



Novel photolactonisation from xanthenoic esters

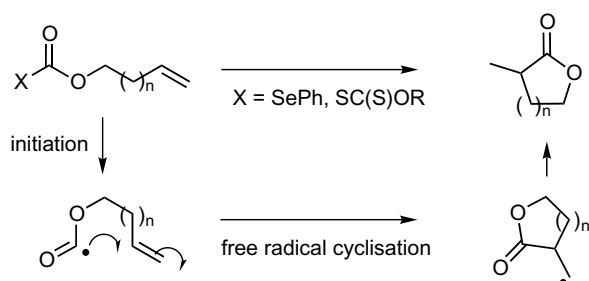
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Abstract—In the context of our work on photocleavable fragrance precursors, we have discovered a new photo-fragmentation of xanthenoic esters into xanthene- and formyl radicals. This homolytic cleavage has not been reported previously. Thus, unsaturated formyl radicals cyclise to lactones of various ring size. © 2001 Elsevier Science Ltd. All rights reserved.

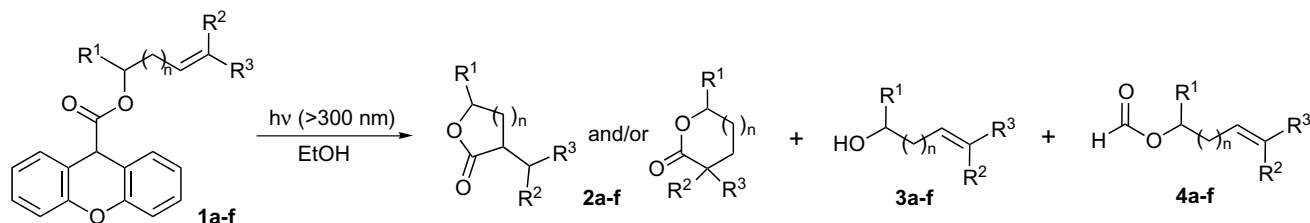
The free radical cyclisation to lactones is well known.¹ In this way, lactones have been made from allyl α -halo-carboxylates,^{1a,b} haloalkyl acrylates,^{1c} vinyl 2-halobenzoates,^{1d} xanthates^{1f,g} and phenylseleno carbonates.^{1h} The latter two classes require tributyltin hydride to generate a formyl radical via homolytic cleavage of either the Se–CO or the S–CO bond, followed by the intramolecular addition of this radical to a carbon–carbon double bond (Scheme 1). We have discovered the photochemical formation of such formyl radicals from xanthenoic esters and their cyclisation to lactones.



Scheme 1.

As part of our work on photocleavable fragrance precursors,² we envisaged that xanthenoic esters may release alcohols, based on a disclosure of Barton and co-workers, who observed the photolytic cleavage of xanthenoic aryl esters into xanthene and the corresponding phenols.³ They rationalised their findings by postulating a homolytic cleavage of the CO–OAr bond (according to the well precedented photochemical Fries rearrangement),⁴ followed by decarbonylation. However, we have found that only a small amount of alcohol is formed from alkenyl xanthenoic esters **1a–f**.⁵ The major products are lactones of various ring size, depending on the location of the unsaturation. These findings are a clear indication that the photolytic cleavage of xanthenoic esters derived from alcohols other than phenols occurs α to the carbonyl group to yield the corresponding formyl and xanthene radicals. To the best of our knowledge this fragmentation of xanthenoates under UV-irradiation has not yet been described.

We report the transformation of such compounds to lactones. Scheme 2 illustrates the general reaction and



Scheme 2.

Keywords: xanthenoic ester; xanthenoate; photo-fragmentation; xanthene radical; formyl radical; lactonisation; lactone.

