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Ozonation of Xanthene

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Synopsis. The ozonation of xanthene was studied using an oxygen stream. Ozone attacks the methylene group of xanthene *via* a 1,3-dipolar insertion reaction to give the hydrotrioxide intermediate, followed by a loss of singlet oxygen to form xanthydrol. The ozonation of xanthydrol gave singlet oxygen, water and xanthone accompanied by autoxidation.

Methylene group ozonation gives the corresponding carbonyl group. In 1949, Cavill *et al.* reported that xanthene ozonation gave xanthyldrol and xanthone.[1] However, a detailed study of this mechanism has not been reported. In this paper, the authors discuss the ozonation mechanism of xanthene which may possibly produce intermediates capable of giving off singlet oxygen.

Experimental

General. Liquid chromatography was performed with a Jasco Twincle liquid chromatography. Mass spectra were obtained with a Hitachi M-52 spectrometer. Gas chromatography was performed with a Shimadzu 4C-PF gas chromatograph. Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Ozone was generated by a Nihon Ozon 0-1-2 type ozonizer.

Materials. Xanthene (Nakarai Kagaku Yakuhin Co.) was recrystallized from ethanol. Mp 100.4 °C (lit, 100.5 °C);[2] NMR (CCl$_4$) δ=4.02 (2H, s) and 6.8—7.3 (8H, m); MS (70 eV) *m/e* (rel intensity) 182(56), 181(100), 152(44), and 76(23). Xanthydrol was synthesized according to the literature.[3] Mp 121.1 °C (lit, 121—123 °C); NMR (CDCl$_3$) δ=2.24 (1H, s), 5.75 (1H, s) and 6.9—7.6 (8H, m); MS (70 eV) *m/e* (rel intensity) 198(16), 197(25), 181(100), and 153(89); IR (KBr disk) 3300 cm^{-1} (OH). Xanthone (Nakarai Kagaku Yakuhin Co.) was recrystallized from ethanol. Mp 175.1 °C (lit, 173.5 °C);[4] MS (70 eV) *m/e* (rel intensity) 196(100), 168(52), and 139(21); IR (KBr disk) 1655 cm^{-1} (C=O).

Ozonation Reaction. Ozonations in all cases were carried out with ozone-oxygen mixtures (ozone: 9.4 mg/min, oxygen: 200 ml/min) on 0.27 mmol of xanthene and xanthydrol in 20 ml of solvent. Products determination was made immediately by liquid chromatography and xanthone was isolated by liquid chromatography. The mass spectra, IR spectra, and mp of xanthone were compared with those of an authentic sample. Though xanthydrol could not be isolated, the NMR and LC analysis of the ozonated solution showed the formation of xanthydrol. Yields were determined by comparison with standard solution of known compounds. The conditions in the liquid chromatography were as follows: column: SS-10, mobile phase: chloroform: hexane=5:1, detector 254 nm. And the conditions in the gas chromatography for the identification of *o*-dibenzoylbenzene and (*Z*)-α,β-dibenzoylstilbene were as follows: column: $3\phi\times 1$ m, 2% OV-1, on Gas Chrom Q, injection temp: 280 °C, detector temp: 280 °C, column temp: 130—240 °C, 10 °C/min, detector: FID.

Results and Discussion

Xanthene reacts with ozone to give water, xanthydrol and xanthone. The results of the reactions are shown in Table 1. It was found that 1.2—1.4 molar equivalents of ozone were consumed in reacting with xanthene, indicating that oxidation of xanthene to xanthone does not proceed only with ozone. The greater the polarity of the solvent, the greater is the conversion of xanthene, suggesting a 1,3-dipolar insertion of ozone to the methylene group. The carbonium ion character of the intermediate should be stabilized by the resonance effect from oxygen at the 10-position. In the case of xanthydrol ozonation, from the facts that (1) only 0.2—0.3 molar equivalent of ozone was consumed in reacting with xanthydrol, (2) the rate of the reaction did not depend on the solvent as in the case of xanthene, and (3) when the xanthydrol solution was allowed to stand, xanthone was formed by autoxidation, it is considered that the role of ozone in the ozonation of xanthydrol to xanthone is not particularly significant compared with that of ozone to oxidize xanthene to xanthydrol. On the other hand, it is of interest to identify molecular oxygen by decomposition of the hydrotrioxides. Stary and Kovač reported that the decomposition of aldehyde- and acetal-hydrotrioxides gave singlet oxygen.[5,6] The ozonation of

Table 1. Ozonation of xanthene and xanthydrol[a]

