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NMR structural elucidation of photochromic quinolone photoproducts

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Abstract—UV irradiation of 3-benzoyl-2-benzyl-6,7-difluoro-1-propyl-1*H*-quinolin-4-one leads to the formation of a mixture of photoproducts, with different evolutions. The structure of each of them has been obtained by one- and two-dimensional multinuclear NMR experiments. Two photoenols, which are thermally reversible, have been identified. All of the other photoproducts have been assigned to degradation. Based on the structural identification and the photochemical and thermal evolution of samples, a plausible mechanism is proposed.

Aromatic ketones containing alkyl substituents in the *ortho* position yield, on irradiation, a mixture of isomeric enols, which decay through a thermal hydrogen shift, regenerating the starting ketone (photoenolisation phenomena).[1–4] Such behaviour is a typical example of photochromism, defined as the photoinduced transformation of a structure A into a structure B, both having different absorption spectra.[5] In 1965, Ullman et al. reported studies on some related chromone derivatives.[6] Photoenolisation did indeed occur, producing a photoenol which thermally faded slowly. However, some irreversible photochemical processes were also observed, leading to a loss of photochromic properties. The same authors also reported briefly the photochromic behaviour of some quinolone derivatives. The only results involving this family concern a strong colour formation on irradiation and considerable thermal stability of the photoenol.[7] To the best of our knowledge, nobody has developed these compounds. In recent years, a renewed interest in photochromic compounds involving photoenolisation has arisen.[8,9] As the reversible hydrogen shift between the two positions has only limited molecular reorganisation, it seems advantageous for its use in constrained media, such as a polymeric matrix and, especially, crystals.[10,11] To this end, some of us have reinvestigated the quinolone family by modifying initial materials.[12] Four isomeric photoenols can be produced by photoinduced hydrogen shift in P_0 (Scheme 1). In addition, undesirable cyclisation and/or oxidation can also occur and leads to irreversible photoproducts, responsible for the loss of photochromic properties. If we take into account all of the structures actually produced and their origin, novel synthetic strategies may then be envisaged to improve the properties of quinolone derivatives. In this letter, multinuclear (^{1}H, ^{13}C, ^{19}F) NMR spectroscopy characterisation of all the detected products of 3-benzoyl-2-benzyl-6,7-difluoro-1-propyl-1*H*-quinolin-4-one[12] (P_0) (Scheme 1) is reported.

Two solutions (degassed and aerated) of P_0 in toluene-d_8 were irradiated with UV light using a 1000 W Xe–Hg lamp, filtered by a band-pass glass filter ($259 < \lambda < 388$ nm), at 273 K, for 30, 300 and 900 s. ^{1}H and ^{19}F NMR spectra were recorded after each of the three UV irradiation periods. Before irradiation, the ^{19}F spectrum consisted of two doublet signals ($^3J_{F-F} = 22.6$ Hz) characterising each fluorine atom (Fig. 1). After 30 s of UV irradiation of the degassed sample, two new doublets, from structure P_1 appeared (Fig. 1a). Increasing the irradiation time led to the appearance of other resonances, named P_2, P_3, P_4 and P_5. The concentration of P_1 increased after 300 s of irradiation then decreased after 900 s under UV light. The same effect was observed for P_2 while the concentrations of other detected photoproducts (P_3, P_4 and P_5) always increased. After 24 h only P_4

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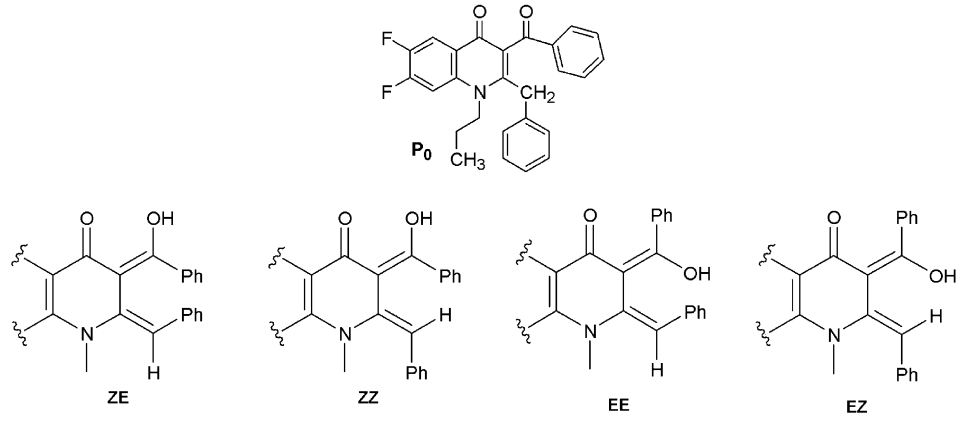


Scheme 1. Structure of P_0 and its four possible isomeric photoenols.

