

Oxidation of 9-Xanthenones with Lead(IV) Acetate. Formation of Di- γ -lactones

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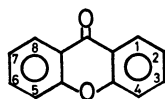
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Synopsis. The oxidation of 9-xanthenones with lead(IV) acetate afforded 3a,3b,6a,12b-tetrahydro-2H-difuro[3,2-a:3',2'-c]xanthene-2,5,7(3H,6H)-triones in addition to other products. Characterization of the di- γ -lactones and the difference between the oxidation reaction of lead(IV) and manganese(III) acetates in the 9-xanthenone system are discussed.

Recently, we have reported that the oxidation of 9-xanthenones with manganese(III) acetate (MTA) affords carboxy-, carboxymethyl-, acetoxymethyl-, and diacetoxymethyl-9-xanthenones, and that carboxyl groups are preferentially introduced at the peri positions of the 9-xanthenones.¹⁾ This regioselectivity was explained in terms of complexation between substrate and MTA.¹⁾ In connection with the MTA oxidation, we have investigated the oxidation of 9-xanthenones with lead(IV) acetate (LTA)²⁾ to give di- γ -lactones, carboxymethyl, acetoxymethyl, and methyl derivatives.

When 9-xanthenone (**1a**) was oxidized with LTA for 3.2 h, di- γ -lactone (**2a**; 22%), 1-carboxymethyl-9-xanthenone (**3a**; 3%), 4-carboxymethyl-9-xanthenone (**4a**; 8%), 4-carboxymethyl-1-methyl-9-xanthenone (**5a**; 1%), 1-acetoxymethyl-9-xanthenone (**7a**; 1%), 4-acetoxymethyl-9-xanthenone (**8a**; 1%),¹⁾ and 1-methyl-9-xanthenone (**10a**; 2%) were obtained. The com-



1a

1b: 1-CH₃O-3-CH₃

3a: 1-HO₂CCH₂

4a: 4-HO₂CCH₂

4b: 1-CH₃O-3-CH₃-4-HO₂CCH₂

4b': 1-CH₃O-3-CH₃-5-HO₂CCH₂

5a: 1-CH₃-4-HO₂CCH₂

6b: 1-CH₃O-3-CH₃-4-HOCH₂-5-HO₂CCH₂

7a: 1-AcOCH₂

8a: 4-AcOCH₂

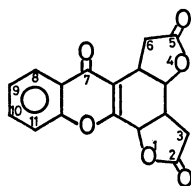
8b: 1-CH₃O-3-CH₃-4-AcOCH₂

9b: 1-CH₃O-3,8-(CH₃)₂-4-AcOCH₂

10a: 1-CH₃

10b: 1-CH₃O-3,8-(CH₃)₂

11a: 1,3-(CH₃O₂CCH₂)₂-4-CH₃O



2a

2b: 8-CH₃O-10-CH₃-11-AcOCH₂

Fig. 1. 9-Xanthenones (**1a**, **b**) and the oxidation products.

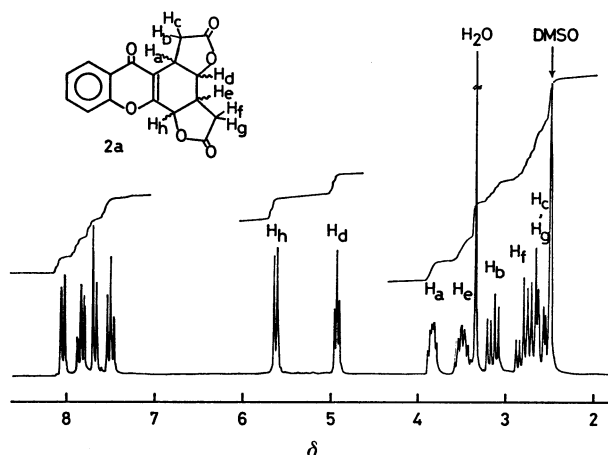


Fig. 2. ¹H-NMR spectrum of di- γ -lactone (**2a**) in DMSO-*d*₆ (δ ppm, 200 MHz).

