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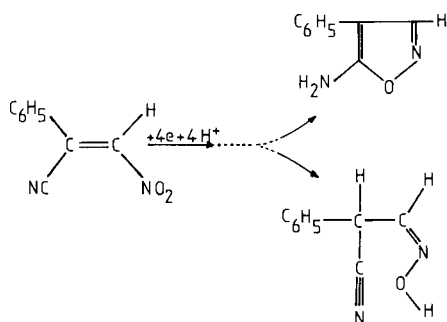
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It is known that the electrochemical reduction of the 1-phenyl-1-cyanonitroethylene leads to the formation of a cyclic compound, the 5-amino-4-phenyl isoxazole, but the mechanism of such a cyclization, which is pH dependent, is not clearly established. Pulse radiolytic methods were used to follow the various stages resulting from the reduction of the 1-phenyl-1-cyanonitroethylene by the radical anion COO^- in order to obtain a better understanding of the preceding reduction. The transient spectra are studied between 250 and 400 nm for times ranging from 4 microseconds to several minutes after the pulse; one of these spectra concerns the ene hydroxylamine. As expected, the changes and evolution of the spectra are pH dependent and corresponding mechanisms are proposed to explain the cyclization following the formation of the ene hydroxylamine. A general scheme is given taking into account all the results obtained.

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Introduction.

It has been shown (1,2) that the electrochemical reduction of 1-phenyl-1-cyanonitroethylene (α -cyano- β -nitrostyrene) in aqueous-organic solutions leads to the formation of 5-amino-4-phenyl isoxazole. At pH 7.7, such a cyclization is stoichiometric, but at pH 1.3, 1-cyano-1-phenylacetaldoxime (*Z*-configuration) also appears.



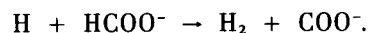
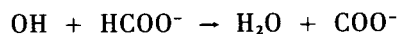
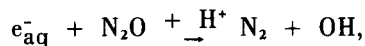
It has been independently shown that the oxime gives isoxazole according to complex kinetics that depends essentially on the pH. For instance, in a mixture of these two products ($5 \times 10^{-4}M$), it has been observed that the characteristic absorption of isoxazole doubled in 13 minutes at pH 1.4 and in 5 minutes at pH 3.7, whereas the reaction becomes quasi instantaneous at pH 7.

Several authors have invoked, either for the chemical formation of oximes (3-8) or for the reduction of the nitroethylenic derivatives (9,10), the intermediate formation of the ene hydroxylamine $>C=C'-NHOH$, but without any

possibility of direct observation. Likewise, classical electrochemical methods (polarography and cyclic voltametry) applied to the study of the preceding reaction, did not allow us to observe this suggested transient species.

Thus, it was interesting to use pulse radiolytic methods in order to study the possible existence of short lived species during the reduction of 1-phenyl-1-cyanonitroethylene and the subsequent cyclization. It is well-known that by these methods, it is possible to form very rapidly oxidizing or reducing radicals (OH , e_{aq}^- , H , O_2^- , COO^- , CO_3^- ...) and to observe spectrophotometrically the kinetics of the induced reactions in time-scales ranging from microseconds to minutes.

The COO^- radical anion was chosen for this work, because it was possible, under our experimental conditions, to produce it in a fraction of a microsecond by irradiating deaerated aqueous solutions of sodium formate, 0.16M, saturated with nitrous oxide. The species produced (OH , H and e_{aq}^-) in the radiolysis of water are then quantitatively transformed into COO^- (11,12) according to:



EXPERIMENTAL

Materials.

The 1-phenyl-1-cyanonitroethylene was prepared by direct nitration of

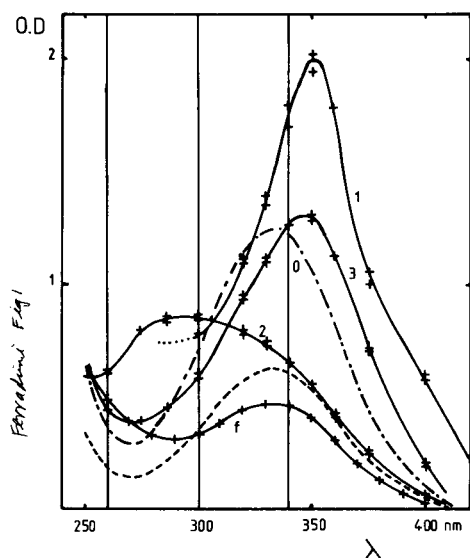


Figure 1-Spectra at pH 3.7 (with respect to the solvent)

