96. Selective Photoinduced Oxidation of Benzylic Methylen Groups through UV Irradiation in Presence of Ferric Chloride

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Summary

Selective oxidation of benzylic methylene groups through UV irradiation in acetone/water/$FeCl_3$ mixtures is reported. This method applied to a series of model compounds, provides an easy access to the corresponding 1-oxo derivative. Thus, tetralin gives a 100% yield of 1-tetralone, indane leads to 60% of 1-indanone, and diphenylmethane is oxidized to benzophenone with 80% yield. However, under the same conditions, alkyl-substituted aromatic hydrocarbons such as toluene, ethyl- and propylbenzene lead to low yields of aldehydes or ketones. Isochromane furnishes a mixture of two substances which can be interconverted, namely the expected 1-isochromanone (9%) and the corresponding hydroxy acid (23%). We failed to apply the method to nitrogen heterocycles containing benzylic groups such as 1,2,3,4- and 5,6,7,8-tetrahydroquinoline as they do not react due to the formation of complexes which precipitate from the solutions.

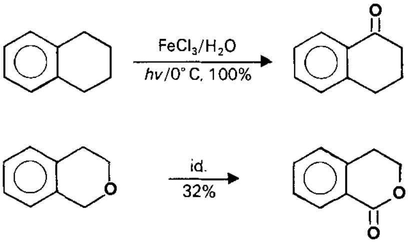
It has been observed many years ago (for a review see [1]) that marasmine-Fe^{3+} chelates were responsible for the wilting properties of some *Aspergillus* species on plants. The importance of the photophase for the phenomenon suggested that Fe^{3+} transported through the stem, was promoting photooxidations at the level of the leaf. During recent investigations on aspergillomarasmine-Fe^{3+} chelate, we considered the *in vitro* photooxidation of EtOH into acetaldehyde [2]. As the same reaction could be observed with $FeCl_3/H_2O$ alone instead of the complex (which then acts as a carrier under natural conditions), we decided to extend this combined Fe^{3+}-UV oxidizing system to a series of compounds such as hydrocarbons with benzylic H-atoms. The results so far obtained are reported in the present publication.

Tetralin, in the mixture of acetone/water/$FeCl_3$, standing over a longer period on the laboratory bench was found to be selectively and quantitatively transformed into 1-tetralone. So, we decided to investigate this reaction in more detail in order to elucidate the optimum conditions for this oxidative transformation.

By using dry acetone, the successive elimination of $FeCl_3$ or of water, or of light, suppressed the formation of the oxo derivative. Hence, this transformation could not be related to the metal-catalyzed autoxidation of tetralin as described by *Robertson & Waters* [3] using iron or copper salts [4], or cobalt salts as published by *Woodward & Mesrobian* [5].

In spite of the fact that light-initiated oxidations in the presence of metal salts through free radical autoxidations are well-documented in the literature [6] [7] the combined action of UV and $FeCl_3$ on hydrocarbons with benzylic H-atom still remained to be explored.

That light in the UV range is necessary was established by using a 330-W UV lamp: a 50% yield of 1-tetralone was obtained after one hour, and after 5 h the reaction was complete (for details see *Exper. Part* and *Table*). TLC analysis showed that the 1-oxo derivative was the only substance formed in this oxidation procedure. Our conclusion was that the remaining methylene group in benzylic position of the 1-tetralone was no longer sensitive to further oxidation under the applied conditions. If tetralin hydroperoxide and 1-tetralol are intermediates under our reaction conditions (as reported in other publications [3] [8]) their existence could only be transient as we were unable to detect these compounds.



The oxidation of indane to 1-indanone was found to proceed at a slower rate: a 50% yield of transformation was observed after 4 h, and 60% was finally isolated after a reaction time of 7 h *(Table)*. Obviously, the 5-membered ring offers a greater resistance to oxidation under our conditions. 1-Indanone was the only oxo derivative which could be isolated from the reaction mixture.

In a similar experiment, diphenylmethane was transformed into benzophenone, 50% and 80% yields were obtained after 4 h and 10 h UV irradiation, respectively *(Table)*.

This reaction was extended to a series of alkyl-substituted aromatic hydrocarbons. However, lower oxidation yields, in function of the side chain, were observed. Thus, toluene gave only 9% benzaldehyde after 8 h (isolated as its 2,4-dinitrophenylhydrazone after spraying the prep. TLC plate with the 2,4-dinitrophenylhydrazine reagent). Ethylbenzene lead to the formation of 3% acetophenone and traces of propiophenone were obtained from propylbenzene (isolated as described for benzaldehyde).

