

## Photochemically Induced Oxidation of Some Steroidal Isoxazolidines by Molecular Oxygen

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**Summary** U.v. irradiation of the steroidal isoxazolidines  $5\alpha,10\alpha$ -imino-oxy-5(10 $\rightarrow$ 1 $\beta$ H)abeo- $5\alpha$ -cholestan-3 $\beta$ -ol acetate (**1a**) and the corresponding *N*-methyl and *N*-acetyl derivatives (**1b**) and (**1c**) in various solvents in the presence of oxygen, gave the nitro products (**2**), (**3**), and (**4**) and the azoxy products (**5**) and (**6**); a mechanism

involving exciplex formation followed by proton transfer from isoxazolidine to molecular oxygen is proposed.

EXAMPLES reported on photo-oxygenation of saturated organic molecules containing heteroatoms (O, S, N) show that reaction may take place at the heteroatom, but, more

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TABLE  
Products obtained by irradiation<sup>a</sup> of the isoxazolidines (**1a**), (**1b**), and (**1c**), in the presence of oxygen

Substrate	Solvent <sup>b</sup>	Time/h	Yields/% <sup>c</sup> of reaction products <sup>d</sup>						S.M. <sup>e</sup>
			(2)	(3)	(4a)	(4b)	(5)	(6)	
(1a)	Acetone	2	9	1	18		8	10	—
"	Dioxan	2	8	1	10		12	9	—
"	Ether	1	11	1	14		27	6	—
"	Benzene	3	8	1	5		30	16	—
"	Methanol	4	18	5	8	16	traces	—	—
(1b)	Acetone	2	6		15		—	—	44
(1c)	Acetone	6	5		7		—	—	22
"	Dioxan	2	9		9		—	—	—

<sup>a</sup> Irradiations were carried out in a cylindrical flask with a medium pressure Hg 250 W lamp contained in a water-cooled jacket of quartz, at room temperature and with stirring. Solutions (not deaerated) were  $2 \times 10^{-3}$  M. <sup>b</sup> Solvents were not dried. <sup>c</sup> All yields refer to crude products, separated and isolated by column chromatography on silica gel (yields after crystallization were lower by 10–30%). Unresolvable mixtures, not further investigated were also obtained. <sup>d</sup> Structures and configurations of the products were determined by microanalysis, spectral data, and chemical transformations. <sup>e</sup> Recovered starting material.

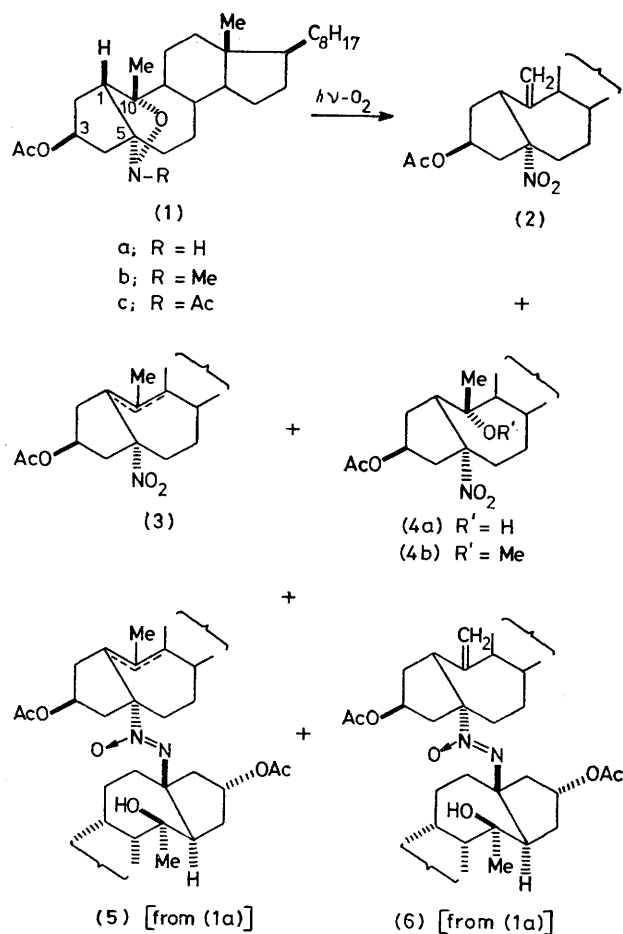
often, involves initially homolytic abstraction of  $\alpha$ -hydrogen atoms (when present).<sup>1</sup> The present study is concerned with the photo-oxygenation of some steroidal isoxazolidines devoid of  $\alpha$ -hydrogen atoms with respect to either heteroatom, *i.e.* compounds (**1a**),<sup>2,3</sup> (**1b**), and (**1c**).<sup>3</sup>