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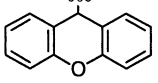
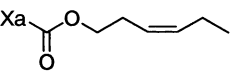
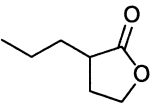
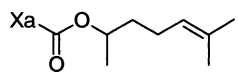
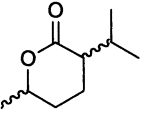
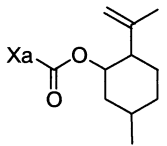
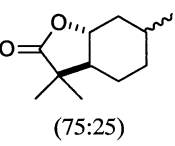
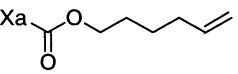
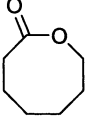
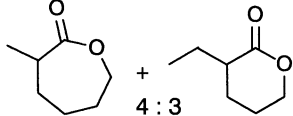
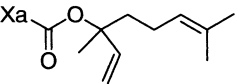
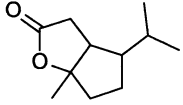
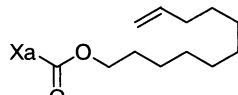
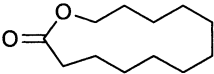
Table 1 summarises the results.⁶ *cis*-3-Hexenyl xanthenoate (**1a**) represents a standard case where the above mentioned reaction conditions led to the γ -lactone **2a**, that was isolated in good yield beside some *cis*-3-hexenol (**3a**, 10%). The formate **4a** was only observed in trace amounts. Xanthenoate **1b** was studied under various conditions: the standard procedure gave a mixture of diastereoisomeric δ -lactones **2b** in 42% yield. In this experiment, the alcohol **3b** and the formate **4b** were isolated in 12 and 5%, respectively. Due to the relatively long reaction times (the half-life of **1b** upon irradiation with a 150 W lamp was approximately 11 h), several alterations to the conditions were made.

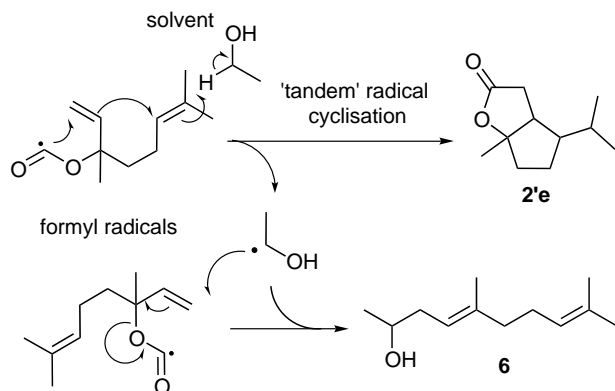
No reaction took place in dioxane and toluene. In acetonitrile and methanol, the disappearance of the xanthenoate was much faster, however, neither lactone **2b** nor the corresponding formate **4b** could be isolated. The only isolable and characterised product was xanthone (**5**). No lactone either was formed by performing the reaction in a quartz vessel. Simonaitis and Pitts described the opening (through homolytic bond cleav-

age) of γ -lactones at 254 nm to yield formates.⁷ Conceivably then, irradiation of **1b** at shorter wave lengths (<300 nm, quartz cell) does either not lead to lactones, or leads to their rapid cleavage. Thus, the initial reaction conditions in ethanol turned out to be the best for our purpose. The (\pm)-isopulegol-derived xanthenoate **1c** gave 50% of a 75:25 mixture of diastereoisomeric lactones *rac*-**2c**. NOESY-spectroscopy confirmed the *trans* ring fusion. Only little alcohol **3c** and formate **4c** was formed. Irradiation of the 5-hexenol derivative **1d** yielded 34% of the eight-membered-ring lactone **2d** beside an inseparable 3:4 mixture of six- and seven-membered lactones **2'd**. The formation of the δ -lactone can be rationalised by isomerisation of the terminal carbon-carbon double bond under the reaction conditions. Again, only small amounts of alcohol **3d** and formate **4d** were formed.

