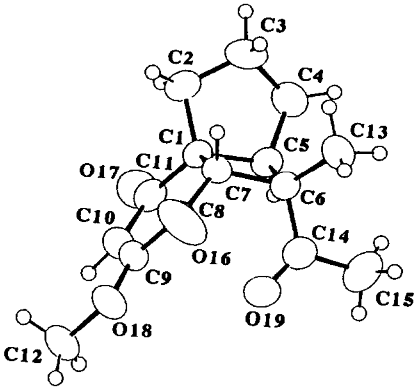
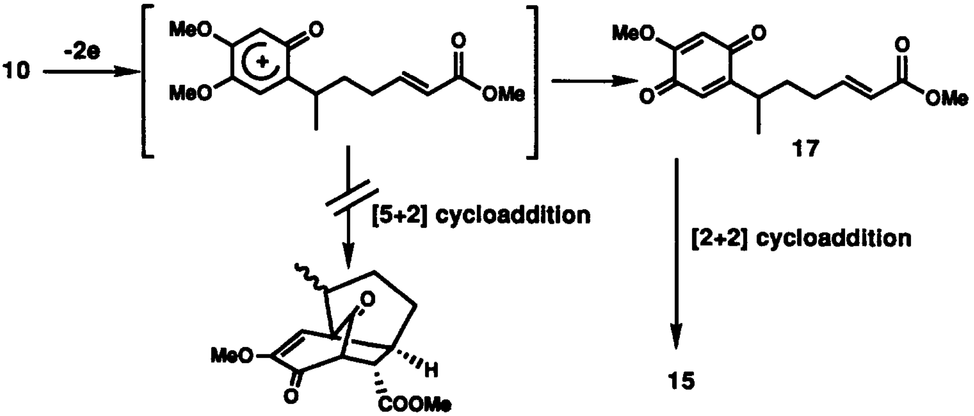


Fig.1. An *ORTEP* drawing of the molecule (12).



Scheme 3.

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1. S. Yamamura, Y. Shizuri, H. Shigemori, M. Okuno, and M. Ohkubo, *Tetrahedron*, **1991**, *47*, 635.

2. S. Maki, K. Toyoda, S. Kosemura, and S. Yamamura, *Chem. Lett.*, **1993**, *in press*

3. In all cases, anodic oxidation was carried out at a constant current [C.C.E. at 0.12~0.15 mA/cm^2 (+750~1300 mV *vs*. SCE); 2 F/mol] using a glassy carbon beaker and a platinum wire tip as an anode and a cathode, respectively.