..... 0 before the pulse
 1 4 μ s after the pulse
 2 3 ms after the pulse
 3 100 ms after the pulse
 f final product
 ----- the half of the initial spectra

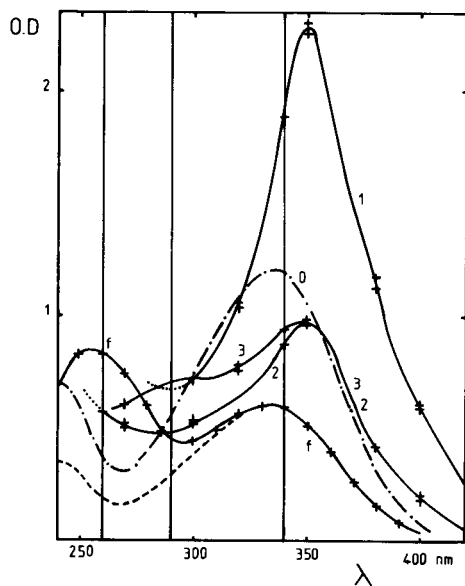


Figure 2-Spectra at pH 6.6 (with respect to the solvent)

..... 0 before the pulse
 0 5 μ s after the pulse
 2 500 μ s after the pulse
 3 10 ms after the pulse
 f final product
 ----- the half of the initial spectra

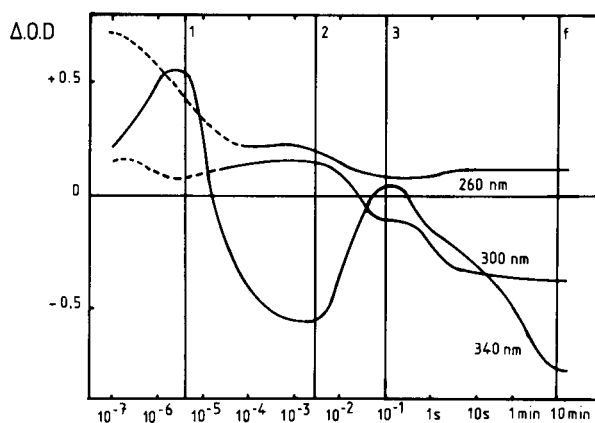


Figure 3-o.d. Changes with Respect to the Initial Spectrum pH 3.7 (curves were directly drawn from the oscillograms)

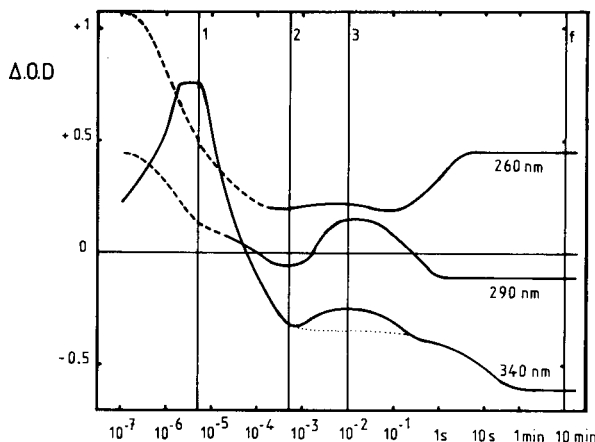


Figure 4-o.d. Changes with Respect to the Initial Spectrum pH 6.6 (curves were directly drawn from the oscillograms)

1-phenyl-1-cyanoethylene with nitrogen peroxide (2). About 50 micromoles of the product was then dissolved in 1 liter of triply distilled water with formic acid 0.08M and sodium formate 0.08M (pH 3.7) or sodium formate 0.16M (pH 6.6). Before each series of irradiations, the concentration was checked spectrophotometrically from known values (2) corrected for our experimental conditions (λ max = 332 nm, ϵ = 9800 $M^{-1}cm^{-1}$ and λ max = 237 nm, ϵ = 6940 $M^{-1}cm^{-1}$).

Irradiation Set-Up.

