

AN UNUSUALLY SELECTIVE PHOTO-INDUCED REARRANGEMENT  
OF 4-ALKOXYCARBONYL-5-FORMYL-2,3-DIHYDRO-6H-1,3-OXAZINES.  
A NEW ROUTE TO PREPARATION OF CONDENSED LACTONES\*

Vladimír OREMUS<sup>a</sup>, Lubor FIŠERA<sup>a</sup>, Hans-Joachim TIMPE<sup>b</sup> and Ute LAMMEL<sup>b</sup>

<sup>a</sup> Department of Organic Chemistry,

Slovak Institute of Technology, CS-812 37 Bratislava, Czechoslovakia and

<sup>b</sup> Department of Photochemistry,

Technical University, DDR-4200 Merseburg, G.D.R.

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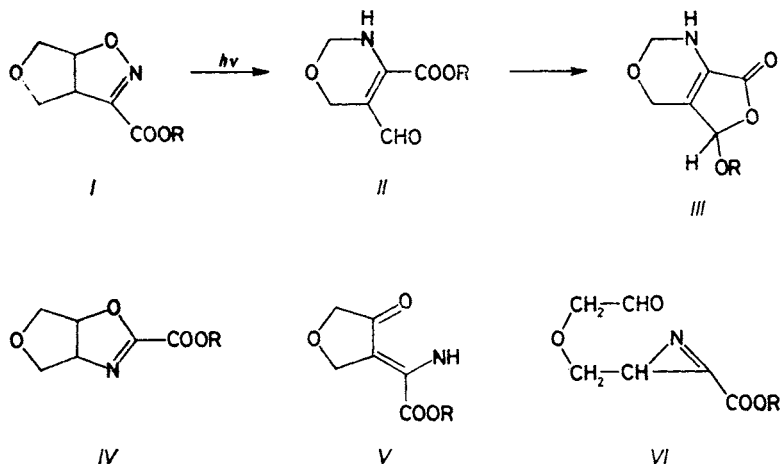
3-R-Alkoxy carbonyl-5-formyl-2,3-dihydro-6H-1,3-oxazines *Ia–Ic* (R = methyl, ethyl, isopropyl) as primary photoproducts formed by a rearrangement of 3-R-alkoxy carbonyl-3a,4,6,6a-tetrahydrofuro[3,4-d]isoxazoles *Ia–Ic* undergo cyclization to bicyclic lactones *IIIa–IIIc* due to further irradiation. The photochemical transformation of compounds *II* into *III* constitutes a new kind of photo-induced rearrangement. The quantum yields are very little dependent on the presence of oxygen and polarity of the solvent. The proposed concerted mechanism of the photo-rearrangement is discussed.

As we recently reported<sup>1–8</sup>, introduction of an oxygen atom to  $\beta$ -position of an isoxazoline oxygen is associated with a highly selective photo-induced rearrangement leading to heterocyclic enaminoaldehydes, e.g. *I*  $\rightarrow$  *II* (aryl or cyano groups can substitute the COOR'). All enaminoaldehydes obtained were found to be photo-unstable towards further irradiation, which was accompanied with formation of polymeric tars. Photochemical reactions of 3-methoxycarbonyl substituted fused isoxazolines, e.g. *Ia*  $\rightarrow$  *IIa* were shown to give one additional product<sup>9</sup>. This paper is, therefore aimed to elucidate its structure and to propose the mechanism of its origination.

The photochemical reaction of 3-methoxycarbonyl-3a,4,6,6a-tetrahydrofuro-[3,4-d]isoxazole (*Ia*) in methanol afforded the expected product of rearrangement – 4-methoxycarbonyl-5-formyl-2,3-dihydro-6H-1,3-oxazine (*IIa*, 69%), and another product (*IIIa*) in 11% yield. Its mass spectrum, showing the molecular radical ion at  $m/z$  174 indicated this substance also to be a product of rearrangement. Spectral data of *IIIa* did not agree with those of any possible rearrangement product of isoxazolines *IV–VI*, which could be expected on grounds of the up-to-date knowledge<sup>10–13</sup>. The absence of a singlet at  $\delta \sim 8–10$  and the doublet at  $\delta \sim 190$  in the

