Pergamon

Tetrahedron Letters, Vol. 37, No. 24, pp. 4179-4182, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00789-7

Oxidation of Ethers to Esters by Photo-Irradiation with Benzil and Oxygen

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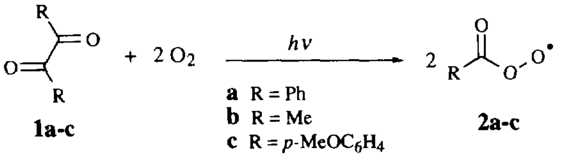
Abstract: A novel method for the conversion of ethers to esters by photo-oxidation using benzil and molecular oxygen, and its plausible reaction mechanism participated by benzoylperoxy radical are described. Copyright © 1996 Elsevier Science Ltd

Acylperoxy radical **2** efficiently generated by photoreaction of α-diketone **1** in an oxygen saturated solution as depicted in Scheme 1[2-4] is an attractive reactive intermediate in a synthetic sense due to its characteristic structural feature different from popularly known oxy radicals, *e.g.*, alkylperoxy radical (ROO•) and acyloxy radical (RCO_2•). This radical consists of a strongly electrophilic oxy radical adding to olefins much faster than ROO• and the adjacent acyloxyl function with the potent departing ability, thus behaving as an efficient one oxygen transfer species to convert olefins to the epoxides, and it is naturally prospected that the strong electrophilicity may coincide with the high ability of electrophilic hydrogen abstraction.[3] However, despite these intriguing reactivities, only epoxidation of olefins has been known as a reaction of acylperoxy radical.[5] We envisaged that this radical would efficiently abstract α-hydrogen of ethers to initiate the oxidation, and found that aliphatic ethers as well as benzylic ones were converted to esters by irradiation with benzil **1a** in an oxygen saturated benzene solution, where intermediary benzoylperoxy radical **2a** seems to serve as a strong hydrogen acceptor. Although there have been a variety of methods for direct conversion of ethers to esters reported so far, few have assumed any synthetic importance, especially to aliphatic compounds, except for the methods based on oxides of chromium and ruthenium.[6] Thus, we now report this photo-oxidation as a new method for conversion of ethers to esters.



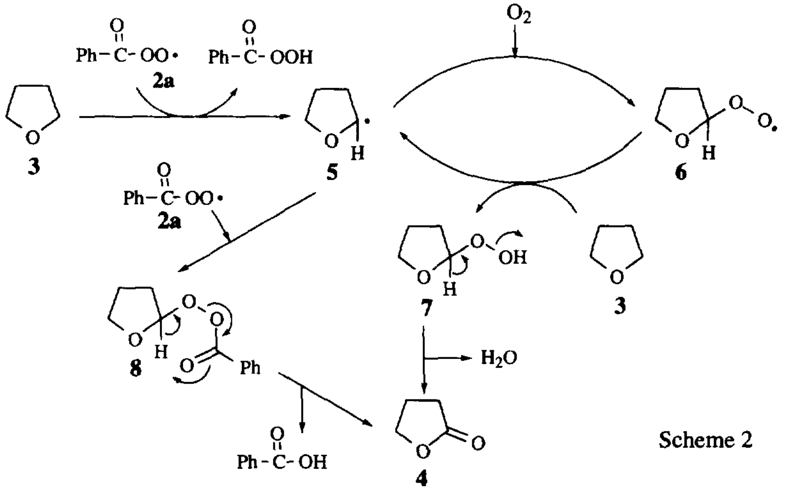
1a-c

2a-c

Scheme 1

The photo-oxidation was first attempted on tetrahydrofuran **3**: a 5.0 x 10^{-2} mol solution of **1a** in **3** placed in a Pyrex tube was irradiated with a 300 W medium pressure mercury lamp at 0°C, with oxygen being bubbled through the solution, until **1a** was completely consumed (*ca.* 6 h). After removal of volatile materials with evaporator, ^{1}H-NMR spectrum of the residue showed the formation of γ-lactone **4** (208%[7] based on the used **1a**). Likewise, tetrahydropyran and an acyclic aliphatic ether, di-*n*-butyl ether, respectively afforded δ-valerolactone (173%) and *n*-butyl *n*-butyrate (169%) under the same reaction conditions.