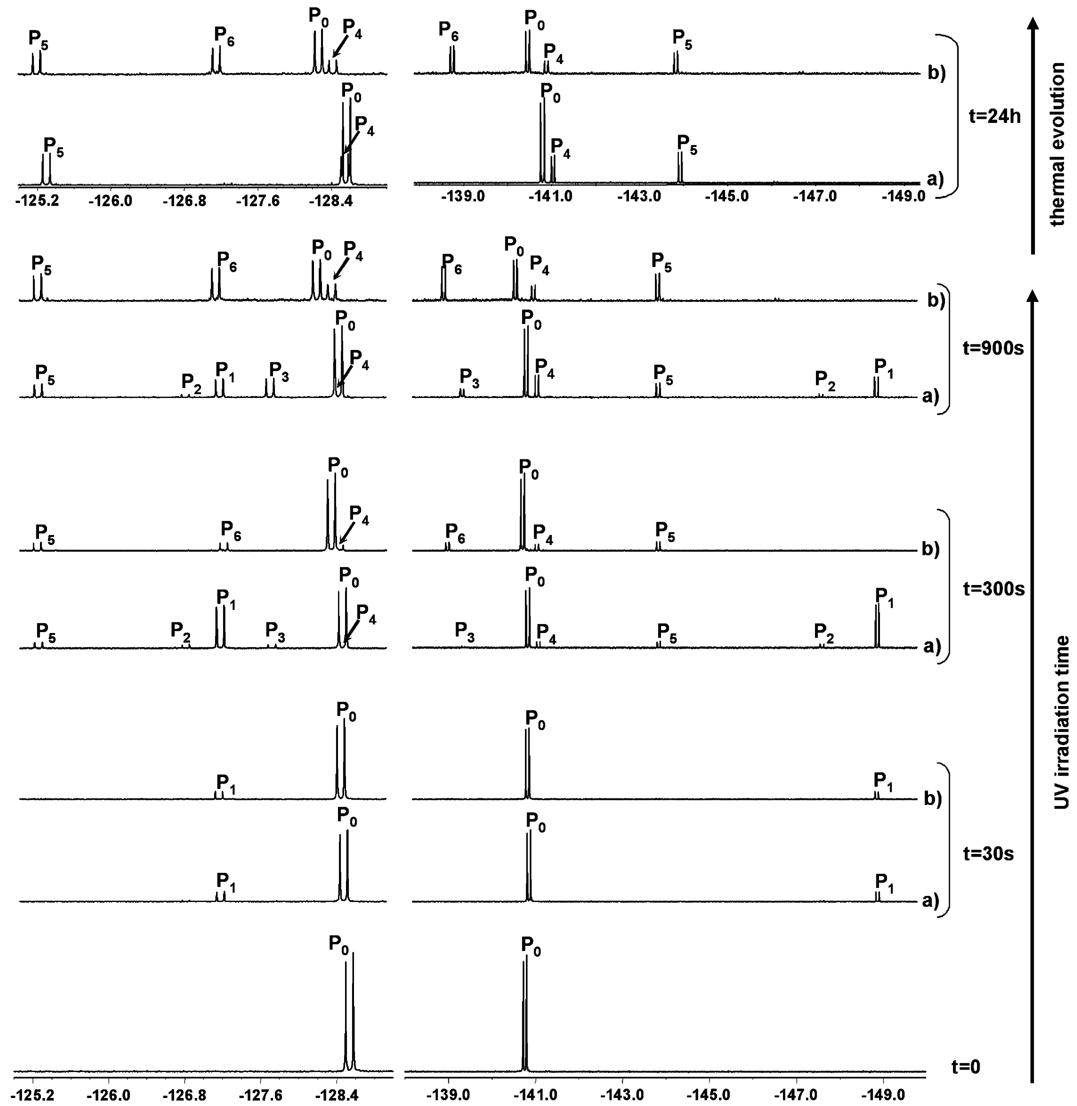


Figure 1. ^{19}F NMR spectra recorded during UV irradiation and after thermal evolution of (a) degassed sample and (b) aerated sample of P_0 at 273 K and after 24 h of thermal evolution at room temperature.