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respective  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra, typical of an aldehyde excludes the structure *VI*, but the presence of singlets at  $\delta$  160.16 and 96.09 evidences the  $\text{C}=\text{C}$  grouping in enaminocarbonyls, triplets at  $\delta$  74.46 and 62.83 prove the preservation of a 2,3-dihydro-6*H*-1,3-oxazine ring and consequently eliminate structures *IV* and *V*. This

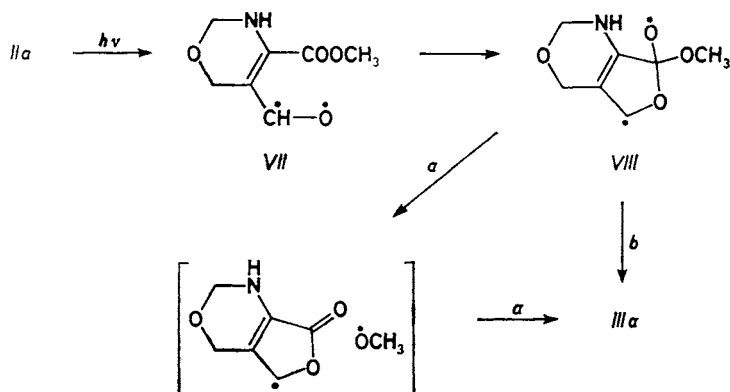


In formulae *I*-*VI*: *a*,  $\text{R} = \text{CH}_3$     *b*,  $\text{R} = \text{C}_2\text{H}_5$     *c*,  $\text{R} = \text{CH}(\text{CH}_3)_2$

finding was further backed by an absorption band at  $\lambda_{\text{max}}$  274 nm excluding the structure of oxazoline *IV* ( $\lambda_{\text{max}}$  reported<sup>5</sup> 257 nm) and 3-aminocarbonyl *V* ( $\lambda_{\text{max}}$  reported<sup>10-13</sup> 330 nm). The ratio of photoproducts *IIa* and *IIIa* is reaction time dependent; an extension of irradiation caused an increase in favour of *IIIa* and decrease of *IIa*. An independent photochemical experiment showed that irradiation of pure *IIa* up to 60% conversion led to *IIIa* as a sole product in 58% yield. Therefore compound *IIIa* was assigned the structure of 6-methoxy-4-oxo-2,3,6-7-tetrahydro[3,4-*d*]1,3-oxazine. In favour of this structure is also the presence of a singlet at  $\delta$  5.66 and a doublet at  $\delta$  99.21 in the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra, respectively, proving the  $\text{CH}_3\text{O}-\text{CHO}$  grouping. Signal at  $\delta$  168.72 and a band at  $1730\text{ cm}^{-1}$  in the IR spectrum are characteristic of lactone. An agreement was found when comparing the 5-alkoxy-2-5*H*-furanone spectral data<sup>14</sup> with those of *IIIa*.

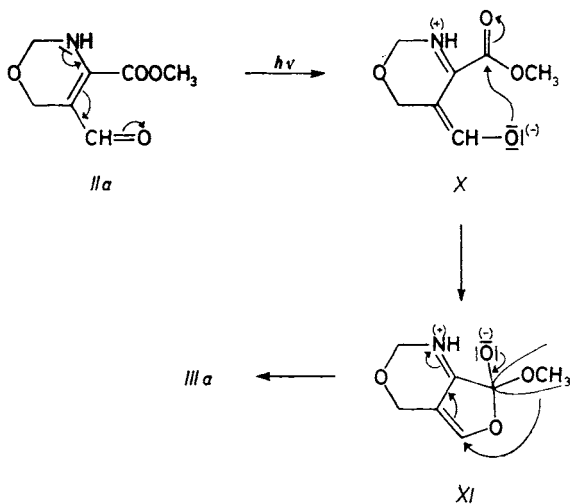
The unsaturated carbonyl compounds are known to undergo various photo-rearrangements and are, therefore, valuable synthons for an easy access to products, the synthesis of which is very complicated<sup>15</sup>. It is our belief that the photochemical rearrangement *IIa*→*IIIa* represents a new kind of selective photorearrangement of unsaturated carbonyl compounds and therefore, we have felt the need to propose its mechanism. The first hypothesis (Scheme 1) considers an excitation in the aldehyde group of *IIa* followed by an attack of an oxygen radical to the methoxycarbonyl