Run	Substrate	Solvent	Conversion	Ozone (10^{-4} mol)	Ozone/Substrate reacting ratio[b]	Yield[c]/%	
			%			Xanthydrol	Xanthone
1	Xanthene[d]	CH$_2$Cl$_2$	98	3.6	1.4	4	74
2	Xanthene[d]	CHCl$_3$	94	3.6	1.4	3	57
3	Xanthene[d]	CCl$_4$	59	3.0	1.9	8	30
4	Xanthydrol[e]	CH$_2$Cl$_2$	58	0.9	0.2	—	45
5	Xanthydrol[e]	CHCl$_3$	50	0.5	0.2	—	41
6	Xanthydrol[e]	CCl$_4$	42	0.8	0.3	—	37

a) Ozonation was carried out with ozone-oxygen mixtures (ozone: 9.4 mg/min, oxgen: 200 ml/min) on 0.27 mmol of xanthene and xanthydrol in 20 ml of solvent at 0 °C. b) The molar ratio of ozone to the substrate reacting. c) Yields were based on the substrate reacting with ozone. d) Ozonation was carried out for 4 min. e) Ozonation was carried out for 1.5 min.

TABLE 2. SINGLET OXYGEN DETERMINATION IN THE OZONATION OF XANTHENE AND XANTHYDROL[a]

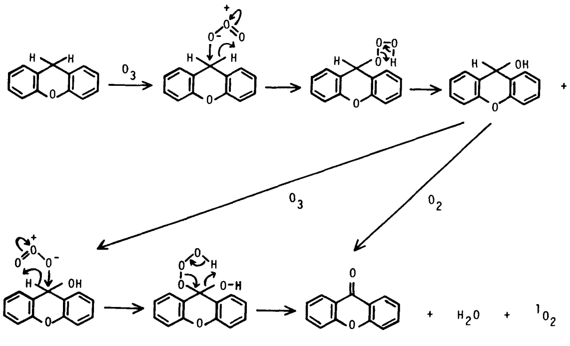
Run	Substrate	Singlet oxygen acceptor	Conversion	Yield[b]/%			
			%	Xanthydrol	Xanthone	*o*-Dibenzoylbenzene	(*Z*)-α,β-Dibenzoylstilbene
1	Xanthene	1,3-Diphenylisobenzofuran	94	4	63	26	—
2	Xanthene	Tetraphenylcyclopentadienone	95	4	61	—	5
3	Xanthydrol	1,3-Diphenylisobenzofuran	62	—	77	16	—
4	Xanthydrol	Tetraphenylcyclopentadienone	87	—	75	—	2

a) The substrates (2.7 mmol) were ozonized in dichloromethane (20 ml) at −78 °C. Singlet oxygen acceptor (0.37 mmol) was then added to the ozonized solutions and allowed to warm to −20 °C.
b) Yields were based on the substrates reacting.

TABLE 3. THE DISTRIBUTION OF SINGLET OXYGEN PRODUCTS IN THE OXIDATION OF 1,2-DIMETHYLCYCLOHEXENE

Method	Product distributions/%	
	1-Methyl-2-methylenecyclohexanol	1,2-Dimethylcyclohex-2-en-1-ol
Xanthene–hydrotrioxide decomposition[a]	93	7
Photooxidation[b]	89	11
Hydrochlorite–hydrogen peroxide method[b]	91	9

a) Xanthene (1.1 mmol) was ozonized in dichloromethane (20 ml) at −78 °C. 1, 2-Dimethylcyclohexene (1.9 mmol) was then added to the ozonized solution and allowed to warm to −20 °C. The hydrotrioxide products were reduced to the corresponding alcohols by sodium borohydride and analyzed by GLC.
b) Ref. 7.



Scheme 1.

xanthene and xanthydrol was carried out at −78 °C and then the excess ozone was removed. 1,3-Diphenylisobenzofuran and tetraphenylcyclopentadienone, singlet oxygen acceptors, were added to the ozonated solution which was then allowed to warm to −20 °C. As expected, *o*-dibenzoylbenzene and (*Z*)-α,β-dibenzoylstilbene were detected. The results are shown in Table 2. The product yields were low because of the instability of the hydrotrioxides. In order to obtain further evidence that decomposition of xanthene–hydrotrioxide gives singlet oxygen, the technique of Foote *et al.* was also used.[7)] The result is shown in Table 3. The products distribution by decomposition of xanthene–hydrotrioxide was the same as that by the sensitized photooxidation and hydrochlorite–hydrogen peroxide method. The probable reaction mechanism of xanthene ozonation is shown in Scheme 1.

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