and P_5 were still detected, indicating that the three others were thermally unstable: P_1 and P_2 thermally converted to P_0, and P_3 to P_5. In the case of the aerated sample, the previously detected photoproducts, P_1, P_2, P_4 and P_5 were observed (Fig. 1b), but the main difference concerned the absence of P_3, while a new compound, P_6 was formed. Once again, after 24 h, no thermal decay was observed for P_4, P_5 and P_6. From the measurement of ^{19}F peak intensities, the corresponding ^{1}H signals of each of the photoproducts were retrieved.

Characterisation of P_1 and P_2: NMR experiments were carried out at 213 K to stabilise P_1 and P_2. In the ^{1}H NMR spectrum (Fig. 2), the singlet signals at 5.28 and 14.74 ppm were assigned to ethylenic proton H_a and to a hydroxy function, respectively, so characterising P_1 as a photoenol. The downfield shift of OH is explained by hydrogen bonding with the carbonyl group. 2D Roesy made it possible to observe dipolar correlations between H_a and protons of propyl chain, $CH_{2\alpha}$ at 3.13 ppm and $CH_{2\beta}$ at 1.41 ppm. This contact along with the hydrogen bonding of OH with C=O prove ZE geometry (Scheme 2) of the photoenol P_1. The photoproduct P_2 presented the same evolution as P_1. Moreover, two singlet resonances at 5.11 and 16.46 ppm in the ^{1}H spectrum (Fig. 2) can be assigned to H_a and OH, respectively. Once again, the deshielded shift of OH function is an indication of hydrogen bonding with the C=O. Consequently, by deduction, P_2 is the ZZ isomer of photoenol.

Characterisation of P_3: In Figure 3, the singlet signal at 12.79 ppm was assigned to the OH function. Scalar couplings measured in the 2D-Cosy experiment elucidated the structure of P_3. Starting from the doublet of H_a at 3.66 ppm, the connection was established via $H_{6'}$ at 4.43 ppm, $H_{5'}$ at 5.21 ppm, $H_{4'}$ at 5.66 ppm and $H_{3'}$ at 5.31 ppm up to $H_{2'}$ at 7.01 ppm. A structure of dihydrobenzo[*b*]acridinone with cyclisation between C_a and $C_{6'}$ can then be proposed. Moreover, the dipolar correlation and the coupling constant ($^{3}J = 7.5$ Hz) between H_a and $H_{6'}$ indicate a *syn* position.

Characterisation of P_4: P_4 was assigned to a cyclised structure, resulting in the bond formation between carbons C_6'' and C_b. Integration of the pattern at 3.52 ppm (Fig. 4a) indicates that it contains two protons, characterising a diastereotopic methylene group, also proved by 2D-HSQC-Dept. This signal is split into two doublets ($^{2}J = 20$ Hz) with a strong roof effect. The scalar correlations measured in the 2D-Tocsy experiment underline the spin–spin coupling between protons $H_{2''}$ at 6.89 ppm, via $H_{3''}$ and $H_{4''}$, and $H_{5''}$ at 8.11 ppm, once again indicating their bearing in an *ortho*-substituted phenyl. As for the OH function, its chemical shift at 8.91 ppm is lower than the other photoproducts. This may be surprising for a tertiary alcohol, but can be explained by the hydrogen bond with C=O.

Characterisation of P_5: In the ^{1}H NMR spectrum (Fig. 4b), except for protons in the propyl group, no other aliphatic proton signals for P_5 were found, which suggests cyclisation between C_a and $C_{6'}$ with the loss of both hydrogen atoms (H_a and $H_{6'}$). 2D Tocsy underlines scalar correlations from $H_{2'}$ at 7.71 ppm via $H_{3'}$ and $H_{4'}$ to $H_{5'}$ at 7.63 ppm. All of these protons are non-equivalent, proving that the phenyl ring is substituted in *ortho* position. An OH function is observed at 16.14 ppm. This data has been used to suggest an aromatic benzo[*b*]acridinone structure for P_5.