U.v. irradiation of (**1a**) in different solvents from which air had not been expelled afforded the nitro products (**2**), (**3**), and (**4**), and the azoxy compounds (**5**) and (**6**) (Scheme 1 and Table). Under similar irradiation conditions (**1b**)

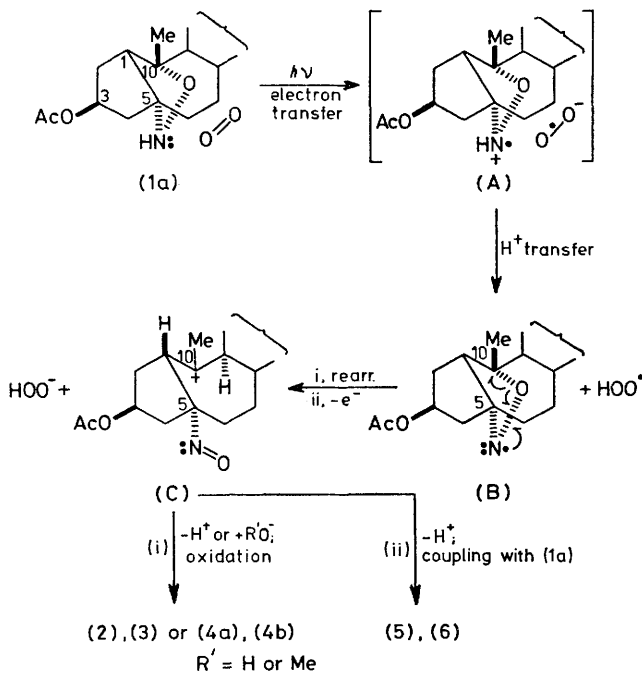
and (**1c**) also underwent oxidative fragmentation, but in these cases only the nitro products (**2**), (**3**), and (**4**) were obtained (Table).

However, when (**1a**) was irradiated in the absence of oxygen (under nitrogen), starting material was recovered in high yield (*ca.* 90%) and none of the products (**2**)–(**6**) could be detected. This shows that molecular oxygen is necessary for the above described photoprocess to occur.

In order to investigate the mechanism of these oxygenations, (**1a**) was irradiated in the presence of Methylene blue or Crystal violet, dyes which are known to be sensitizers for singlet oxygen. However, they proved to be inefficient in inducing oxygenation, indicating that the reaction does not proceed by the intermediacy of singlet oxygen.



SCHEME 1



SCHEME 2

All these results are consistent with a mechanism (Scheme 2) which involves as the primary photoprocess electron transfer from the substrate (**1a**) to molecular oxygen. The exciplex (**A**) so formed undergoes internal proton transfer

to give the isoxazolidine radical (**B**) and a hydroperoxyl radical. Rearrangement of (**A**) to the more stable 5-nitroso C(10) radical followed by one-electron oxidation at C(10) (by the hydroperoxyl radical)<sup>4</sup> results in the formation of the C(10)-carbonium ion intermediate (**C**), from which all the products isolated can be derived. Thus, upon stabilization of the cationic site in (**C**), by removal of the adjacent proton, *i.e.* double bond formation, or addition of water or methanol followed by proton elimination (reactions which are all characteristic only of carbocations, but not of other conceivable intermediates, such as carbon-centred radicals, alkyl hydroperoxides, alkoxy radicals, *etc.*), the 5-nitroso group can undergo (i) either further oxidation to give the nitro products (**2**)—(**4**), or (ii) coupling with the starting isoxazolidine (**1a**) to give the azoxy products (**5**) and (**6**).

Control experiments have shown that the nitro-products (**2**) and (**4**) remain unchanged upon u.v. irradiation in acetone or dioxan for 2 h, while the azoxy compounds (**5**) and (**6**), under the same conditions, undergo reversible [*e.g.* (**6**)] or irreversible [*e.g.* (**5**)] transformation<sup>5</sup> to the extent of 20—30%, affording products not observed in the photo-oxygenation of (**1a**).

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