group to form a biradical *VIII* or a radical pair *IX* (reaction path  $\alpha$ ). The step of a similar radical pair was also considered with a photorearrangement of 2-benzoyloxyoxazole<sup>16</sup>. Both radicals *VIII* and *IX* are stabilized by the overlap of radical



SCHEME 1

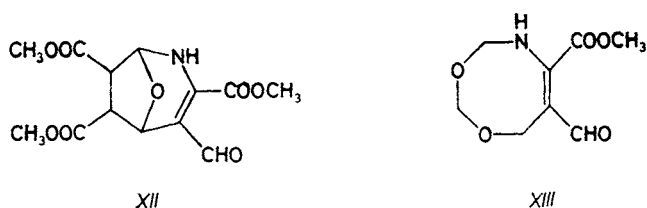
centre with a non-bonding *p*-electron of oxygen and  $\pi$ -electrons of the double bond. A fundamental problem arises, whether the methoxyl group of *IIIa* stems from the starting derivative *IIa* or from the solvent (methanol). To be sure, two complementary experiments were carried out, namely irradiation of *IIa* in acetonitrile and employment of other than methoxy derivatives. The first experiment afforded the same



SCHEME 2

rearrangement product *IIIa* in 71% yield, thus proving that the methoxy group did not come from methanol. Ethyl (*Ib*) and isopropyl (*Ic*) esters needed for the second experiment were prepared by a 1,3-dipolar cycloaddition of the corresponding alkoxy-carbonylnitrile oxides to 2,5-dihydrofuran. Photorearrangement up to 80% conversion afforded the primary photo-products *IIb*, *IIc*. Further irradiation in methanol led to 6-ethoxylactone *IIIb* and 6-(1-methylethoxy)lactone *IIIc*, respectively, thereby proving the universality and intramolecular course of the photorearrangement. The structures of *Ib*, *Ic*, *IIIb*, *IIIc* were deduced by analogy as detailed for compounds *Ia–IIIa*.

The second possible mechanism (Scheme 2) is parallel with that proposed for the photorearrangement of dienones as described in literature<sup>17</sup>. A similar zwitter-ionic structure as *X* was considered for [2 + 2] photocycloadditions of enamino-carbonyl compounds<sup>18</sup>. Irradiation of the oxabicyclic derivative *XII* (monitored by UV spectroscopy, no preparative experiments) has an analogous course leading to a fused lactone. It is worth noting that rearrangement *II* → *III* proceeded only under irradiation and that cyano derivatives did not undergo this rearrangement<sup>8</sup> like the eight-membered 1,3-dioxo-5-azocine (*XIII*). The latter, of course, underwent a *cis–trans* isomerization, as we have recently reported<sup>2,3</sup>.



To throw more light on the mechanism, we monitored the photolysis of *IIa* → *IIc* applying the monochromatic light  $\lambda$  254 and 356 nm, respectively, by UV spectra at low concentrations ( $10^{-4}$  mol l<sup>-1</sup>) in various solvents. Irradiation of unsaturated  $\gamma$ -oxoesters *IIa–IIc* with a light of  $\lambda > 300$  nm in heptane, dioxane, acetonitrile, methanol, and water caused a typical situation plotted in Fig. 1. The long-wave absorption maximum at  $\lambda \sim 320$  nm disappeared under formation of another one at  $\lambda \sim 270$  nm. This photoreaction is extraordinarily selective as can be concluded from isosbestic points shown in Fig. 1. Evaluation of the time versus spectral course by an extinction-difference diagram<sup>19</sup> indicated a simple A → B reaction. The same photoreaction course was also observed when applying the  $\lambda$  254 nm wavelength (*IIa*, the presence of isosbestic points at 233 and 291 nm).