Characterisation of P_6: To elucidate its structure (Fig. 4c), 2D-HMBC was explored. ^{1}H and ^{13}C long-range correlations through three bonds were observed between aromatic protons at 7.77 and 7.84 ppm, assigned to $H_{2'} = H_{6'}$ and $H_{2''} = H_{6''}$, respectively, and quaternary deshielded carbons at 190 and 194 ppm, corresponding to C_a and C_b. These connections, as well as the formation of this structure only in the aerated medium, are coherent with an oxidised product with two benzoyl substituents.

Consequently, the UV irradiation of quinolone P_0 led to the formation of two photoenols, unambiguously identified by NMR as $ZE = P_1$ and $ZZ = P_2$ isomers, although previous investigations on chromones[6] and

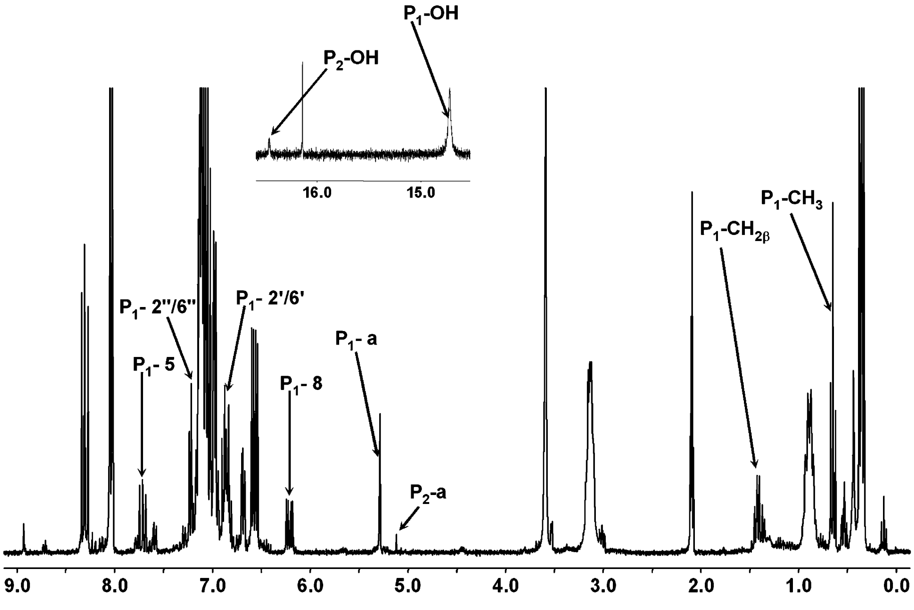
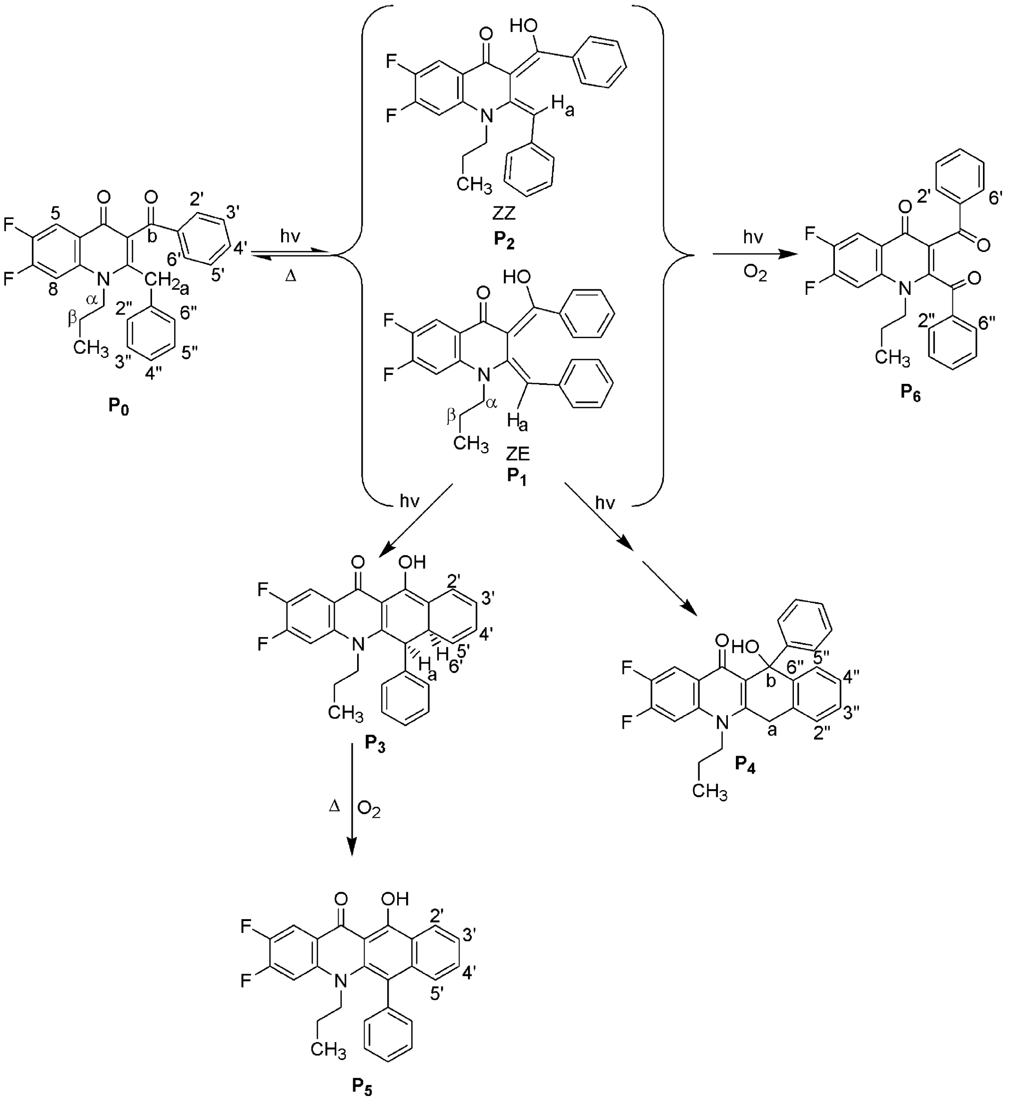