The oxidation of tetralin and of indane was subsequently compared with the oxidation of isochromane in which the ether function was supposed to activate the adjacent benzylic methylene group. We found, however, that the oxidation to 1-isochromanone through UV irradiation in presence of $FeCl_3$ and water proceeds at a slower rate than expected. After 8 h, a 32% overall yield of two compounds, which could be easily interconverted, was obtained, namely, 1-isochromanone (9%) and the corresponding hydroxy-acid (23%). These products were identified by the comparison of their R_f-values and MS with those of authentic samples prepared according to a known method [9]. The smooth formation of 1-isochromanone (3,4-dihydroisocoumarine) at 0° seems

Table. *Photo-oxidation of Substrates with Benzylic H-Atoms by UV Irradiation in a* $Acetone/H_2O/FeCl_3$ *Mixture*[a])

Reactant	Time of irradiation [h]	Product (% yield)	Product characterization
Tetralin		1-Tetralone	$R_f = 0.35$; Semicarbazone:
	1	(50)	m.p. 213–216°, MS
	3	(90)	
	5	(100)	
Indan		1-Indanone	$R_f = 0.35$, m.p. 38–40°;
	1	(10)	2,4-DNP[b]): m.p. 254–257°,
	4	(50)	MS
	7	(60)	
Diphenylmethane		Benzophenone	$R_f = 0.45$, m.p. 45–48°;
	1	(15)	2,4-DNP: m.p. 233–236°,
	3	(45)	MS
	6	(70)	
	10	(80)	
Toluene		Benzaldehyde	$R_f = 0.55$,
	1	(traces)	2,4-DNP: m.p. 234–237°
	8	(*ca.* 9)	
Ethylbenzene		Acetophenone	$R_f = 0.45$,
	1	(traces)	2,4-DNP: m.p. 235–236°
	8	(*ca.* 3)	
Isochromane		1-Isochromanone	$R_f = 0.80$ hydroxy acid[b]):
	8	(32)[c])	$R_f = 0.60$, m.p. 82–85°, MS

[a]) For details see *Exper. Part.*

[b]) 9% of 1-isochromanone and 23% of 2-(2-hydroxyethyl)benzoic acid.

[c]) 2,4-DNP = 2,4-Dinitrophenylhydrozone.

to provide a new accessibility to this family of substances, which, in general, requires a stronger oxidizing reagent. The low yield, in comparison with tetralin, may be explained in terms of interactions of the heterocyclic oxygen in isochromane with the metal ions, interfering on the attack of the neighbouring methylene group.

Attempts performed on nitrogen heterocycles such as 1,2,3,4- and 5,6,7,8-tetrahydroquinoline led to the immediate formation of a highly colored complex which precipitated from the solution, thus blocking the photo-oxidation.

Methyl benzyl ether chosen as a model for comparison, was totally unchanged after 8 h of irradiation. That no methyl benzoate nor benzoic acid could be detected seems to be an argument in favor of our hypothesis of the hindering effect of the oxygen ether function due to interaction with the metal.

In conclusion, the combined $FeCl_3$, UV, H_2O-promoted oxidation of benzylic methylene groups represents an efficient and smooth method for the access of mono-oxo products in aromatic alicyclic compounds, whereas low yields or unreactivity are noticed with alkyl-substituted aromatic hydrocarbons or analogue nitrogen-containing heterocycles.

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Experimental Part

In a typical experiment, 0.2 mmol tetralin in 30 ml of acetone (distilled over $KMnO_4$), 4 drops of H_2O (120 mg) and 350 mg of $FeCl_3$ were irradiated by means of a 330-W *Hanau* UV lamp under ice-cooling. Control TLC's were carried out on *Schleicher-Schüll* fluorescent SiO_2-films with hexane/AcOEz 95:5 (80:20 in the case of isochromane and isochromanone), using UV observation. Prep. TLC's were carried out under similar conditions in SiO_2 fluorescent plates (1 mm thickness) or by using a preliminary column chromatography on *Merck 60 PF 254* SiO_2.

Experiments with higher amounts of H_2O and $FeCl_3$ did not increase the yields of the oxo compounds, which were decreased by using lower amounts of reagents.

The *Table* indicates the yields and methods of identifications of the products isolated after oxidation. All products mentioned have also been directly compared with authentic samples.

Mass spectrometric determinations have been carried on an *AEI MS 50* apparatus and the melting points were determined under the *Kofler* microscope and are corrected.

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