Spectral changes during photolysis made it possible to determine in a simple way the quantum yields ( $\Phi$ ) of the reaction. The measured data listed in Table I reveal a minute influence of both the solvent and oxygen on the photorearrangement of

*II* → *III*. Different values  $\Phi$  measured in heptane and water are probably due to a possible enamine-imine tautomerism. Also the alkoxy substituent was found to have little influence on the photorearrangement. On the other hand, the irradiation wavelength is important, this being probably due to population of various excited states. The data obtained, i.e. the independence of  $\Phi$  on the solvent effect contrasted with the presence of zwitter-ionic intermediate (mechanism shown in Scheme 2) but is in accordance with the mechanism via the biradical *XI* (Scheme 1). The most probable rationalization is to presume concerted processes *VII* → *VIII* and *VIII* → *III* like with a classical di- $\pi$ -methane rearrangement<sup>20</sup>.

TABLE I

Quantum yields<sup>a</sup> of photorearrangement *II* → *III* at 365 nm

Compound	Solvent						
	heptane	benzene	dioxane	acetonitrile	methanol	water	
<i>IIa</i>	0.033	0.13	0.081	0.13	0.10	0.032 <sup>b</sup>	0.045
	—	0.14	0.096	0.15	0.097	0.025 <sup>b</sup>	—
<i>IIb</i>	—	—	0.046	—	0.099	0.033 <sup>b</sup>	—
	—	—	0.039	—	0.089	0.028 <sup>b</sup>	—
<i>IIc</i>	—	—	—	—	0.081	—	0.06

<sup>a</sup> Upper value obtained in the presence of oxygen, the lower one after a 30 min passing of argon through the mixture prior to measurement; <sup>b</sup> the  $\Phi$  value at irradiation with a light of a 254 nm wavelength.

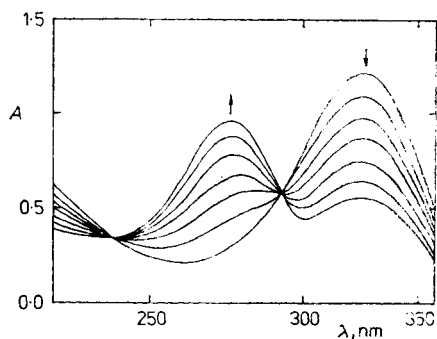


FIG. 1

Spectral change during irradiation of *I* ( $1 \cdot 10^{-4} \text{ mol l}^{-1}$  in methanol) by UV radiation (365 nm), at 0, 1, 2, 3, 4, 5, and 6 min of irradiation time

## EXPERIMENTAL

The melting points are uncorrected. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of deuteriochloroform solutions were recorded with a Tesla 487 C (80 MHz) and Jeol FX-60 apparatuses, respectively, tetramethylsilane being the internal reference. The UV spectra ( $\epsilon$  in  $\text{m}^2 \text{mol}^{-1}$ ) of methanolic solutions were measured with a Perkin-Elmer, model 323 spectrophotometer in tempered cells. The electron-impact mass spectra were taken with an MS 902 S instrument at an ionization energy 70 eV, trap current 100  $\mu\text{A}$ . The IR spectra of chloroform solutions were run with a Specord IR-60 spectrophotometer. Methyl-, ethyl- and isopropylchlorooximido acetates were prepared according to literature<sup>21</sup>. A low-pressure quartz mercury lamp Tohiba GL-15 (15 W) and a tempered quartz 300 ml-reactor with a forced circulation were employed at irradiation temperature 15°C. The reaction course was monitored either by chromatography on Silufol sheets, or by UV spectroscopy. The reactions were carried out till the starting isoxazolines *I*, or oxazines *II* were consumed. Measurement of quantum yields by monochromatic light  $\lambda$  254 and 365 nm was described in our previous papers, i.e. ref.<sup>8</sup> and ref.<sup>22</sup>, respectively.

