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NMR kinetic analysis of photochromic quinolone photoproducts

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Abstract—The whole photochromic reaction, photocolouration, thermal bleaching and photodegradation, of a quinolone derivative has been kinetically monitored by product-by-product NMR spectroscopy. The mechanism of reactions has been established from quantitative kinetic data analysis.

The reversible photoenolization of ortho-alkyl substituted aromatic ketones[1–4] is an example of photochromism.[5] Among the heteroaromatic ketones, photochromism has been observed with 2-benzyl-3-benzoylchromones and 2-benzyl-3-benzoyl-4-quinolones.[6,7] In the framework of the photochromism involving hydrogen transfer/cyclization sequence,[8,9] we recently reported[10] the complete NMR structural elucidation of the photoproducts of the photochromic 3-benzoyl-2-benzyl-6,7-difluoro-1-propyl-1*H*-quinolin-4-one $\mathbf{P_0}$. It was shown that UV irradiation of this new photochromic quinolone led to the formation of two reversible photoenols $\mathbf{P_1}$ and $\mathbf{P_2}$ together with several other cyclized permanent photoproducts $\mathbf{P_3}$, $\mathbf{P_4}$ and $\mathbf{P_5}$ which have been assigned to photodegradation. On the basis of structural elucidation and qualitative observation of their photochemical and thermal evolution, a plausible mechanism was assumed, but the details of the thermal and photochemical pathways were not investigated quantitatively.

The purpose of this work is to provide a quantitative analysis of the whole photochromic and photodegradation processes based on a NMR product-by-product monitoring followed by a numerical modelling of the recorded kinetics. After UV irradiation in degassed toluene-d_8,[11] quinolone $\mathbf{P_0}$ gives rise to the formation of two photoenols, $\mathbf{P_1}$ and $\mathbf{P_2}$ which were attributed, respectively, to the ZE and ZZ configurations and to three other cyclized photoproducts, 2,3-difluoro-6,6a-dihydro-11-hydroxy-6-phenyl-5-propyl-5*H*-benzo[*b*]-acridin-12-one ($\mathbf{P_3}$), 2,3-difluoro-6,11-dihydro-11-hydroxy-11-phenyl-5-propyl-5*H*-benzo[*b*]-acridin-12-one ($\mathbf{P_4}$) and 2,3-difluoro-11-hydroxy-6-phenyl-5-propyl-5*H*-benzo[*b*]-acridin-12-one ($\mathbf{P_5}$) (see Scheme 1). The reaction was followed by irradiating the sample at 273 K for 10 min by UV periods of 30 s. After each UV period, the sample was rapidly transferred into the probe of the NMR spectrometer and ^{19}F NMR spectrum was recorded. Then, another irradiation period was added. After 20 periods (cumulative time of irradiation = 600 s), the thermal evolution of the sample was monitored. By measuring the peak intensities of each resonance, the time-evolution concentrations were plotted taking into account the duration of irradiation, the duration of transfer and the duration of ^{19}F NMR acquisition (Fig. 1). From this plot, homemade software[12–14] was used to perform the quantitative kinetic analysis aimed to establish the detailed mechanism.

The dark relaxation kinetics were analyzed first to reach the thermal part of the mechanism. Except the acridinone $\mathbf{P_4}$ which remains strictly constant, it has been shown that all the other compounds $\mathbf{P_0}$, $\mathbf{P_1}$, $\mathbf{P_2}$, $\mathbf{P_3}$ and $\mathbf{P_5}$ are involved in the thermal relaxation process. From the kinetic analysis,[15] the back-conversion of the metastable photoenol $\mathbf{P_1}\rightarrow\mathbf{P_0}$ ($k_{10} = 1.6\times10^{-4}\ \mathrm{s}^{-1}$) and the very slow process $\mathbf{P_3}\rightarrow\mathbf{P_5}$ ($k_{35} = 5.55\times10^{-7}\ \mathrm{s}^{-1}$) were clearly demonstrated. In order to determine the fate of $\mathbf{P_2}$, that is, if $\mathbf{P_2}\rightarrow\mathbf{P_1}$ or $\mathbf{P_2}\rightarrow\mathbf{P_0}$ (k_{21} or $k_{20} = 6.8\times10^{-5}\ \mathrm{s}^{-1}$) it was necessary to consider the residual quadratic error which nevertheless suggested a slight preference for the second one: $\mathbf{P_2}\rightarrow\mathbf{P_0}$.[16]

