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Electrochemical Oxidation of α,β-Unsaturated Ketones

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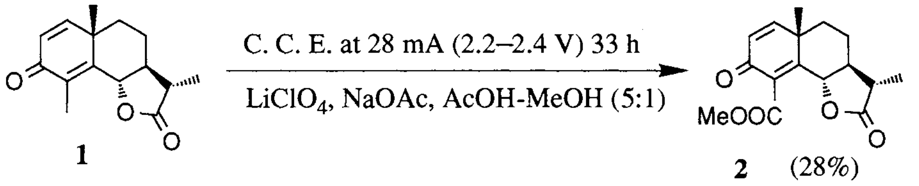
α,β-Unsaturated ketones were successfully oxidized by using electrochemical method. In this oxidation reaction, allylic methyl or methylene groups were converted into acetoxylmethyl group or methoxy carbonyl group. In contrast, these unsaturated ketones were stable to Sharpless's method (a combination of selenium dioxide and ^{t}butyl hydroperoxide).

Selective oxidation of allylic methyl or methylene groups utilizing no metal oxides would be of great importance. Among the oxidation reactions of allylic positions, Sharpless's method 1) has been extensively used by many chemists during their synthetic works. But, the allylic positions of α,β-unsaturated ketones were quite stable to Sharpless's reagent. We report herein the useful oxidation of allylic positions of α,β-unsaturated ketones by using electrochemical method.

On anodic oxidation of santonin (**1**) in AcOH-MeOH, we have obtained quite unusual oxidation product (**2**) 2) in 28% yield. Though the yield of the reaction was rather low, this result was fascinating, since there are very few methods known to oxidize allylic methyl group attached to α,β-unsaturated ketones.

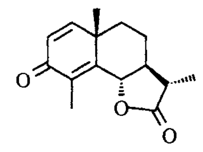
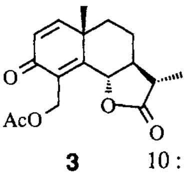
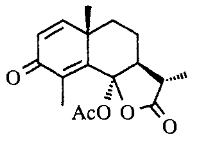
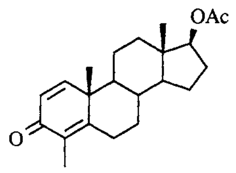
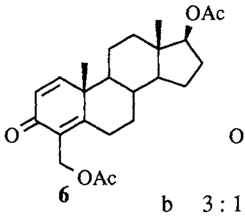
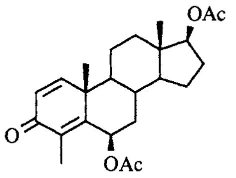
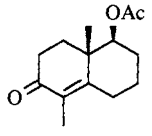
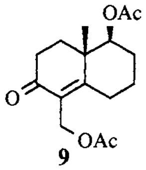
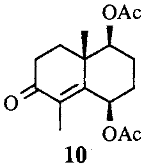
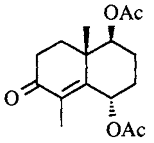
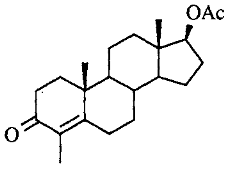
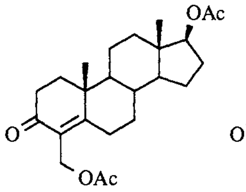
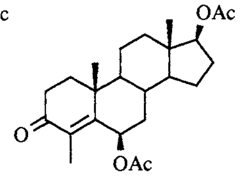


1 **2** (28%)

Thus, reaction conditions were examined to obtain better yield, resulting in the development of new oxidation method. When these reactions were applied to dienones and enones with methyl group α to the carbonyl group, and carried out in acetic acid, allylic methyl groups were mainly oxidized to give acetoxymethyls. Thus, acetoxylated derivatives (**3**, 3) **6**, 4) **9**, 5) and **13** 6)) were obtained in moderate yields by this method. Byproducts (**4**, 7) **7**, 8) **10**, 9) **11**, 10) and **14** 11)) were formed by the oxidations at methine or methylenes at C-6 positions. The results are shown in Table 1. Dienones showed much better regioselectivity than enones. Although the selectivity in the oxidation of **8** was the worst, and oxidation of methylene took place predominantly, desired product **9** was obtained as a major product by changing the solvent system from AcOH to ^{t}BuOH-AcOH (4 : 1). The same tendency was observed in entries 2 and 4. Interestingly, esters and lactones were unreacted in all cases.