3-Alkoxy-carbonyl Substituted Isoxazolines *Ia*–*Ic*

A solution of alkyl chlorooximidoacetate (10 mmol) in ether (20 ml) was added dropwise to a stirred solution of 2,5-dihydrofuran (5 ml) and triethylamine (10 mmol) in ether (20 ml) at room temperature during 5 h. The mixture was then stirred for additional 1 h, the separated triethylammonium chloride was filtered off and the solvent was removed under reduced pressure. The product was chromatographed over a silica gel-packed column with chloroform to yield the respective isoxazolines *Ia*–*Ic*; the first fractions contain the corresponding dimers of alkoxy-carbonylformyl nitrile oxide in 30 to 50% yields.

3-Methoxycarbonyl-3a,4,6,6a-tetrahydrofuro[3,4-d]isoxazole (*Ia*) was characterized in our previous paper<sup>9</sup>.

3-Ethoxycarbonyl-3a,4,6,6a-tetrahydrofuro[3,4-d]isoxazole (*Ib*), yield 35%, m.p. 57–60°C. For  $\text{C}_8\text{H}_{11}\text{NO}_4$  (185.2) calculated: 51.9% C, 5.99% H, 7.56% N; found 52.07% C, 6.14% H, 7.41% N.  $^1\text{H}$  NMR: 5.35 dd, 1 H (H-6a,  $J(1) = 3.5$  Hz,  $J(2) = 9$  Hz); 4.46–3.91 m, 5 H ( $2 \times$  H-6, H-3a,  $\text{CH}_2$ -ester); 3.77–3.52 m, 2 H ( $2 \times$  H-4); 1.29 t, 3 H ( $\text{CH}_3$ -ester,  $J$  7 Hz). UV spectrum,  $\lambda_{\text{max}}$  (log  $\epsilon$ ): 240 nm (2.60).

3-(1-Methylethoxycarbonyl)-3a,4,6,6a-tetrahydrofuro[3,4-d]isoxazole (*Ic*), yield 43%, m.p. 47–50°C. For  $\text{C}_9\text{H}_{13}\text{NO}_4$  (199.2) calculated: 54.26% C, 6.58% H, 7.05% N; found: 54.43% C, 6.39% H, 7.13% N.  $^1\text{H}$  NMR: 5.36–4.97 m, 2 H (H-6a, O–CH-ester); 4.25–3.42 m, 5 H ( $2 \times$  H-6,  $2 \times$  H-4, H-3a); 1.31 d, 6 H ( $2 \times$   $\text{CH}_3$ ,  $J$  7 Hz). UV spectrum,  $\lambda_{\text{max}}$  (log  $\epsilon$ ): 242 nm (2.81).

Photochemical Rearrangement of *I*, *II*

A solution of the respective isoxazoline *Ia*–*Ic*, or oxazine *IIa*–*IIc* (3 mmol) in methanol (300 ml) was irradiated till the starting compound was consumed. The solvent was evaporated under reduced pressure and the product was purified by column chromatography (silica gel, chloroform).

Irradiation of *Ia* afforded: a) 4-methoxycarbonyl-5-formyl-2,3,6,7-tetrahydro-6H-1,3-oxazine (*IIa*) in 69% yield (ref.<sup>9</sup>); b) 6-methoxy-4-oxo-2,3,6,7-tetrahydrofuro[3,4-d]-1,3-oxazine (*IIIa*), yield 11%, m.p. 148–150°C. For  $\text{C}_7\text{H}_9\text{NO}_4$  (171.1) calculated: 49.12% C, 5.30% H, 8.18% N; found: 49.33% C, 5.16% H, 8.01% N.  $^1\text{H}$  NMR: 5.70–5.62 m, 1 H (H-6); 5.27 bs, 1 H (NH); 4.80 to 4.69 m, 2 H ( $2 \times$  H-2); 4.46 s, 2 H ( $2 \times$  H-7); 3.51 s, 3 H ( $\text{OCH}_3$ ).  $^{13}\text{C}$  NMR: 168.72 s (C=O);

