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

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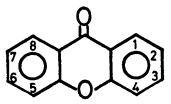
Synopsis. The oxidation of 9-xanthenones with lead (IV) acetate afforded 3a,3b,6a,12b-tetrahydro-2*H*-difuro[3,2-*a*:3′,2′-*c*]xanthene-2,5,7(3*H*,6*H*)-triones in addition to other products. Characterization of the di-γ-lactones and the difference between the oxidation reaction of lead(IV) and manganese(III) 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 compound (**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 ^{1}H-NMR spectrum (200 MHz) of **2a** in DMSO-d_6 is shown in Fig. 2. Decoupling the triplet at δ=4.95 (H_d) collapsed the multiplet at δ=3.85 (H_a) to four peaks. Decoupling the H_a collapsed the triplet of H_d and two double doublets at δ=3.15 (H_b) and 2.64 (H_c) to three doublets. When the multiplet at δ=3.50 (H_e) was decoupled, the doublet at δ=5.64 (H_h), the triplet (H_d), the double doublets at δ=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 ^{13}C-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-xanthenone (**11a**; 16 mg, 31%). It is known that the addition of a $\cdot CH_2COOH$ 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-2*H*-difuro[3,2-*a*:3′,2′-*c*]-xanthene-2,5,7(3*H*,6*H*)-trione, though the configurations at C-3a, 3b, 6a, and 12b could not be determined.



1a

1b : 1-CH_3O-3-CH_3

3a : 1-HO_2CCH_2

4a : 4-HO_2CCH_2

4b : 1-CH_3O-3-CH_3-4-HO_2CCH_2

4b′: 1-CH_3O-3-CH_3-5-HO_2CCH_2

5a : 1-CH_3-4-HO_2CCH_2

6b : 1-CH_3O-3-CH_3-4-$HOCH_2$-5-HO_2CCH_2

7a : 1-$AcOCH_2$

8a : 4-$AcOCH_2$

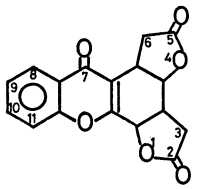
8b : 1-CH_3O-3-CH_3-4-$AcOCH_2$

9b : 1-CH_3O-3,8-$(CH_3)_2$-4-$AcOCH_2$

10a : 1-CH_3

10b : 1-CH_3O-3,8-$(CH_3)_2$

11a : 1,3-$(CH_3O_2CCH_2)_2$-4-CH_3O



2a

2b: 8-CH_3O-10-CH_3-11-$AcOCH_2$

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

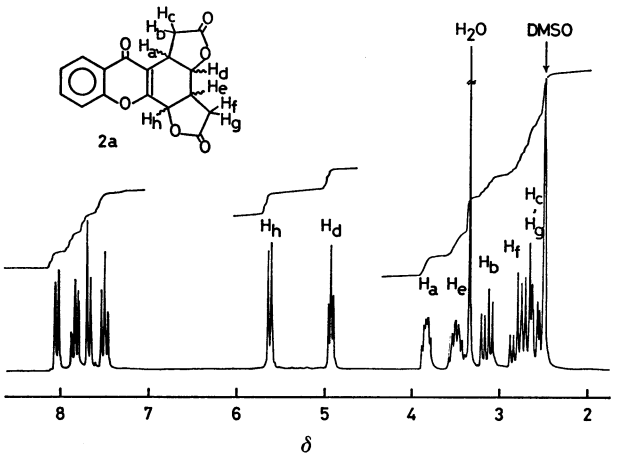


Fig. 2. ^{1}H-NMR spectrum of di-γ-lactone (**2a**) in DMSO-d_6 (δ ppm, 200 MHz).

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-2*H*-difuro-[3,2-*a*:3′,2′-*c*]xanthene-2,5,7(3*H*,6*H*)-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 $\cdot CH_3$ radicals[4] which react with acetic acid to afford $\cdot CH_2COOH$ radicals.[5] The $\cdot CH_2COOH$ radicals attack aromatic compounds and the CH_2-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 $\cdot CH_2COOH$ radicals.[6] $\cdot CH_3$ 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, $\cdot CH_2COOH$ 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 $\cdot CH_2COOH$ radicals add to the aromatic rings to give di-γ-lactones.

Experimental

Measurements. The ^{1}H-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); ^{1}H-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 $C_{17}H_{12}O_6$: 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 $C_{16}H_{12}O_4$: 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, $H_{(2)}$), 7.44 (1H, d, J=7.8 Hz, $H_{(3)}$), 7.15—8.40 (4H, m, ArH); *m/e* 282.0798 (52, M$^+$), 223 (100), 194 (20). Calcd for $C_{17}H_{14}O_4$: 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 $C_{16}H_{12}O_4$: 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×CO_2CH_3), 3.77 (2H, s, CH_2), 4.03 (3H, s, OCH_3), 4.19 (2H, s, CH_2), 7.00 (1H, s, $H_{(2)}$), 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 $C_{20}H_{18}O_7$: 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×CH_2, 2×CH), 2.52 (3H, s, CH_3), 3.95 (3H, s, OCH_3), 4.80 (1H, t, J=6.0 Hz, $H_{(3b)}$), 5.30 (2H, s, CH_2), 5.38 (1H, d, J=6.6 Hz, $H_{(12b)}$), 6.70 (1H, s, $H_{(9)}$); *m/e* 428.1113 (2, M$^+$), 384 (19), 326 (23), 325 (100), 253 (63). Calcd for $C_{22}H_{20}O_9$: 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, $H_{(2)}$), 7.20—8.37 (4H, m, ArH). Found: C, 69.01; H, 5.12%. Calcd for $C_{18}H_{16}O_5$: 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, $H_{(2)}$), 7.10—8.20 (3H, m, ArH). Found: C, 66.57; H, 5.28%. Calcd for $C_{19}H_{18}O_6$: 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, $H_{(2)}$), 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 $C_{19}H_{18}O_5$: 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, $H_{(2)}$), 6.79 (1H, d, J=1.8 Hz, $H_{(4)}$), 6.94—7.59 (3H, m, ArH); *m/e* 254.0942 (55, M$^+$), 236 (100). Calcd for $C_{16}H_{14}O_3$: M, 254.0943.

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