The source of pulsed electrons was a modified Febetron 707 accelerator used at CEN Saclay (DRA-SRIRMa). In this apparatus the discharge from a series of capacitor-inductance modules is applied to the field emission cathode of a vacuum tube. A magnetic selection of 1.8 MeV electrons is then used to reduce the total pulse length to about 20 nanoseconds (13). The solutions are contained in a spectro-sil cell ($2.5 \times 2.5 \times 0.25$ cm). At each pulse, the energy absorbed by the solution was about 25 krad so that the initial concentration of COO^- produced was about $1.5 \times 10^{-4}M$.

Measurements.

The spectrophotometric analysis was carried out with a standard device including a xenon lamp, a monochromator and a photomultiplier.

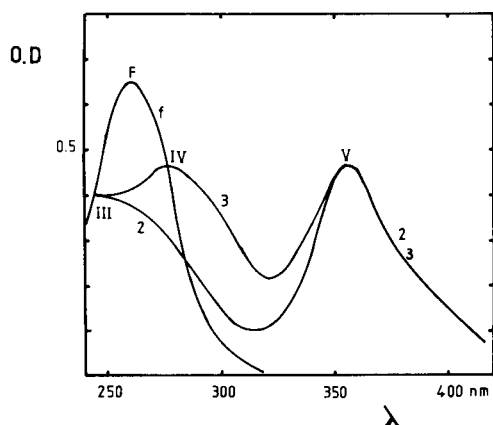


Figure 5-Spectra of the Transient Formed after the Disproportionation pH 6.6 (with respect to the solvent containing 50% of the initial product)

- 2: after 0.5 ms (transients III + V)
 3: after 10 ms (transients IV + V)
 f: final product (F)

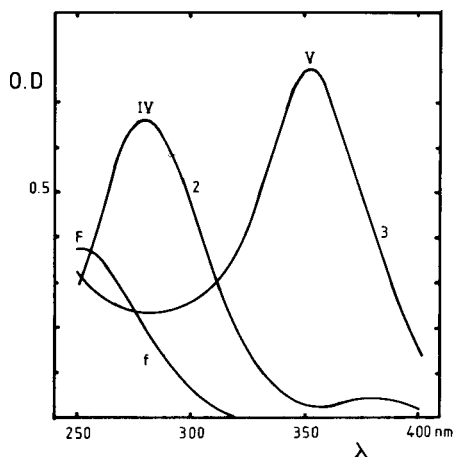


Figure 6-Spectra of the Transients Formed after the Disproportionation pH 3.7 (with respect to the solvent containing 3/8 of the initial product)

- 2: after 3 ms (transient IV)
 3: after 100 ms (transient V)
 f: final product (F)

The analyzing light-path in the solution was 2.5 cm. For each wavelength employed, the changes of the absorption with time were recorded photographically using an oscilloscope (Tektronix 454), the start of the pulse being taken as the origin of the time-scale. All measurements were made at room temperature ($\sim 20^\circ$).

Results.

Absorption Spectra.

The concentration of 1-phenyl-1-cyanonitroethylene ($\sim 5 \times 10^{-5}M$) was chosen less than that of COO^- initially formed ($\sim 1.5 \times 10^{-4}M$) (see interpretation). Preliminary