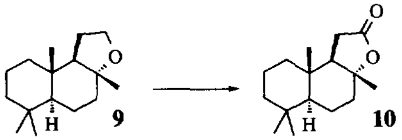
The mechanism of this reaction may be tentatively explainable in terms of either a radical chain reaction [**3** → **5** → **6** → **7**→ **4**] or oxygen transfer reaction of **2a** to the α-methylene carbon of **3** [**3** → **5** → **8** → **4**] as illustrated in Scheme 2. Radical **2a** generated by photoreaction of **1a** and oxygen abstracts the α-hydrogen of **3**, leading to the formation of perbenzoic acid and tetrahydrofuranyl radical **5**. In the chain mechanism, radical **5** then reacts with oxygen to form tetrahydrofuranylperoxy radical **6**, followed by abstraction of the α-hydrogen of **3**, giving **5** and tetrahydrofuranyl hydroperoxide **7**. Dehydration of **7** finally generates **4**. This mechanism is similar to the benzophenone-sensitized photo-oxidation of **3** reported by Schenck *et. al.*,[8] where the radical initiator is triplet benzophenone in place of **2a** and hydroperoxide **7** only was obtained. However, we assume that lactone **4** must have been missed, because our reinvestigation of the Schenck's reaction afforded **4** (86% based on benzophenone) as a major product. Thus, photo-exited triplet benzil **1a** should be considered as another hydrogen abstractor in this mechanism, but we assume that the contribution may be small if any, because it is well documented that triplet **1a** efficiently decays through two processes in an oxygen saturated solution: quenching by oxygen leading to **1a** and singlet oxygen, and reaction with oxygen finally leading to **2a**.[2] Alternatively, in oxygen transfer mechanism from **2a**, radical **5** combines with a second molecule of **2a** to form tetrahydrofuranyl perbenzoate **8**, which then easily decomposes into benzoic acid and lactone **4** due to the leaving ability of the benzoyloxyl group. The stoichiometry of the formed **4** to **1a** was beyond one, suggesting the contribution of the radical chain mechanism.



Scheme 2

In order to refine the reaction conditions, the photo-oxidation of an aliphatic five-membered ether, (-)-ambroxide **9**, to γ-lactone, 3a*R*-(+)-sclareolide **10**, was attempted in a benzene solution, with varying the amounts of **1a** (entries 1-4 in Table 1) and then replacing acylperoxy radical source **1a** with biacetyl **1b**,[4] *p*-anisil **1c**[9] and benzoin[10] (entries 5-7) which are known to efficiently generate acylperoxy radicals, **2b**, **2c** and **2a**, respectively, upon irradiation in the presence of oxygen. Lactone **10**[11] was obtained in a moderate yield (60% isolated yield after flash-chromatography on silica gel) after reasonable reaction time (6 h) when 2.0 equivalent of **1a** was used (entry 3). Among acylperoxy radical sources tested, **1a** was found to be best. In addition, this reaction surpassed benzophenone-sensitized photo-oxidation (entry 8) with regard to its efficiency, which may be accounted for in part by the efficient hydrogen abstraction from **9** by highly electrophilic **2a** more than the triplet benzophenone.

Table 1 Photo-oxidation of **9** to **10** under various conditions[a]



Entry	Reagent	Molar Equiv.	Time / h	Conversion (%)	Yield(%)[b] of **10**
1	**1a**	0.5	6	36	72
2	**1a**	1.0	6	79	45
3	**1a**	2.0	6	100	62
4	**1a**	4.0	4	100	47
5	**1b**	2.0	6	87	22
6	**1c**[c]	2.0	6	98	22
7	Benzoin[c]	2.0	6	39	26
8	Benzophenone	2.0	6	57	49

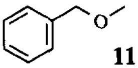
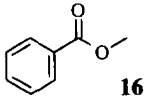
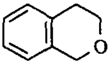
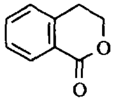
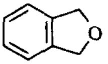
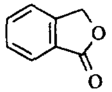
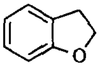
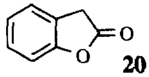
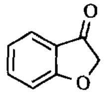
[a] Unless otherwise indicated, a 5.0×10^{-2} mol solution of **9** in benzene containing reagent in a Pyrex tube was irradiated with a 300 W medium pressure mercury lamp at 5–10°C: oxygen was continuously bubbled through the solution during irradiation.