pound (**2a**) showed a parent ion peak at *m/e* 312 in the MS spectrum, and strong IR absorption bands at 1775 and 1640 cm⁻¹ in KBr. The ¹H-NMR spectrum (200 MHz) of **2a** in DMSO-*d*₆ is shown in Fig. 2. Decoupling the triplet at $\delta=4.95$ (*H_a*) collapsed the multiplet at $\delta=3.85$ (*H_d*) to four peaks. Decoupling the *H_a* collapsed the triplet of *H_d* and two double doublets at $\delta=3.15$ (*H_b*) and 2.64 (*H_e*) to three doublets. When the multiplet at $\delta=3.50$ (*H_e*) was decoupled, the doublet at $\delta=5.64$ (*H_b*), the triplet (*H_d*), the double doublets at $\delta=2.82$ (*H_f*) and 2.64 (*H_g*) were collapsed to a sharp singlet and three doublets, respectively. The coupling constants are as follows: *J_{ab}*=8.8, *J_{ac}*=4.4, *J_{bc}*=17.8, *J_{ad}*=5.9, *J_{de}*=4.9, *J_{ef}*=8.3, *J_{eg}*=4.4, *J_{fg}*=17.3, and *J_{eh}*=7.3 Hz. In the ¹³C-NMR spectrum of **2a** seventeen peaks appeared. In addition, **2a** (44 mg) was hydrolyzed with 50% KOH-ethanol, then treated with 3 M (1 M=1 mol dm⁻³) sulfuric acid, followed by methylation to give 1,3-bis(methoxycarbonylmethyl)-4-methoxy-9-xanthene (**11a**; 16 mg, 31%). It is known that the addition of a $\cdot\text{CH}_2\text{COOH}$ radical to olefins occurs by cis-addition.³⁾ Therefore, the γ -lactone rings of **2a** may add cis to the cyclohexene ring. From the results described above the structure of **2a** was deduced to be 3a,3b,6a,12b-tetrahydro-2H-difuro[3,2-a:3',2'-c]-xanthene-2,5,7(3H,6H)-trione, though the configurations at C-3a, 3b, 6a, and 12b could not be determined.

The oxidation of 1-methoxy-3-methyl-9-xanthenone (**1b**) with LTA for 2.5 h gave 11-acetoxymethyl-8-methoxy-10-methyl-3a,3b,6a,12b-tetrahydro-2H-difuro[3,2-a:3',2'-c]xanthene-2,5,7(3H,6H)-trione (**2b**; 6%), 4-carboxymethyl-1-methoxy-3-methyl-9-xanthenone (**4b**; 3%), 5-carboxymethyl-1-methoxy-3-methyl-9-xanthenone (**4b'**; 1%),¹⁾ 5-carboxymethyl-4-hydroxymethyl-1-methoxy-3-methyl-9-xanthenone (**6b**; 5%), 4-acetoxymethyl-1-methoxy-3-methyl-9-xanthenone (**8b**; 12%),¹⁾ 4-acetoxymethyl-1-methoxy-3,8-dimethyl-9-xanthenone (**9b**; 1%), and 1-methoxy-3,8-dimethyl-9-

xanthenone (**10b**; 1%).

It is known that LTA decomposes in acetic acid to yield $\cdot\text{CH}_3$ radicals⁴⁾ which react with acetic acid to afford $\cdot\text{CH}_2\text{COOH}$ radicals.⁵⁾ The $\cdot\text{CH}_2\text{COOH}$ radicals attack aromatic compounds and the $\text{CH}_2\text{-COOH}$ group is then introduced; this is also converted into a CH_2OAc group.⁵⁾ Therefore, these groups are substituted at the positions ortho or para to electron-donating groups because of the electrophilic nature of $\cdot\text{CH}_2\text{COOH}$ radicals.⁶⁾ $\cdot\text{CH}_3$ radicals also attack 9-xanthenones to yield methylated products, which can be further oxidized with LTA to give acetoxymethyl-9-xanthenones.⁵⁾ In MTA oxidation, on the other hand, $\cdot\text{CH}_2\text{COOH}$ radicals predominantly attack the peri positions regardless of the effect of the electron-donating groups.¹⁾ However, in the present LTA oxidation such a tendency was not observed and the yields of products were not so good as those in MTA oxidation. Consequently, the interaction between the substrate and oxidant which was assumed in MTA oxidation is not important in LTA oxidation.¹⁾ It is known that the reaction of olefins with LTA gives γ -lactones.³⁾ The present reaction is, however, the first example that $\cdot\text{CH}_2\text{COOH}$ radicals add to the aromatic rings to give di- γ -lactones.