Although the other pathway could be considered, reaction mechanism of this oxidation would be

Table 1. Oxidation of dienones and enones with methyl groups α to the carbonyl groups

Entry	Starting material	Conditions, Yields/%[a)]	Products (ratio)
1	 **1**	b 54 (62)	  **3** 10 : 1 **4**
2	 **5**	b 42 (52) c 23 (44)	  **6** b 3 : 1 **7** c 25 : 1
3	 **8**	b 75 (78) c 80	   **9** **10** **11** b 12 : 20 : 7 c 8 : 5 : 2
4	 **12**	b 58 (76) c 34 (46)	  **13** b 1.6 : 1 **14** c 2 : 1

a) Yields in parenthesis are based on reacted starting materials
b) Constant current electrolysis at 15-60 mA using an undevided cell, Supporting electrolyte; $LiClO_4$-NaOAc, Solvent; AcOH, Molecular Sieves 4Å
c) Constant current electrolysis at 29.5 mA using an undevided cell, Supporting electrolyte; $LiClO_4$-NaOAc, Solvent; ^{t}BuOH-AcOH (4 : 1), Molecular Sieves 4Å

classified to two independent processes. The first one (path A) involves hydrogen abstraction from methyl group by the radical cation formed from ketone group. As to the second one, dienol radical [B] would be an important intermediate (see Fig. 1). From this mechanistic point of view, enones or dienones with no methyl group α to the carbonyl groups should be oxidized only at the allylic methylene groups (path B). Thus, these electrochemical oxidation reactions were further applied to simple enones, and acetoxylated products (**16** [12)] and **19** [12)]) were obtained as expected. Stereoselectivity of the newly formed asymmetric carbon were high in entry 2, and β isomer was the major one. Unfortunately, yields were low because of the formation of epoxides (**17** [12)] and **20** [12)]) as primary products. Although, the reaction mechanism of epoxide formation was unknown, it is noteworthy that yields of the epoxides were lowered to 4% on bubbling

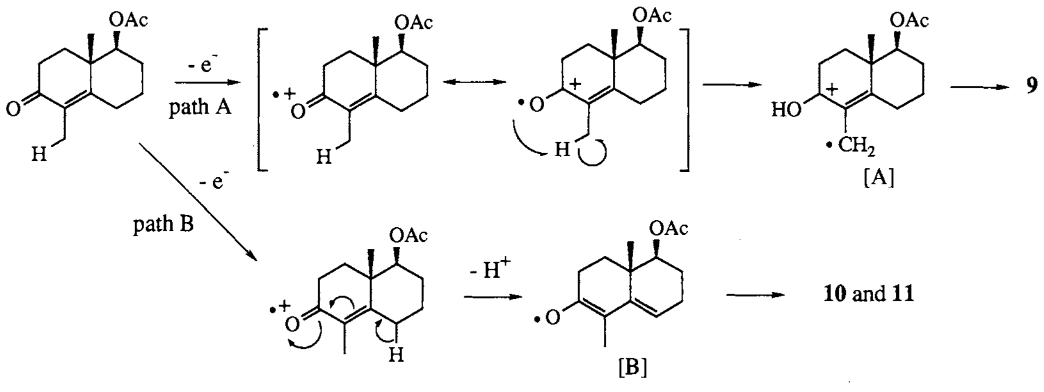
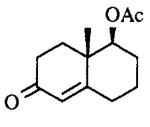
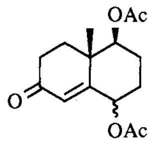
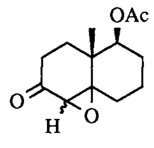
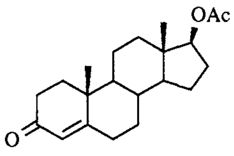
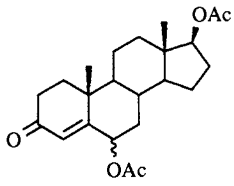
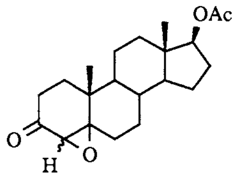
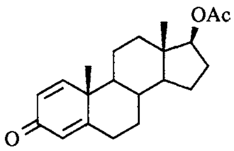


Fig. 1. Possible reaction mechanism.