[b] Yields based on converted starting material, determined by ^{1}H NMR analysis.

[c] Due to the low solubility of the reagent, twice amount of solvent was used.

The photo-oxidation with **1a** and oxygen in a benzene solution was then applied to several commercially available aromatic ethers and the results are presented in Table 2. As expected, benzylic ethers, **11**, **12**, **13** and **14**, were oxidized smoothly to give the corresponding benzoyloxyl derivatives, **16**, **17**, **18** and **19** in

Table 2 Photo-oxidation of aromatic ethers with benzil and oxygen in a benzene solution[a]

Entry	Ether	Time / h	Product	Yield (%)[b]
1	 **11**	2	 **16**	97
2	*O*-benzyl-β-cholestanol **12**	2	β-cholestanol benzoate **17**	94
3	 **13**	1	 **18**	67
4	 **14**	3	 **19**	61
5	 **15**	2	 **20**	3
			 **21**	23

[a] A 5.0×10^{-2} mol solution of ether in benzene containing 2.0 equivalents of **1a** was reacted under the same photo-oxydation conditions given in the note *a* to Table 1.

[b] Yields determined by ^{1}H NMR analysis.

moderate to excellent yields, respectively (entries 1-4). Whilst, in the case of benzofuran **15** (entry 5), the benzyl methylene rather than the α-methylene of oxygen atom was preferentially oxidized, 3(2*H*)-benzofuranone **21** (23%) being obtained predominantly along with a mall amount of lactone **20** (3%). The observed regioselectivity would be explainable in the terms of SOMO-HOMO interaction in electrophilic hydrogen abstraction.[12] Namely, the C–H bond of the benzyl methylene on **15** is conjugated to both aromatic ring and oxygen atom, which raises the energy of the HOMO. Therefore, this bond should be more reactive to electrophilic radical than that of the methylene conjugated to oxygen atom alone. This effect raising HOMO energies should be also true of **11**, **12**, **13** and **14**, which reflected well their reaction times much shorter than that of an aliphatic ether, **9**. It is noteworthy that oxidative debenzylation of *O*-benzyl-β-cholestanol **12** was attained through a reaction sequence of the photo-oxidation (entry 2) and alkali hydrolysis [2N NaOH *aq*., MeOH, reflux] to give β-cholestanol in 88 % isolated yield.[15]

As described, we demonstrated a synthetic utility of benzoylperoxy radical generated by photo-irradiation of benzil and oxygen, which provided a novel method for direct oxidation of aliphatic ethers as well as benzilic ones to esters. Currently we are studying this oxidation reaction in more detail with a view to establishing the mechanism and scope.

Acknowledgment: This research was supported in part by a Grant-in-Aid for Scientific Research to H. Seto (No. 07672306) from the Ministry of Education, Science and Culture, Japan and by a Special Coordination Fund from the Science and Technology Agency, Japan.

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11. All photo-products except for **18** and **21** were identical to commercially available authentic samples with respect to ^{1}H and ^{13}C NMR spectra, and ^{1}H NMR spectra of **18** [300 MHz, $CDCl_3$; δ 3.07 (2H, t, *J*=6.0 Hz, 4-H_2), 4.55 (2H, t, *J*=6.0 Hz, 3-H_2), 7.27 (1H, dm, *J*=7.5 Hz, 5-H), 7.40 (1H, ddd,*J*=8.0, 7.5 and 0.6 Hz, 7-H), 7.55 (1H, td, *J*=7.5 and 1.4 Hz, 6-H), 8.11 (1H, dd, *J*=8.0 and 1.2 Hz, 8-H)] and **21** [δ 4.64 (2H, s, 2-H_2), 7.10 (1H, ddd, *J*=7.6, 7.2 and 0.6 Hz, 5-H), 7.15 (1H, br d, *J*= 8.4 Hz, 7-H), 7.62 (1H, ddd, *J*=8.4, 7.2 and 1.5, 6-H), 7.69 (1H, ddd, *J*=7.6, 1.5, 0.6 Hz, 4-H)] were well consistent with those reported.[13,14]
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(*Received in Japan* 26 *February* 1996; *revised* 10 *April* 1996; *accepted* 24 *April* 1996)