Experimental

Measurements. The ^1H -NMR spectra were recorded on a Hitachi Perkin-Elmer R-24 spectrometer (60 MHz) in CDCl_3 and a JEOL FX-200 spectrometer (200 MHz), while the ^{13}C -NMR spectrum was measured on a JEOL FX-90Q spectrometer. The IR spectra were taken on a JASCO IRA-1 grating spectrometer in CHCl_3 . The Mass spectra were measured on a JEOL DX-300 mass spectrometer. The UV spectra were recorded for methanol solution with a Hitachi EPS-3T spectrophotometer. The melting points were determined with a Yanagimoto micromelting point apparatus and were not corrected.

Oxidation of 9-Xanthenones. A mixture of 9-xanthenone (**1a** or **1b**; 1 mmol), LTA (5 mmol), and acetic acid (25 ml) was heated under reflux. The work-up procedure including the esterification of the acidic products was the same as described elsewhere.¹⁾ The yields are based on the amount of substrate consumed.

2a: Mp 281–283 °C (EtOH); λ_{max} nm (log ϵ), 231 (4.28), 253^{sh} (3.95), 268^{sh} (3.73), 307 (3.80); ^1H -NMR δ =2.64 (1H, dd, J =17.3, 4.4 Hz, H_c or H_g), 2.65 (1H, dd, J =17.8, 4.4 Hz, H_c or H_g), 2.82 (1H, dd, J =17.3, 8.3 Hz, H_f), 3.15 (1H, dd, J =17.8, 8.8 Hz, H_b), 3.50 (1H, m, H_e), 3.85 (1H, m, H_a), 4.95 (1H, t, H_d), 5.46 (1H, d, J =7.3 Hz, H_h), 7.5–8.1 (4H, m, ArH); ^{13}C -NMR δ =30.2 (t, CH_2), 31.4 (d, CH), 34.3 (t, CH_2), 36.1 (d, CH), 72.5 (d, H–C–O), 75.7 (d, H–C–O), 117.3 (d, ArC), 118.3 (s, ArC), 122.5 (s, ArC), 125.0 (d, ArC), 125.7 (d, ArC), 134.8 (d, ArC), 155.5 (s, C=), 156.0 (s, C=), 174.6 (s, C=O), 175.3 (s, C=O), 176.3 (s, C=O); m/e 312 (96), 268 (100), 226 (64), 197 (43). Found: C, 65.23; H, 4.05%. Calcd for $\text{C}_{17}\text{H}_{12}\text{O}_6$: C, 65.38; H, 3.87%.

Methyl Esters of 3a and 4a: The methyl ester of **3a** was not separated from the methyl ester of **4a** because they have the same R_f values on TLC; mp 148–150 °C (MeOH); IR (CHCl_3) 1670, 1745 cm^{-1} (C=O); **3a** (CDCl_3) δ =3.69 (3H, s, CO_2CH_3), 4.25 (2H, s, CH_2), 6.95–8.35 (7H, m, ArH); **4a** δ =3.69 (3H, s, CO_2CH_3), 3.93 (2H, s, CH_2), 6.95–8.35 (7H, m, ArH). Found: C, 71.34; H, 4.55%. Calcd for $\text{C}_{16}\text{H}_{12}\text{O}_4$: C, 71.63; H, 4.51%.

Methyl Ester of 5a: Mp 149–150 °C (MeOH); IR 1665, 1740 cm^{-1} (C=O); δ =2.89 (3H, s, CH_3), 3.70 (3H, s, CO_2CH_3), 3.91 (3H, s, CH_2), 7.04 (1H, d, J =7.8 Hz, $\text{H}_{(a)}$), 7.44 (1H, d, J =7.8 Hz, $\text{H}_{(a)}$), 7.15–8.40 (4H, m, ArH); m/e 282.0798 (52, M^+), 223 (100), 194 (20). Calcd for $\text{C}_{17}\text{H}_{14}\text{O}_4$: M, 282.0892.

7a: Mp 132–133 °C (EtOH); IR 1665, 1745 cm^{-1} (C=O); δ =2.20 (3H, s, OAc), 5.87 (2H, s, CH_2), 7.19–8.42 (7H, m, ArH); m/e 268.0711 (8, M^+), 225 (100), 197 (28). Calcd for $\text{C}_{16}\text{H}_{12}\text{O}_4$: M, 268.0736.