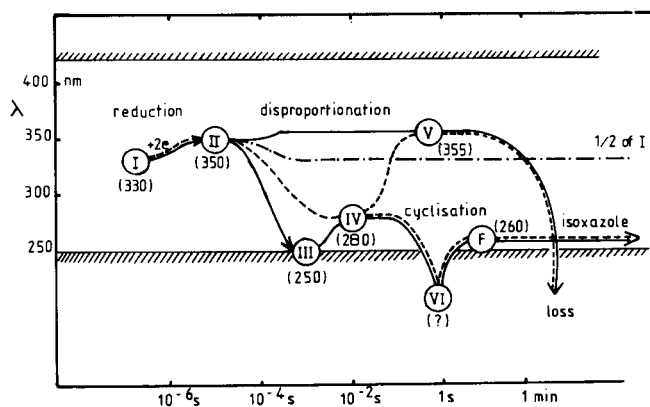


Figure 7-Evolution Scheme of the Transient
 ——— pH 6.6
 - - - - pH 3.7

results showed that various transients play a role in the reaction and that their life-times are very different. Hence we determined the absorption spectra of the irradiated solution after different times which were chosen to correspond, as well as possible, to the plateau of the kinetic changes. Figures 1 and 2, respectively, give the results obtained at pH 3.7 and 6.6. The optical densities are given with respect to a 0.16M formate aqueous solution. Curves 0 are the spectra of the initial product before irradiation. Curves 1, 2 and 3, respectively, show the spectra determined after 4 μs , 3 ms and 100 ms (pH 3.7, Figure 1), 5 μs , 0.5 ms and 10 ms (pH 6.6, Figure 2). The curve f is the final spectrum determined with a conventional spectrophotometer at about 10 minutes after the pulse. It can be seen that: (1) For times of about 4-5 μs after the pulse at both pH values, the same species appears with a maximum of absorption at $\lambda = 350$ nm (curves 1, Figures 1 and 2). (2) At pH 3.7 the decay of this absorption leads in about 3 ms to a new absorption spectrum with $\lambda_{max} = 290$ nm (curve 2, Figure 1). At pH 6.6 the phenomenon seems more complex: an intermediate spectrum is observed after 0.5 ms (curve 2, Figure 2) with a maximum at about 350 nm and the spectrum obtained after 10 ms shows, beyond this remaining maximum, only a shoulder at 290 nm instead of the maximum found in the acid medium. At pH 3.7 the characteristic absorption at 350 nm appears only at about 100 ms (curve 3, Figure 1), whereas the transient which absorbs at 290-300 nm strongly decays. (3) The final spectrum presents two maxima at 335 nm and near 250 nm. At pH 6.6 its intensity corresponds quantitatively for $\lambda \geq 310$ nm to half that of the spectrum of the initial product (curve f, Figure 2). For the same wavelength region in the solution at pH 3.7, the final intensity corresponds only to 3/8 of the original value (curve f, Figure 1).

Kinetics.

The spectral changes as a function of time were observed near the characteristic wavelengths of the preceding spectra, *i.e.*, 260, 290-300 and 340 nm. Figures 3 and 4 respectively give for *pH* 3.7 and 6.6, the o.d. changes measured at these wavelengths with respect to the initial spectra versus the logarithm of time. The observation times range from 100 nanoseconds to 10 minutes and the values corresponding to the spectra in the preceding figures are indicated as 1, 2, 3, f vertical lines.

At *pH* 3.7 (Figure 3) and 340 nm an intense absorption appears in some microseconds which then decreases and becomes stable at about 3 ms. During the same time the o.d. at 300 nm slightly increases. From 3 to 100 ms the absorption at 340 nm strongly increases again and then decreases. The stable final value is reached slowly at 340 nm and quickly at 260 and 300 nm.

At *pH* 6.6, after a similar rapid absorption formation and decay at 340 nm, the absorption increase at 290 nm appears but later (10 ms) and after a period of relative stability (Figure 4). There is not, as at *pH* 3.7, the same reappearance of the large increase at 340 nm.

Interpretation and Discussion.

Analysis of Spectra.

This analysis is based on the following considerations: (1) The duration of uv absorption of COO^- (especially at 260 and 290 nm) cannot be greater than 50 μs since it is limited by the second order reaction of COO^- with itself ($k = 1.5 \times 10^9 \text{M}^{-1}\text{second}^{-1}$) (14). Thus, COO^- is not involved in the subsequent kinetics. (2) The absorption at 340 nm decreases until about 1-2 minutes, *i.e.*, even after the complete stabilization (some seconds) at 260 nm, characteristic wavelength of the final product. With regard to the yield of cyclization, this absorption at 340 nm corresponds to a loss which is greater at *pH* 3.7 than at *pH* 6.6. (3) The fact that, at *pH* 6.6, the final spectrum shows that half of the initial 1-phenyl-1-cyanonitroethylene is still present in spite of the excess of the reducing COO^- employed, strongly suggests that two electrons per molecule are involved in the reduction: the species absorbing at 350 nm and formed after some microseconds would come from two successive reduction reactions and its disproportionation (~ 1 ms) would give back 50% of the initial compound thus present during all the ulterior steps.

a) *pH* 6.6.

On this basis the optical densities corresponding to 50% of the initial concentration have been subtracted from the final spectrum and from those observed at 0.5 and 10 ms. The results of this correction are shown in Figure 5. It can be seen that the final spectrum (f) with $\lambda_{\text{max}} = 260$ nm (species F) is similar to the known spectrum of the 5-amino-4-phenylisoxazole (1) produced by electrochemical reduction (2). The yield of the cyclization,

calculated with $\epsilon_{260} = 15,000 \text{M}^{-1}\text{cm}^{-1}$, is then equivalent to 70% of the 1-phenyl-1-cyanonitroethylene consumed.

