CONVERSION OF ISOXAZOLE DERIVATIVES INTO β -AMINOENONES BY PENTACARBONYLIRON, WATER AND PHOTOIRRADIATION

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Abstract. 3,5-Disubstituted isoxazole derivatives, when irradiated in the presence of pentacarbonyliron and water undergo reductive cleavage of the N-O bond to give β -aminoenones in good yields.

It has been well established that 2,5-diarylisoxazoles photoisomerize to the azirines, which recyclize to the starting isoxazoles or oxazoles, depending on the wavelength of further irradiation.¹ The thermal reaction of isoxazoles have also been noted to undergo N-O bond cleavage to afford azirines.² Recently much attention has been focussed on azirines, which undergo a variety of interesting and useful ring cleavage reactions in the presence of transition metal carbonyls such as $Fe_2(CO)_9$, $^3 Co_2(CO)_8$, 4 and $M(CO)_6$ (M=Mo, 5,6 Cr, 6 W⁶). Among these ring cleavage reactions, Mo(CO)₆-induced efficient intramolecular cycloaddition of 2-formyl-3-phenyl-2H-azirine to 3-phenylisoxazole stands in contrast to the photochemical and thermal behaviors of isoxazoles.⁵ However, the reaction of isoxazole with transition metal carbonyls has not been reported so far.

In connection with the above investigations, we would like to present here the Fe(CO)₅-induced reductive cleavage of 3,5-disubstituted isoxazole derivatives $\underline{1}$ which result in the formation of β -aminoenones $\underline{2}$ under photoirradiation⁷ as shown in Scheme 1.

The general procedure of photoirradiation was as follows. A solution of isoxazole (1 mmol) and an adequate amount of $Fe(CO)_5$ in 20 cm³ of anhydrous or moist solvent containing an equivalent amount of water was irradiated with sunlight⁸ or RPR-350 nm lamps⁹ under a nitrogen atmosphere for a period indicated in Table 1.



Scheme 1

3925

3926

The yields of the products summarized in Table 1 were determined through pyrification by TLC or column chromatography.

Photoirradiations of la, lb and lc (entries A-F) with Fe(CO), in moist acetonitrile afforded β -aminoenones 2a, 2b and 2c in good yields, respectively. In the reactions of <u>la</u>, <u>lb</u> and <u>lc</u> with $Fe(CO)_5$ in anhydrous acetonitrile or benzene (entries G-J), however, 2a, 2b and 2c were obtained in low yields, along with the other products (ca 10-17% yield) in each case. The latter products ¹⁰ are not separated and thus the structures have not been determined at the present stage. Water seems to be a hydrogen source in the present transformations. Even in the reaction in anhydrius solvents, the possibility of stray water can not be ruled The reaction of <u>la</u> or <u>lc</u> with $Fe(CO)_5$ in moist acetonitrile in the dark at out. ambient temperature resulted in the quantitative recovery of <u>la</u> or <u>lc</u>. Furthermore, photoirradiation of lc in moist acetonitrile with RPR-350 nm lamps in the absence of Fe(CO)₅ for 6 h gave no product and <u>lc</u> was recovered quantitatively. Therefore, it is clear that light and Fe(CO) 5 as well as water are indispensable for the present transformations.

Photoirradiation of Fe(CO)₅ has been shown to originate Fe(CO)₄ species in low-temperature matrices.¹¹ In solution and in the absence of nucleophile Fe(CO)₄ collapses to Fe₂(CO)₉ with good efficiency,¹² while in the presence of nucleophile such as pyridine, Fe(CO)₄(pyridine) complex is formed.¹³ Therefore the photochemically generated Fe(CO)₄ species seems to cause the present reactions. With this in mind, the thermal reactions of <u>la</u> with Fe₂(CO)₉ was investigated. Heating a sample of <u>la</u> and Fe₂(CO)₉ at 50 °C for 5 h in moist acetonitrile or anhydrous benzene gave the similar results (entries K and L). Therefore it is also shown that the reductive cleavage of isoxazoles to β-aminoenones is effectively performed by thermal condition using Fe₂(CO)₉.