Figure 2. ^{1}H NMR assignment of characteristic signal of P_1 and P_2.



Scheme 2. Proposed mechanism model showing the photoconversion paths between all the identified structures.

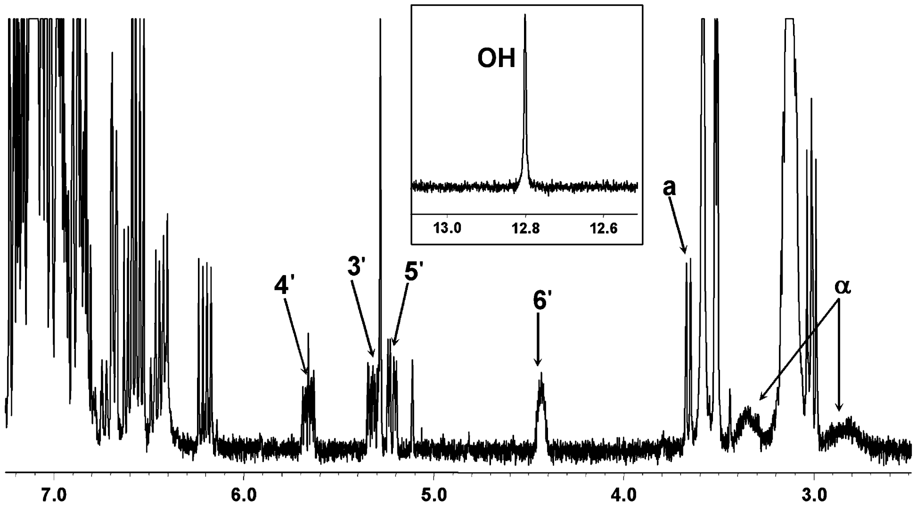


Figure 3. ^{1}H NMR assignment of characteristic signals of P_3.