10a: Mp 113 °C (MeOH) (lit.⁷⁾ mp 114 °C).

11a: Mp 137 °C (MeOH); IR 1660, 1740 cm^{-1} (C=O); δ =3.71 (6H, s, $2 \times \text{CO}_2\text{CH}_3$), 3.77 (2H, s, CH_2), 4.03 (3H, s, OCH_3), 4.19 (2H, s, CH_2), 7.00 (1H, s, $\text{H}_{(a)}$), 7.25–8.34 (4H, m, ArH); m/e 370.1080 (20, M^+), 338 (66), 323 (100), 311 (38), 295 (38), 237 (50). Calcd for $\text{C}_{20}\text{H}_{18}\text{O}_7$: M, 370.1051.

2b: Mp 199–204 °C (EtOH); λ_{max} nm (log ϵ), 237 (4.33), 265^{sh} (4.07), 285^{sh} (3.62), 324 (3.73); IR 1645, 1745, 1785 cm^{-1} (C=O); δ =2.07 (3H, s, OAc), 2.46–3.88 (6H, m, $2 \times \text{CH}_2$, $2 \times \text{CH}$), 2.52 (3H, s, CH_3), 3.95 (3H, s, OCH_3), 4.80 (1H, t, J =6.0 Hz, $\text{H}_{(ab)}$), 5.30 (2H, s, CH_2), 5.38 (1H, d, J =6.6 Hz, $\text{H}_{(12b)}$), 6.70 (1H, s, $\text{H}_{(a)}$); m/e 428.1113 (2, M^+), 384 (19), 326 (23), 325 (100), 253 (63). Calcd for $\text{C}_{22}\text{H}_{20}\text{O}_9$: M, 428.1107.

Methyl Ester of 4b: Mp 160–161 °C (MeOH); IR 1655, 1740 cm^{-1} (C=O); δ =2.41 (3H, s, CH_3), 3.71 (3H, s, CO_2CH_3), 3.88 (2H, s, CH_2), 3.97 (3H, s, OCH_3), 6.66 (1H, s, $\text{H}_{(a)}$), 7.20–8.37 (4H, m, ArH). Found: C, 69.01; H, 5.12%. Calcd for $\text{C}_{18}\text{H}_{16}\text{O}_5$: C, 69.22; H, 5.16%.

Methyl Ester of 6b: Mp 224–225 °C (MeOH); IR 1655, 1740 (C=O), 3250–3600 cm^{-1} (OH); δ =2.45 (3H, s, CH_3), 3.08 (1H, br. s, OH), 3.70 (3H, s, CO_2CH_3), 3.89 (2H, s, CH_2CO_2), 3.91 (3H, s, OCH_3), 4.86 (2H, s, CH_2O), 6.47 (1H, s, $\text{H}_{(a)}$), 7.10–8.20 (3H, m, ArH). Found: C, 66.57; H, 5.28%. Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_6$: C, 66.66; H, 5.30%.

9b: Mp 184–186 °C (EtOH); IR 1655, 1740 cm^{-1} (C=O); δ =2.06 (3H, s, OAc), 2.50 (3H, s, CH_3), 2.91 (3H, s, CH_3), 4.00 (3H, s, OCH_3), 5.42 (2H, s, CH_2), 6.63 (1H, s, $\text{H}_{(a)}$), 6.98–7.69 (3H, m, ArH); m/e 326.1165 (100, M^+), 297 (31), 267 (89), 250 (25), 249 (95), 238 (26). Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_5$: M, 326.1154.

10b: Mp 168–170 °C (MeOH); IR 1655 cm^{-1} (C=O); δ =2.43 (3H, s, CH_3), 2.89 (3H, s, CH_3), 4.00 (3H, s, OCH_3), 6.56 (1H, d, J =1.8 Hz, $\text{H}_{(a)}$), 6.79 (1H, d, J =1.8 Hz, $\text{H}_{(a)}$), 6.94–7.59 (3H, m, ArH); m/e 254.0942 (55, M^+), 236 (100). Calcd for $\text{C}_{16}\text{H}_{14}\text{O}_3$: M, 254.0943.

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