The mechanism by which the isoxazole system undergoes reductive N-O bond cleavage is of considerable interest. It seems to be possible that the reaction proceeds via nitrene complex, which has been postulated in the reaction of azirines with Fe₂(CO)₀.³ Evidence concerning the mechanistic aspect of the present transformation was obtained by studying the reaction of 2-benzoy1-3-pheny1-2H-azirine 3 (Table 1, entries M-O). Photoirradiation⁸ of 3 (0.5 mmol) and $Fe(CO)_5$ (0.6 mmol) in 10 cm^3 of acetonitrile containing an equivalent amount of water for 4 h resulted in the formation of 2a and isoxazole 1a in 43% and 39% yields, respectively (entry M). However, photoirradiation⁸ of $\frac{3}{2}$ in the absence of Fe(CO)₅ under similar condition, afforded la in 27% yield leaving the starting azirine 3 in a 69% yield (entry N). These facts seem to suggest that $Fe(CO)_5$ induces 3 to undergo the reductive cleavage to give 2a as well as the rearrangement to give la, under photoirradiaiton. Furthermore, heating 3 with Fe₂(CO)₉ in moist acetonitrile at 50 °C afforded 2a and la in 57% and 31% yields, respectively (entry 0). The formation of <u>la</u> from <u>3</u> is noticeable and similar to the case of Mo(CO)₆-induced reaction of 2-formyl-3-phenyl-2H-azirine to give 3-phenylisoxazole. The reaction sequences

Entry	Compound	Solvent	Molar Ratio of Fe(CO) ₅	Lıght	Irradiation Time (h)	Product Yield (%)
A	la	CH ₃ CN-H ₂ O	1.2	Sun ^b	24	2a (74)
В	lb	CH ₃ CN-H ₂ O	1.2	Sun	24	2b (79)
С	lc	CH ₃ CN-H ₂ O	1.2	Sun	24	2c (65)
D	la	CH ₃ CN-H ₂ O	1.2	350 ^C	24	2a (68)
Е	lb	CH ₃ CH-H ₂ O	1.2	350	24	2b (76)
F	lc	CH ₃ CN-H ₂ O	1 2	350	6	2c (72)
G	la	PhH	2.0	350	24	2a (56) ^d
Н	lb	PhH	2.0	350	24	2b (12) ^d
I	lc	PhH	2.0	350	6	2c (59) ^d
J	lc	CH 3 CN	1.2	350	6	2c (10) ^d
K	la	CH ₃ CN-H ₂ O	(1 0) ^e	None	5	2a (66)
\mathbf{L}	la	PhH	(1 0) ^e	None	5	2a (41) ^d
М	3	CH ₃ CN-H ₂ O	1 2	Sun	4	2a (43) + la (39)
N	3	CH ₃ CN-H ₂ O	None	Sun	4	la (23) + 3 (69)
0	3	CH ₃ CN-H ₂ O	(1.0) ^e	None	0.7	2a (57) + la (31)

Table 1. Reductive Cleavage of Isoxazoles and an Azirine^a

a. All products are known compounds and were identified by comparison of spectral data with those of authentic materials.
b. Ref. 8.
c. Ref. 9
d. In this case, minor amount of products (ca 10-17%) was obtained Ref 10
e. Heated at 50 °C in the presence of an equivalent amount of Fe₂(CO)₉.

of <u>3</u> are summarized in Scheme 2. The initial step in this reaction should be Ndonor complexation to give <u>4</u> followed by carbon-nitrogen bond cleavage to give nitrene complex <u>5</u>.³ This intermediate <u>5</u> is trapped by water to give β -aminoenone <u>2a</u>. Another pathway for <u>5</u> should be the cyclization to give 6, of which decomplex-



ation gives <u>la</u>. The isoxazole <u>la</u> could also afford <u>2a</u>, therefore the present reaction of <u>la</u>,<u>b</u>,<u>c</u> with $Fe(CO)_5$ under photoirradiation (entries A-J) or the thermal reaction with $Fe_2(CO)_9$ (entries K and L) should proceed via a common nitrene complex such as <u>5</u>

It is reported that azirines undergo coupling and insertion reactions in the presence of Fe₂(CO)₉ in anhydrous benzene to give pyrroles, ureadiiron hexacarbonyl complexes, diimide complexes, and minor amount of ketones ³ The formation of ketones via a nitrene complex is consistent with the formation of β -aminoenones in the present reactions.

The reductive cleavage of isoxazoles by catalytic hydrogenation is widely applicable to the synthetic transformations of various compounds.¹⁴ The present reaction might serve as another convenient method for the conversion of isoxazoles to β -aminoenones. Further studies including scope and limitation as well as the detailed mechanistic aspect are now underway.

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