Table 2. Oxidation of enones and dienone without methyl group α to carbonyl groups

Entry	Starting material	Yield/%[a]	Products
1	 **15**	66 (72) **16** : **17** = 2:3	 **16** α:β = 2:3  **17** α:β = 4:1
2	 **18**	52 (72) **19** : **20** = 1:2	 **19** α:β = 1:10  **20** α:β = 3:1
3	 **21**		No reaction under the same conditions

a) Yields in parenthesis are based on reacted starting materials.

b) Reaction conditions: Constant current electrolysis at 20-60 mA using an undevided cell, Supporting electrolyte; $LiClO_4$ -NaOAc, Solvent; AcOH, Molecular Sieves 4Å.

molecular oxygen to the reaction solutions. Interestingly, no oxidation product was obtained in the case of simple dienone (**21**) (see Table 2).

Finally, attempts to oxidize enones (**8** and **15**) with SeO_2 - ^{t}BuOOH in CH_2Cl_2 (the most commonly used reaction conditions reported by Sharpless)$^{1)}$ turn out to be complete recovery of starting enones, even after 3 days. Thus, our new electrochemical reactions seemed to be useful tool for oxidation of allylic positions of α,β-unsaturated ketones.

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References

1) M. A. Umbreit and K. B. Sharpless, *J. Am. Chem. Soc.*, **99**, 5526 (1977).

2) **2**: HRMS, Found: 290.1154. Calcd for $C_{16}H_{18}O_5$: 290.1154; ^{1}H NMR ($CDCl_3$, δ): 1.24 (3H, d, J=8 Hz), 1.42 (3H, s), 3.88 (3H, s), 4.70 (1H, d, J=11 Hz), 6.19 (1H, d, J=10 Hz), 6.78 (1H, d, J=10 Hz); ^{13}C NMR ($CDCl_3$, δ): 12.4 (q), 22.4 (t), 24.5 (q), 38.3 (t), 40.1 (s), 41.2 (d), 52.5 (q), 53.8 (d), 78.6 (d), 126.2 (d), 127.2 (s), 154.6 (s), 155.1 (d), 166.2 (s), 176.1 (s), 181.9 (s); IR(film): 1660, 1740 cm^{-1} .

3) **3**: HRMS, Found: 304.1309. Calcd for $C_{17}H_{20}O_5$: 304.1311; ^{1}H NMR ($CDCl_3$, δ): 1.29 (3H, d, J=7 Hz), 1.40 (3H, s), 1.97 (3H, s), 4.84 (1H, d, J=10 Hz), 5.01 (1H, d, J=10 Hz), 5.08 (1H, d, J=10 Hz), 6.28 (1H, d, J=9 Hz), 6.73 (1H, d, J=9 Hz);^{13}C NMR ($CDCl_3$, δ): 12.6 (q), 20.8 (q), 23.0 (t), 25.2 (q), 38.2 (t), 40.7 (d), 41.8 (s), 53.7 (d), 56.5 (t), 80.7 (d), 126.0 (d), 126.8 (s), 154.8 (d), 157.9 (s), 170.4 (s), 176.8 (s), 184.1 (s); IR(film): 1670, 1740, 1790 cm^{-1}.

4) **6**: HRMS, Found: 400.2250. Calcd for $C_{24}H_{32}O_5$: 400.2250; ^{1}H NMR ($CDCl_3$, δ): 0.87 (3H, s), 1.28 (3H, s), 2.05 (6H, s), 4.58 (1H, t, J=8 Hz), 4.95 (1H, d, J=12 Hz), 5.03 (1H, d, J=12 Hz), 6.29 (1H, d, J=10 Hz), 7.05 (1H, d, J=10 Hz); ^{13}C NMR ($CDCl_3$, δ): 12.1 (q), 19.2 (q), 21.0 (q), 21.1 (q), 22.5 (t), 23.6 (s), 27.4 (t), 27.8 (t), 29.7 (t), 33.0 (t), 35.2 (d), 36.5 (t), 42.8 (s), 43.8 (s), 49.8 (d), 53.0 (d), 56.7 (t), 82.3 (d), 127.0 (d), 127.7 (s), 155.2 (d), 171.0 (s), 171.1 (s), 184.0 (s); IR(film): 1630, 1660, 1740 cm^{-1} .