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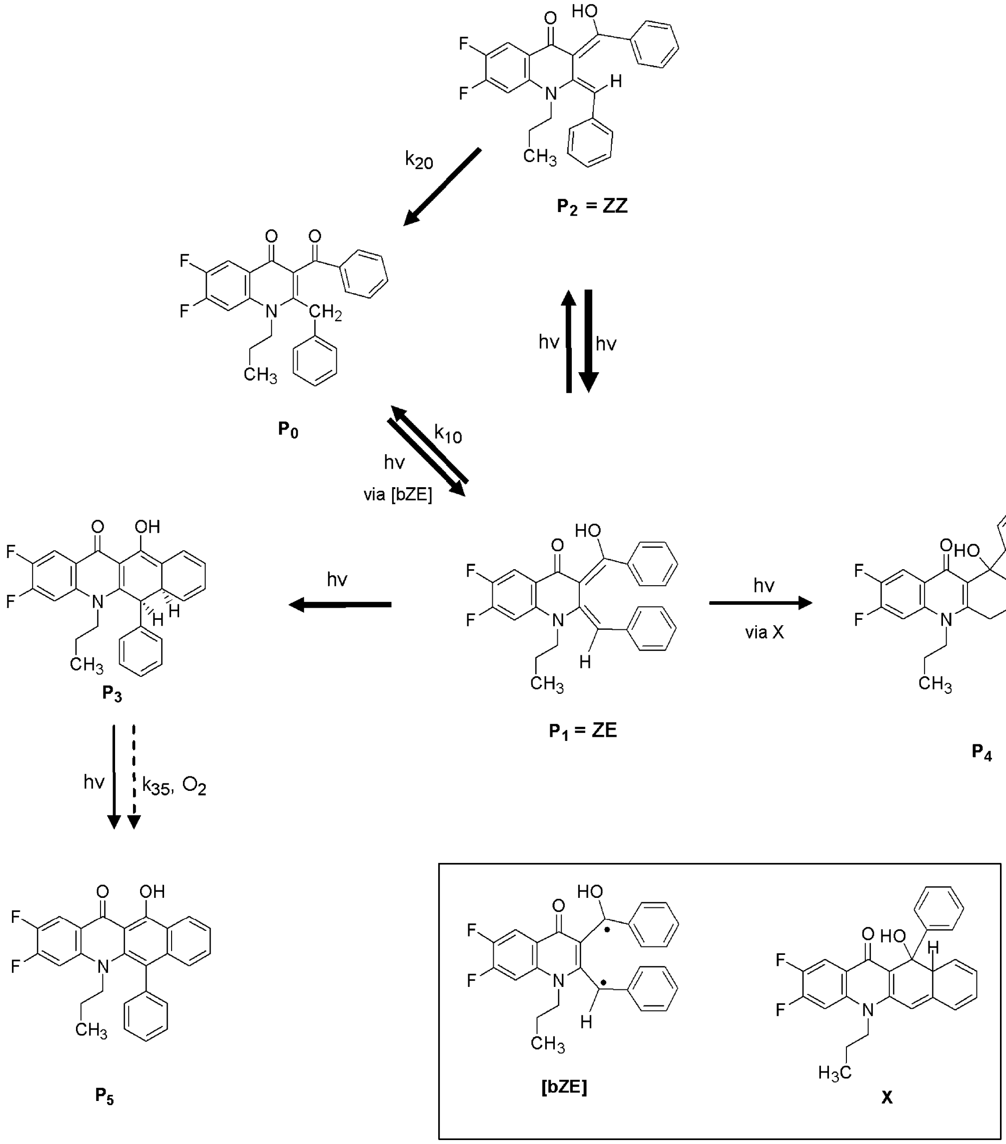

Scheme 1. Photochromic processes of $\mathbf{P_0}$ (the widths of the arrows are a visual indication of the relative values of the corresponding apparent rate constants; *k*: thermal processes; *hv*: photochemical processes).

In order to analyze the photochemical part of the mechanism, all the previously determined thermal relaxation paths need to be taken into account as there always occur spontaneous processes.

Among all possible, we found the presence of six significant photochemical processes. Irradiation of $\mathbf{P_0}$ gives rise to the ZE enol $\mathbf{P_1}$ with an apparent photochemical rate constant $h_{\mathrm{P0}\rightarrow\mathrm{P1}} = 3.18\times10^{-4}\ \mathrm{s}^{-1}$. The other ZZ enol, $\mathbf{P_2}$ does not arise from $\mathbf{P_0}$ but results from a reversible photoisomerization of $\mathbf{P_1}$ whose respective apparent photochemical rate constants are $h_{\mathrm{P1}\rightarrow\mathrm{P2}} = 2.92\times10^{-4}\ \mathrm{s}^{-1}$ and $h_{\mathrm{P2}\rightarrow\mathrm{P1}} = 3.20\times10^{-3}\ \mathrm{s}^{-1}$. Note that no (E)-enols have been detected as H-bonding in $\mathbf{P_0}$ favours the Z-isomerism. A possible interpretation or the prior formation of the photoenol ZE ($\mathbf{P_1}$) is the presence of a triplet biradical intermediate [bZE], provided by the γ-hydrogen abstraction by the triplet-excited carbonyl.[17] This intermediate undergoes fast internal rotations around single bonds, thereby relaxing to energetically favourable conformations.[18,19] Hence the primary formation of ZE leads us to conclude that the preferential conformation of biradical is the precursor of ZE. Another interesting feature is the ratio between the two rates of photoisomerization. The conversion $\mathbf{P_2}\rightarrow\mathbf{P_1}$ is about 10 times higher than the reverse, confirming that the triplet biradical (= triplet enol) has a configuration closer to $\mathbf{P_1}$ than $\mathbf{P_2}$.