160·16 s (C-3a); 99·21 d (C-6); 96·09 s (C-6a); 74·46 t (C-2); 62·83 t (C-7); 55·36 q (OCH<sub>3</sub>). IR spectrum, cm<sup>-1</sup>: 3 216, 3 045, 2 910, 1 730 (C=O), 1 640, 1 540, 1 396, 1 310, 1 202. Mass spectrum, *m/z*: 171 (M<sup>+</sup>), 154 (M - OH), 112 (M - COOCH<sub>3</sub>), 81, 70, 59. UV spectrum, λ<sub>max</sub>(log ε): 273 nm (3·13).

Irradiation of *Ila* under the same conditions furnished *IIIa* in 71% yield.

Irradiation of *Ib* led to: a) 4-ethoxycarbonyl-5-formyl-2,3-dihydro-6H-1,3-oxazine (IIb), yield 63%, m.p. 78–80°C. For C<sub>8</sub>H<sub>11</sub>NO<sub>4</sub> (185·2) calculated: 51·89% C, 5·99% H, 7·56% N; found: 51·77% C, 6·23% H, 7·81% N. <sup>1</sup>H NMR: 10·07 s, 1 H (CHO); 5·93 bs, 1 H (NH); 4·77–4·65 m, 2 H (2 × H-2); 4·52 s, 2 H (2 × H-6); 4·36 q, 2 H (OCH<sub>2</sub>); 1·35 t, 3 H (CH<sub>3</sub>). UV spectrum (acetonitrile), λ<sub>max</sub>(log ε): 319 nm (3·02); b) 6-ethoxy-4-oxo-2,3,6,7-tetrahydrofuro[3,4-d]-1,3-oxazine (IIIb), yield 9%, m.p. 218–220°C. For C<sub>8</sub>H<sub>11</sub>NO<sub>4</sub> (185·2) calculated: 51·89% C, 5·99% H, 7·56% N; found: 51·65% C, 5·74% H, 7·81% N. <sup>1</sup>H NMR: 5·95 bs, 1 H (NH); 5·72 s, 1 H (H-6); 4·80–4·67 m, 2 H (2 × H-2); 4·42 s, 2 H (2 × H-7); 4·50–4·40 m, 2 H (OCH<sub>2</sub>); 1·22 t, 3 H (CH<sub>3</sub>, *J* 7·0 Hz).

Irradiation of *Ic* yielded: a) 4-(1-methylethoxycarbonyl)-5-formyl-2,3-dihydro-6H-1,3-oxazine (IIc), yield 60%, m.p. 70–72°C. For C<sub>9</sub>H<sub>13</sub>NO<sub>4</sub> (199·2) calculated: 54·26% C, 6·58% H, 7·03% N; found: 54·45% C, 6·39% H, 7·22% N. <sup>1</sup>H NMR: 9·91 s, 1 H (CHO); 6·60 bs, 1 H (NH); 5·40 to 4·92 m, 1 H (CH-ester); 4·66 s, 2 H (2 × H-2); 4·45 s, 2 H (2 × H-6); 1·27 d, 6 H (2 × CH<sub>3</sub>-ester, *J* 6 Hz); b) 6-(1-methylethoxy)-4-oxo-2,3,6,7-tetrahydrofuro[3,4-d]-1,3-oxazine (IIIc), yield 9%, m.p. 204–206°C. For C<sub>9</sub>H<sub>13</sub>NO<sub>4</sub> (199·2) calculated: 54·26% C, 6·58% H, 7·03% N; found: 54·33% C, 6·71% H, 6·93% N. <sup>1</sup>H NMR: 5·70 s, 1 H (H-6); 5·25–5·00 m, 1 H (OCH); 4·82–4·69 m, 2 H (2 × H-2); 4·42 s, 2 H (2 × H-7); 1·37 d, 6 H (2 × CH<sub>3</sub>, *J* 7·0 Hz). UV spectrum, λ<sub>max</sub>(log ε): 285 nm (2·34).

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