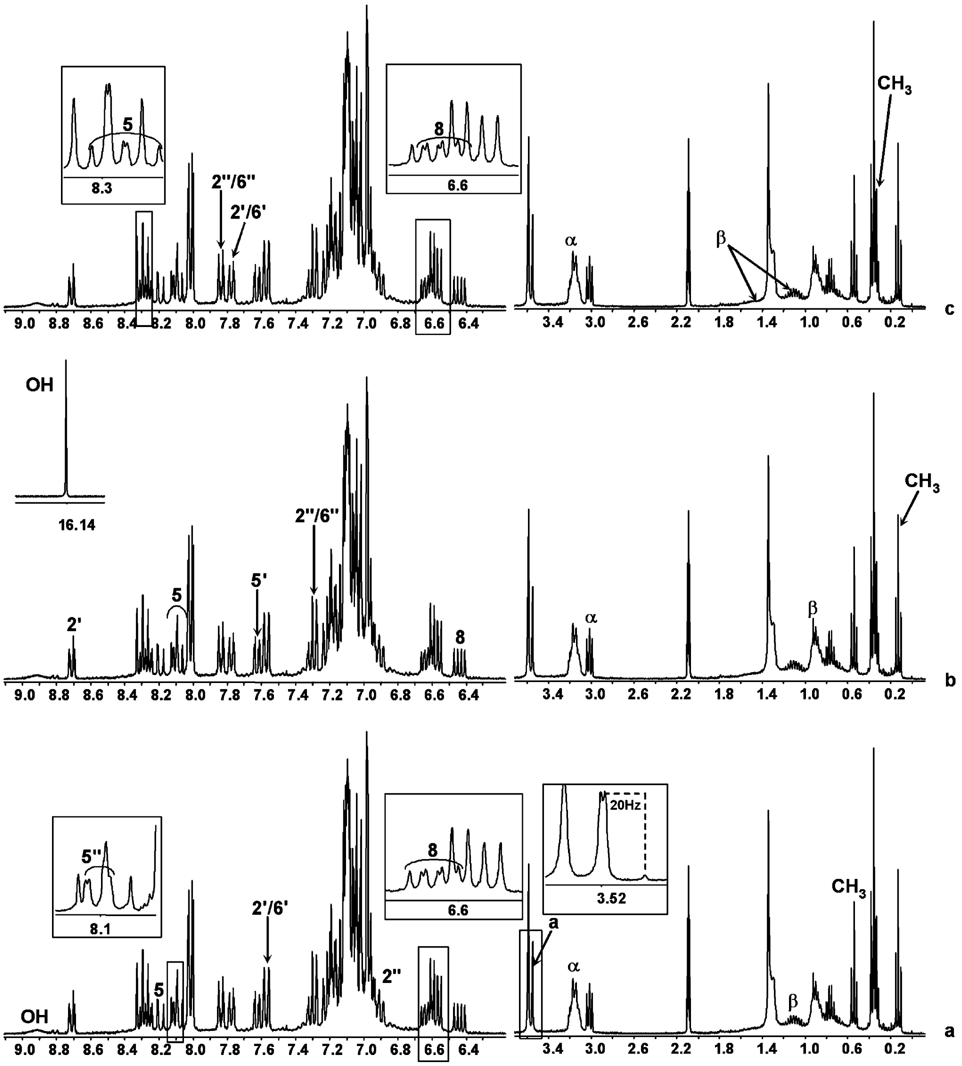


Figure 4. ^{1}H NMR assignment of characteristic signals of (a) P_4, (b) P_5 and (c) P_6.

benzophenones[4] suggested the predominance of photoenol with OH and phenyl opposite (here, ZZ) and also the possible presence of photoenol with both phenyl opposite (here, EZ). These proposals were made on the basis of steric constraint. Here, P_1 appeared as the non-expected isomer, which would be stabilised by π–π interactions between both phenyl groups. In addition to reversible photoenolisation, non-desired photoreactions also occurred. In degassed solution, the decrease in photoenol concentrations is concomitant with an accumulation of degradation products, P_3 and P_4. According to Woodward–Hoffman's rules, only P_1 can undergo conrotatory cyclisation, giving rise to a dihydro-structure with protons in *syn* position. This thermally reacts with residual oxygen to lead, after a loss of hydrogen atoms $H_{6'}$ and H_a, to P_5. Such a product is observed without its precursor P_3 when the solution is not degassed. As for P_4, it also comes from P_1 after photocyclisation between $C_{6''}$ and C_b. This reaction is supposed to pass through an intermediate (not detected under our applied conditions), which undergoes 1,3 hydrogen transfer to produce P_4. Finally, the summarised Scheme 2 shows that the principal pathway for the photodegradation of quinolone P_0 involves photocyclisation of its enol, ZE. Understanding of the degradation origin makes it possible to envisage other structures, in which the formation of resistant photoenol ZZ = P_2 will be selected.

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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.

2005.07.032. Supplementary material contains 2D NMR spectra of P_1, P_3, P_4, P_5 and P_6.

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