5) **9**: HRMS, Found: 294.1464. Calcd for $C_{16}H_{22}O_5$: 294.1467; ^{1}H NMR ($CDCl_3$, δ): 1.23 (3H, s), 1.97 (3H, s), 2.02 (3H, s), 4.63 (1H, dd, J=5, 7 Hz), 4.74 (2H, s); IR(film): 1670, 1730 cm^{-1} .

6) **13**: HRMS, Found: 402.2386. Calcd for $C_{24}H_{34}O_5$: 402.2406; ^{1}H NMR ($CDCl_3$, δ): 0.85 (3H, s), 1.24 (3H, s), 2.03 (3H, s), 2.07 (3H, s), 4.61(1H, t, J=8 Hz), 4.82 (1H, d, J=10 Hz), 4 .89 (1H, d, J=10 Hz); IR(film): 1690, 1760 cm^{-1}.

7) **4**: HRMS, Found: 304.1313. Calcd for $C_{17}H_{18}O_5$: 304.1311; ^{1}H NMR ($CDCl_3$, δ):1.28 (3H, d, J=8 Hz), 1.42 (3H, s), 2.09 (3H, s), 2.15 (3H, s), 6.26 (1H, d, J=10 Hz), 6.68 (1H, d, J=10 Hz); IR(film): 1660, 1780 cm^{-1}.

8) **7**: HRMS, Found: 400.2260. Calcd for $C_{24}H_{32}O_5$: 400.2250; ^{1}H NMR ($CDCl_3$, δ): 0.91 (3H, s), 1.33 (3H, s), 2.04 (3H, s), 2.07 (3H, s), 4.61 (1H, t, J=8 Hz), 6.09 (1H, t, J=3 Hz), 6.24 (1H, d, J=9 Hz), 7.00 (1H, d, J=9 Hz); IR(film): 1630, 1660, 1750 cm^{-1}.

9) **10**: HRMS, Found: 294.1466. Calcd for $C_{16}H_{22}O_5$: 294.1467; ^{1}H NMR ($CDCl_3$, δ): 1.38 (3H, s), 1.89 (3H, s), 2.08 (3H, s), 2.10 (3H, s), 4.66 (1H, dd, J=5, 10 Hz), 5.99 (1H, t, J=3 Hz); ^{13}C NMR ($CDCl_3$, δ): 11.4 (q), 17.8 (q), 21.1 (q), 21.2 (q), 21.6 (t), 28.6 (t),33.3 (t), 34.7 (t), 40.0 (s), 68.2 (d), 79.1 (d), 135.2 (s), 152.1 (s), 169.5 (s), 170.4 (s), 198.9 (s); IR(film): 1720, 1750 cm^{-1}.

10) **11**: HRMS, Found: 294.1458. Calcd for $C_{16}H_{22}O_5$: 294.1467; ^{1}H NMR ($CDCl_3$, δ): 1.31 (3H, s), 1.80 (3H, s), 2.10 (3H, s), 2.11 (3H, s), 4.96 (1H, dd, J=7, 10 Hz), 5.78 (1H, d, J=6 Hz); IR(film):1740, 1680 cm^{-1}.

11) **14**: HRMS, Found: 402.2409. Calcd for $C_{24}H_{34}O_5$: 402.2406; ^{1}H NMR ($CDCl_3$, δ): 0.87 (3H, s), 1.28 (3H, s), 1.87 (3H, s), 2.05 (6H, s), 4.62 (1H, t, J=8 Hz), 6.04 (1H, t, J=3 Hz); IR(film):1680, 1740 cm^{-1}.

12) Fully characterized by ^{1}H NMR and ^{13}C NMR spectroscopy and accurate mass measurement.

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