Linalyl xanthenoate **1e** gave a complex mixture of products. However, the four diastereoisomers of bicyclic lactone **2'e** were identified by GLC-MS analysis of an enriched fraction. The combined GLC-yield

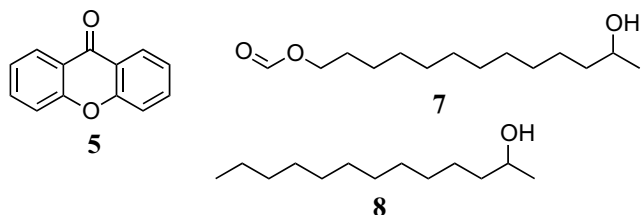
Table 1. Results of the photolysis of alkenyl xanthenoates **1a–f**

	Xanthenoate  Xa =	Products (Yield %)			
		Lactones	Alcohol	Formate	recovered Xanthenoate
1a		 2a (55)	3a (10)	4a (<1)	1a (36)
1b		 2b (42) (<i>trans-cis</i> 56:44)	3b (12)	4b (5)	1b (8)
1c		 <i>rac</i> - 2c (50) (75:25)	3c (3)	4c (1)	1c (9)
1d		 2d (34) +  2'd (10) 4 : 3	3d (4)	saturated formate 4'd (1)	1d (5)
1e		 2'e (9)	3e (4)	-	-
1f		 2f (6)	3f (13)	4f (12)	1f (7)



Scheme 3.

amounts to about 9%. Linalool (**3e**) was obtained in 4% beside alcohol **6** (7%). The latter resulted from intermolecular radical reaction with ethanol (Scheme 3). None of the formate **4e** was observed. A mechanism for the formation of these bicyclic lactones is proposed in Scheme 3, involving a 'tandem' radical addition first to the vinylic then to the prenylic carbon–carbon double bond. Such a behaviour of formyl radicals derived from xanthates was also observed by Iwasa and co-workers.^{1g} Finally, 10-undecenol-derived xanthenoate **1f** gave only 6% of the expected 13-membered ring lactone **2f**, showing the limitations of this method. The formation of formate **3f** (12%) as well as intermolecular side reactions became predominant. Among the by-products we identified in particular **7** (12%) and **8** (5%). 10-Undecenol (**3f**) was obtained in 13% yield.



In conclusion, we have shown for the first time that alkenyl xanthenoates fragment under UV-irradiation ($\lambda > 300$ nm) to generate xanthene and unsaturated formyl radicals that may cyclise to give the corresponding lactones in acceptable yields. The optimisation of the system with regard to reaction conditions and additives, as well as the alteration of the chromophore are subject of continued efforts.

Acknowledgements

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- The xanthenoates, prepared in good yields via the DCC-mediated coupling of the xanthenoic acid with the alcohols, were fully characterised by ¹H and ¹³C NMR, IR and mass spectroscopy.
- Approximately three-millimolar solutions of the starting materials **1a–f** in ethanol were irradiated with a 150 W medium pressure Hg-lamp in a water cooled Pyrex® photoreactor (>300 nm). Larger scale experiments were conducted with a 700 W lamp. A typical experiment consists of irradiating an ethanolic solution of the xanthenoate **1a–f** (3 g in 3 l) with a 700 W lamp. The conversion was monitored by GLC-analysis. Reaction times varied from 48 to 96 h for a conversion of >80%.

The solvent was evaporated and the residue taken up in MTBE (200 ml). This was washed with saturated aq. NaHCO_3 (200 ml) and brine (100 ml), dried (MgSO_4) and concentrated in vacuo. The crude, a yellow oil, was diluted with poly(ethylene glycol) ($M_n \sim 400$, 5 g) and the volatiles collected by Kugelrohr distillation under reduced pressure. The products were separated by flash chromatography on silica. Compounds **2a–d** and **2f**, **2'd**, **3a–d**, **4b** and **5** were isolated and fully characterised by

^1H and ^{13}C NMR, IR and MS, the others were identified by GLC or GLC–MS from enriched fractions (all formates **4** were prepared independently from their corresponding alcohols for GLC-identification purposes). Solid xanthone was obtained by further Kugelrohr distillation and the structure of other xanthene-derivatives was tentatively assigned on the basis of a GLC–MS analysis.

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