4. The synthetic phenols gave satisfactory spectral data consistent with the assigned structures.

5. S. Maki, N. Asaba, S. Kosemura, and S. Yamamura, *Tetrahedron Lett.*, **1992**, *33*, 4169.

6. The spectral data for the new compounds are in accord with the structures assigned, and only selected data are cited: **4**: $C_{19}H_{19}O_5N$ [m/z 341.1223 (M^+)]; IR (film) 1690, 1645, 1595, and 1520 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 0.94 (3H, d, J= 6.8 Hz), 3.24 (1H, dd, J= 4.9, 7.3 Hz), 3.58 (1H, dd, J= 4.9, 11.7 Hz), 3,68 (1H, d, J= 11.7 Hz), 3.69 (3H, s), 6.20 (1H, s), 7.27 (2H, d, J= 8.8 Hz), 8.11 (2H, d, J= 8.8 Hz); ^{13}C-NMR δ ($CDCl_3$) 115.43 (d), 123.73 (d), 123.73 (d), 128.77 (d), 128.77 (d), 146.37 (s), 146.97 (s), 163.49 (s), 191.69 (s), 200.55 (s). **5**: $C_{19}H_{19}O_5N$ [m/z 341.1309 (M^+)]; IR (film) 1760, 1690, 1600, and 1520 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 1.18 (3H, d, J= 7.3 Hz), 3.48 (1H, d, J= 10.3 Hz), 3.76 (3H, s), 3.92 (1H, s), 6.39 (1H, s), 7.23 (2H, d, J= 8.8 Hz), 8.17 (2H, d, J= 8.8 Hz); ^{13}C-NMR δ ($CDCl_3$) 118.96 (d), 123.87 (d), 123.87 (d), 128.54 (d), 128.54 (d), 147.01 (s), 147.55 (s), 152.63 (s), 190.89 (s), 202.52 (s). **6**: $C_{19}H_{19}O_5N$ [m/z 341.1230 (M^+)]; IR (film) 1670, 1640, and 1600 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 1.10 (3H, d, J= 7.0 Hz), 3.81 (3H, s), 5.83 (1H, dt, J= 10.5, 7.3 Hz), 5.89 (1H, s), 6.42 (1H, s), 6.43 (1H, d, J= 10.5 Hz), 7.35 (2H, d, J= 8.9 Hz), 8.17 (2H, J= 8.9 Hz); ^{13}C-NMR δ ($CDCl_3$) 107.87 (d), 123.49 (d), 123.49 (d), 126.38 (d), 127.86 (d), 129.31 (d), 129.31 (d), 135.47 (d), 144.04 (s), 146.27 (s), 154.27 (s), 158.27 (s), 182.31 (s), 186 89 (s). **12**: $C_{15}H_{18}O_4$ [m/z 262.1221 (M^+)]; IR (film) 1690, 1640, and 1600 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 2.72 (1H, s), 2.82 (1H, d, J= 7.2 Hz), 3.84 (3H, s), 6.00 (1H, s); ^{13}C-NMR δ ($CDCl_3$) 112.23 (d), 164.64 (s), 192 48 (s), 200.84 (s), 208.64 (s); m.p. 162-163°C. **13**: $C_{17}H_{20}O_7$ [m/z 336.1236 (M^+)]; IR (film) 1765, 1695, 1650, and 1600 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 1.96 (3H, s), 2.00 (3H, s), 2.72 (1H, ddd, J= 3.8, 5.7, 10.2 Hz), 2.93 (1H, t, J= 5.7 Hz), 3.19 (1H, d, J= 10.2 Hz), 3.82 (3H, s), 6.16 (1H, s), 6.78 (1H, d, J= 3.8 Hz); ^{13}C-NMR δ ($CDCl_3$) 88.79 (d), 113.87 (d), 163.13 (s), 168.11 (S), 168.23 (s), 191.51 (s), 200.07 (s). **14**: $C_{14}H_{16}O_5$ [m/z 264.1030 (M^+)]; IR (film) 1730, 1695, 1645, and 1600 cm^{-1}; ^{1}H-NMR δ (C_6D_6) 2.68 (1H, d, J= 11.2 Hz), 2.77 (1H, dd, J= 5.0, 11.2 Hz), 2.89 (3H, s), 2.99 (1H, dd, J= 6.4, 5.0 Hz), 3.23 (3H, s), 5.84 (1H, s); ^{13}C-NMR δ ($CDCl_3$) 113.97 (d), 163.52 (s), 172.92 (s), 192.45 (s), 199.51 (s). **15**: $C_{15}H_{18}O_5$ [m/z 278.1167 (M^+)]; IR (film) 1730, 1695, 1645, and 1595 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 0.89 (3H, d, J= 6.6 Hz), 2.99 (1H, dd, J= 4.3, 5.9 Hz), 3.10 (1H, dd, J= 4.3, 10.9 Hz), 3.34 (1H, d, J= 10.9 Hz), 3.62 (3H, s) 3.84 (3H, s), 6.18 (s); ^{13}C-NMR δ ($CDCl_3$) 114.61 (d), 163.32 (s), 172.97 (s), 192.63 (s), 199.93 (s). **16**: $C_{16}H_{20}O_5$ [m/z 292.1284 (M^+)]; IR (film) 1725, 1690, 1640, and 1600 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 0.85 (3H, d, J= 6.3 Hz), 1.39 (3H, s), 2.90 (1H, s), 3.02 (1H, d, J= 7.8 Hz), 3.58 (3H, s), 3.82 (3H, s), 6.12 (1H, s); ^{13}C-NMR δ ($CDCl_3$) 114.18 (d), 160.38 (s), 175.48 (s), 192.44 (s), 201.10 (s). **17**: $C_{15}H_{18}O_5$ [m/z 278.1153 (M^+)]; IR (film) 1720, 1675, 1645, and 1600 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 1.15 (3H, d, J= 6.9 Hz), 3.71 (3H, s), 3.83 (3H, s), 5.81 (1H, d, J= 15.5 Hz), 5.94 (1H, s), 6.47 (1H, s), 6.91 (1H, dt, J= 15.5, 6.9 Hz); ^{13}C-NMR δ ($CDCl_3$) 107.85 (d), 121.37 (d), 129.30 (d), 148.16 (d), 154.25 (s), 158.25 (s), 166.78 (s), 182.30 (s), 186.82 (s). The stereochemistry of each product was elucidated by NOE experiments.

7. Anodic oxidation was carried out at a constant current [C.C.E. at 0.12~0.15 mA/cm^2 (+400~1300 mV *vs*. SCE); 2 F/mol] in 80% aqueous MeCN including $LiClO_4$ using a glassy carbon beaker and a platinum wire tip as an anode and a cathode, respectively.

8. CRYSTALLOGRAPHIC DATA; $C_{15}H_{18}O_4$, MW 262.3, monoclinic, $P2_1/a$, a = 23.253(4), b = 6.664(1), c = 8.807(2)Å, β = 100.27(1)°, V = 1342.9(4) Å^3, Z = 4, Dx = 1.30 g cm^{-3}, μ(Mo Kα) = 0.087 mm^{-1}. The X-ray intensities up to 2θ = 45° were measured on a Rigaku AFC-5 four-circle diffractometer with graphite-monochromatized Mo Kα radiation. Non-hydrogen atoms were refined with anisotropic thermal parameters. Final R is 0.043 for 1048 reflections. Tables of atomic parameters, bond lengths and bond angles have been deposited with the Cambridge Crystallographic Data Center.

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