The step at 10 ms (curve 3) corresponds to two transients with distinguishable maxima, which decay at different rates. One of them, (IV), with a maximum near 280 nm, could be the ene-hydroxylamine which has been invoked as an intermediate in this kind of reaction: it may be noticed that compounds with similar type of bonds absorb in the same region, $\text{C}_6\text{H}_5\text{-C}(\text{CN})=\text{CH}(\text{NHCH}_3)$ at 313 nm ($\epsilon = 11,400 \text{M}^{-1}\text{cm}^{-1}$) and 293 nm ($\epsilon 12,600 \text{M}^{-1}\text{cm}^{-1}$), $\text{C}_6\text{H}_5\text{-C}(\text{CN})=\text{CH}(\text{O}^-)$ at 286 nm ($\epsilon = 14,200 \text{M}^{-1}\text{cm}^{-1}$) (15). The other one, (V), with a maximum at 355 nm and decaying very slowly would lead to the above decrease.

The step at 0.5 ms (curve 2) already contains the spectrum of this transient (V) and also evidence of a precursor (III) of the ene-hydroxylamine, precursor which seems to come directly from the disproportionation ($2 \times \text{II} \rightarrow \text{III} + \text{I}$).

b) *pH* 3.7.

Concerning the acid solutions, the o.d. corresponding to the half of the initial amount of 1-phenyl-1-cyanonitroethylene has been also subtracted from the spectra at steps 3 and 100 ms (Figure 6).

After this correction the step at 3 ms (curve 2) shows also the ene-hydroxylamine (IV) spectrum with $\lambda_{\text{max}} \cong 280$ nm but, unlike the corresponding stage at *pH* 6.6, does not contain any contribution of V at 355 nm.

It is only after 100 ms (curve 3) that the absorption of this slowly decaying species V becomes maximal: this species V seems then, in this case, to be formed by the disappearance of a fraction of the ene-hydroxylamine ($\text{IV} \rightarrow \text{V}$).

In the final spectrum the correction has only taken into account 3/8 of the initial o.d. for the reason noted above which implies that another undetected loss reaction occurs. At this *pH* 3.7, the isoxazole F seems also to be formed during the decay of the ene-hydroxylamine (IV) but its maximum is slightly shifted probably because of the accumulation of other stable products coming from the various loss-processes. The yield is then only 33% of the amount of the 1-phenyl-1-cyanonitroethylene effectively disappeared.

Evolution Scheme.

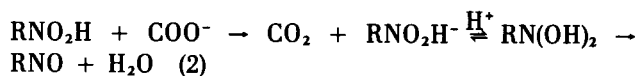
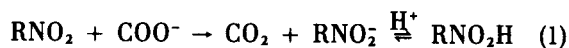
The scheme of Figure 7 summarizes the filiations that may be proposed between the various transients.

The species I (330 nm) is the initial compound. Species II (350 nm) would be formed from the double-reduction of I by COO^- radicals before their complete disappearance. Species III and V (*pH* 6.6) or IV (*pH* 3.7) would be produced after the disproportionation of II by which the half of I

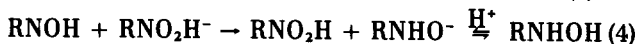
would be regenerated. The overall reduction corresponds, then, to a transfer of 4 electrons.

It has been indicated that transient IV (280 nm) can be identified as the ene-hydroxylamine that finally leads to the cyclization into 5-amino-4-phenylisoxazole F (260 nm). But its precursor III (250), appearing only at pH 6.6, is not yet identified. This is also true for V (355) which is directly formed after the disproportionation at pH 6.6 but comes from IV at pH 3.7. Species V (355) leads to a loss in the cyclization process without any concomitant appearance of the absorption of another species in the wavelength range studied.

Concerning the overall four equivalent reduction leading to the formation of the ene-hydroxylamine (IV or its precursor III) through the disproportionation of II, the exchange of two electrons with COO^- radicals can be written:

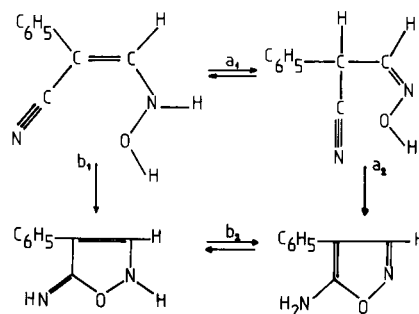


The initial step when nitro-compounds are reduced, either electrochemically (16) or using chemical reducing agents (17,18) and particularly COO^- (19) has been shown to involve the addition of a single electron, the nitro-radical anion RNO_2^- giving a characteristic esr spectrum. In the presence of an excess of COO^- the reaction (2) could intervene and, after the complete disappearance of COO^- , the nitroso-compound ($\text{II} = \text{RNO}_2\text{H}^-$, RN(OH)_2 or RNO) is then formed in quantities approximately equivalent to the initial concentration of RNO_2 (I). However, small concentrations of the nitro-radical RNO_2H^- still remaining in the solution could initiate a chain reaction leading to the here observed disproportionation of the compound II, e.g.:

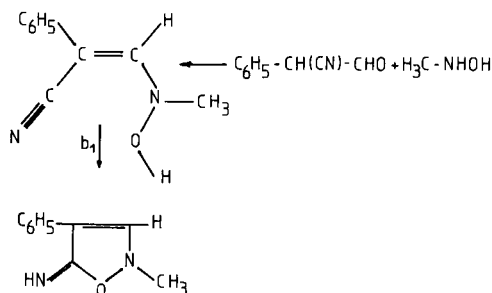


Following this mechanism, the chosen experimental conditions ($[\text{RNO}_2]_0 < [\text{COO}^-]_0$) lead then to the stoichiometry observed at pH 6.6 ($[\text{RNO}_2]_\infty = \frac{1}{2} [\text{RNO}_2]_0$). In such a way the cyclization yield was better than that would be obtained in the opposite condition ($[\text{RNO}_2]_0 > [\text{COO}^-]_0$), since the disproportionation reaction following the first electron exchange would have led to a greater back-formation of RNO_2 ($[\text{RNO}_2]_\infty = \frac{3}{4} [\text{RNO}_2]_0$).

Concerning the cyclization following the decay of the ene-hydroxylamine IV, two hypotheses may be formulated: (a) one of the possible pathways supposes in the first stage the tautomeric equilibrium (a_1) with the oxime form followed by the cyclization of this oxime into isoxazole (a_2); and (b) the other way implies a direct cyclization (b_1) into isoxazole imide with a subsequent tautomeric shift to isoxazole (b_2).



The route (a) seems more probable than (b) since, as was mentioned in the introduction, the transformation oxime-isoxazole has been observed. However, although the electrons are more delocalized in the ene-hydroxylamine than in its tautomer oxime, the route (b) cannot be excluded. Indeed the cyclisation obtained by the reaction of hydroxylamines with the 1-phenyl-1-cyano acetaldehyde occurs even when methylhydroxylamine is used, leading then to the formation of isoxazolone imide (1): due to the blocked structure the two tautomeric equilibria are then impossible and the only possible mechanism is the route (b_1).



In fact, the pulse radiolytic results give a clue to a possible choice between the two hypotheses. It can be seen on figure 4 that the decay of the ene-hydroxylamine followed at 290 nm, is finished nearly 5 seconds before the production of isoxazole observed at 260 nm. Thus the occurrence of a non-absorbing supplementary transient must be supposed (VI on Figure 7). This transient cannot be the isoxazolone which strongly absorbs (8) at 285 nm ($\epsilon \sim 6,400 \text{ M}^{-1}\text{cm}^{-1}$) and at 257 nm ($\epsilon \sim 7,300 \text{ M}^{-1}\text{cm}^{-1}$). These results are then rather in agreement with the route (a) which implies the nonabsorbing oxime transient than with the route (b).

Conclusion.

This study shows that pulse radiolytic methods are able to furnish information necessary for the knowledge of reaction mechanisms. In this specific case it was possible to produce in very short times (some μs) a mild reducing radical able to initiate a sequence of reactions leading to the required effect: reduction of the 1-phenyl-1-cyano-nitroethylene with cyclization to 5-amino-4-phenylisox-

azole. After this initial radiolytic step, the history of the overall process could be traced using fast spectrophotometric methods (Figures 3 and 4). The existence of transient species has been clearly demonstrated either by kinetic analysis or through their characteristic absorption spectra.

It has been experimentally shown that the reduction of the 1-phenyl-1-cyanonitroethylene in isoxazole involved an ene-hydroxylamine as a transient and some details were obtained about the mechanism following the decay of this transient. However, other experiments concerning compounds with structures similar to this one here studied are necessary in order to precisely determine the nature of some other transients and the mechanism of their decays.

Acknowledgement.

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