On the contrary, the faster regeneration of $\mathbf{P_0}$ by a thermal 1,5-sigmatropic rearrangement of the photoenol ZE ($\mathbf{P_1}$) is not surprising as the ZE conformation is sterically more crowded than the ZZ. On the other hand, it is noteworthy that the photoenol ZE ($\mathbf{P_1}$) is highly photoreactive as it is the precursor of all ways of degradation through photocyclization. According to Woodward–Hoffman's rules, a single-step conrotatory process leads to the dihydro-structure with protons in

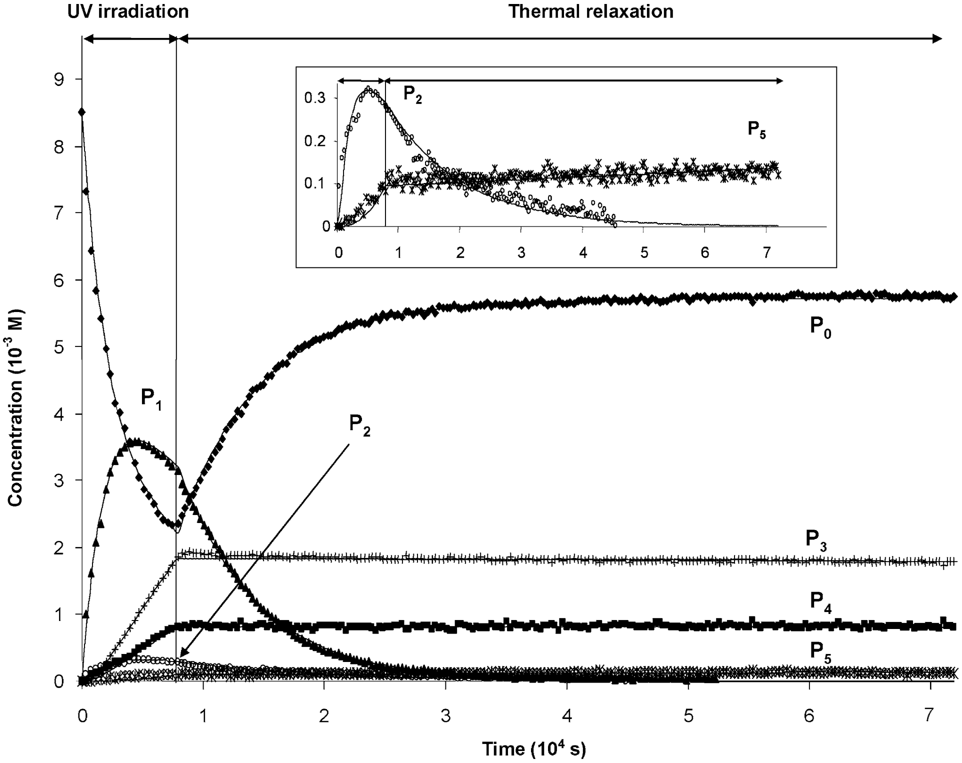

Figure 1. Evolution of the concentrations of the quinolone $\mathbf{P_0}$ and of the five photoproducts ($\mathbf{P_1}$–$\mathbf{P_5}$) during the photocolouration under UV irradiation and the thermal relaxation in the dark of a 8.5×10^{-3} M degassed toluene solution of $\mathbf{P_0}$. Signs are the experimental concentrations from ^{19}F NMR measurements, continuous lines are best fit from the model (see text). Insert: magnification of the $\mathbf{P_2}$ and $\mathbf{P_5}$ kinetics.

syn position,[10] $\mathbf{P_3}$ ($h_{P1\rightarrow P3} = 8.11 \times 10^{-5}\ \mathrm{s}^{-1}$). The formation of $\mathbf{P_4}$ is supposed to pass through a not-detected intermediate, here X, which undergoes rapid 1,3-sigmatropic shift to generate $\mathbf{P_4}$ ($h_{P1\rightarrow P4} = 3.41 \times 10^{-5}\ \mathrm{s}^{-1}$).

$\mathbf{P_5}$ came from $\mathbf{P_3}$ by a loss of two hydrogen atoms, then by oxidation. Comparison of the photochemical ($h_{P3\rightarrow P5} = 1.42 \times 10^{-5}\ \mathrm{s}^{-1}$) and the thermal rates ($k_{P3\rightarrow P5} = 5.55 \times 10^{-7}\ \mathrm{s}^{-1}$) indicates that this reaction is photochemically favoured. Nevertheless, if oxygen is present, the thermal disappearance of $\mathbf{P_3}$ is highly accelerated. This was nicely confirmed by the aeration of solution at the end of thermal relaxation. Indeed, the NMR tube was opened and ^{19}F NMR spectra were recorded. This affected only $\mathbf{P_3}$ which oxidized spontaneously to give $\mathbf{P_5}$.

Consequently, the present work gives precise details about the exact location of processes in the photochemical and thermal reactions of $\mathbf{P_0}$.[10] Indeed, only one photoenol (ZE) can be produced by irradiation of initial compound and it is reversibly photoisomerized into the second enol, ZZ. Moreover, kinetic analysis has underlined the existence of photochemical transformation of $\mathbf{P_3}$ into $\mathbf{P_5}$.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tetlet.2006.02.061. Supplementary data contains details of experiments, NMR spectra and kinetic analysis.

References and notes

1. Yang, N. C.; Rivas, C. *J. Am. Chem. Soc.* **1961**, *83*, 2213.
2. Sammes, P. G. *Tetrahedron* **1976**, *32*, 405–422.
3. Scaiano, J.-C. *Acc. Chem. Res.* **1982**, *15*, 252–258.
4. Netto-Ferreira, J. C.; Wintgens, V.; Scaiano, J.-C. *Can. J. Chem.* **1994**, *72*, 1565–1569.
5. *Photochromism*; Brown, G. H., Ed.; Wiley: New York, 1971; *Photochromism: Molecules and Systems*; Dürr, H., Bouas-Laurent, H., Eds.; Elsevier: Amsterdam, 1990; *Organic Photochromic and Thermochromic Compound*; Crano, J. C., Guglielmetti, R. J., Eds.; Plenum Press: New York, 1999.

6. Huffman, K. R.; Loy, M.; Ullman, E. F. *J. Am. Chem. Soc.* **1965**, *87*, 5417–5423.
7. Henderson, W. A., Jr.; Ullman, E. F. *J. Am. Chem. Soc.* **1965**, *87*, 5424–5433.
8. Lokshin, V.; Valès, M.; Samat, A.; Pèpe, G.; Metelitsa, A. V.; Khodorkovsky, V. *Chem. Commun.* **2003**, 2080–2081.
9. Rossollin, V.; Lokshin, V.; Samat, A.; Guglielmetti, R. *Tetrahedron* **2003**, *59*, 7725–7731.
10. Berthet, J.; Lokshin, V.; Vales, M.; Samat, A.; Vermeersch, G.; Delbaere, S. *Tetrahedron Lett.* **2005**, *46*, 6319–6324.
11. The degassing of solution to remove oxygen was made by the technique of freeze–pump–thaw cycles (six cycles) directly in the J. Young valve NMR sample tubes (Wilmad 507-JY-7).
12. Kaps, K.; Rentrop, P. *Comp. Chem. Eng.* **1984**, *8*, 393–396.
13. Minoux, M. In *Programmation Mathématique*; Dunod, Ed.; Bordas: Paris, 1983; Vol. 1, pp 95–168.
14. Deniel, M. H.; Lavabre, D.; Micheau, J. C. In *Organic Photochromic and Thermochromic Compounds*; Crano, J. C., Guglielmetti, R. J., Eds.; Plenum Press: New York, 1999; Vol. 2, pp 167–209.
15. Details of fitting procedure are reported in the Supplementary data.
16. The minimal value of residual quadratic error ($\chi^2 = \Sigma_n ([C]_{\mathrm{cal}} - [C]_{\mathrm{obs}})^2$, n is the number of experimental data points) is an indication of location of process. With process $\mathbf{P_2 \rightarrow P_1}$ $\chi^2 = 7.26 \times 10^{-10}$, while with $\mathbf{P_2 \rightarrow P_0}$, $\chi^2 = 7.02 \times 10^{-10}$.
17. Das, P. K.; Encinas, M. V.; Small, R. D., Jr.; Scaiano, J.-C. *J. Am. Chem. Soc.* **1979**, *101*, 6965–6970.
18. Scaiano, J.-C. *Tetrahedron* **1982**, *38*, 819–824.
19. Eckert, G.; Goez, M. *J. Am. Chem. Soc.* **1994**, *116*, 11999–12009.