

Sunlight induced functionalisation of some heterocyclic bases in the presence of polycrystalline TiO_2

T. Caronna,^{*a} C. Gambarotti,^b L. Palmisano,^c C. Punta^b and F. Recupero^b

^a Università di Bergamo, Facoltà di Ingegneria, Via Marconi 5, I-24044 Dalmine, Bergamo, Italy

^b Dipartimento di Chimica, Materiali ed Ingegneria Chimica “Giulio Natta”, Via Mancinelli 7, I-20131 Milano, Italy

^c Dipartimento di Ingegneria Chimica dei Processi e dei Materiali, Viale delle Scienze, I-90128 Palermo, Italy. E-mail: tullio.caronna@unibg.it

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The functionalisation of various heterocyclic bases induced by sunlight is reported. The photoreaction occurred with higher yield in a liquid–solid heterogeneous system in the presence of polycrystalline TiO_2 (anatase) than in a homogeneous system under the same experimental conditions.

Research into processes with less environmental impact has resulted in the development of reactions in which the use of the solar energy is one of the most renewable and less polluting reagents. Unfortunately, except in the presence of a chromophoric group, most organic substances do not absorb light in the visible or UV-A regions, hence most research has developed in the search for substances able to absorb sunlight and induce reactions on organic substrates. TiO_2 is the most widely employed substance for its (photo)chemical stability and harmlessness, although it is able to absorb only <5% of the solar radiation. The mechanism of its action involves the photochemical induced promotion of an electron to a higher energy level, and in this way an electron may be more easily given as well as accepted. Photooxidation reactions, especially of volatile organic compounds (VOCs) which are air pollutants, are widely reported,¹⁻⁵ but also a few reduction reactions have been reported.^{6,7} Protonated heterocyclic bases are known to be attacked by nucleophilic radicals created *via* reaction of hydroxyl or *tert*-butoxy radicals with amides, aldehydes, ethers, etc.⁸ Here we present data regarding the free radical functionalisation of heterocyclic bases induced by sunlight in which the presence of TiO_2 is beneficial as the irradiation times drastically diminished in comparison to the homogeneous system without affecting the regioselectivity or the kind of radical formed.

In a typical experiment 10 mg of polycrystalline anatase TiO_2 (Merck, BET specific surface area: $10 \text{ m}^2 \text{ g}^{-1}$) were added to a solution in formamide (40 mL) of quinoline (1 mmol), H_2SO_4 (1 mmol) and H_2O_2 (4 mmol), and the resulting suspension was irradiated with sunlight⁹ with mechanical stirring (700 rpm) for 5 h. After the irradiation, most of the amide was removed by distillation under low pressure, the solution was alkalinized with aq. 10% NaOH and extracted with CH_2Cl_2 . The reaction products were identified via GC-MS and by comparison with authentic samples. Quantitative analyses were carried out by GC with the use of an internal standard, showing almost quantitative (90%) transformation of quinoline into 2-formamidoquinoline. In parallel reactions in the dark or without TiO_2 , no products were obtained. Note also that the mono substitution product in position 2 (**5**) was formed, while when the formamido radicals were created via redox reaction, (**5**) and 2,4-diamidoquinoline were obtained in 40/60 ratio.¹⁰ In Scheme 1 and Table 1 are reported the heterocyclic bases irradiated in formamide in the presence or absence of TiO_2 , the yields and the obtained products.

Other amides, namely dimethylformamide and dimethylacetamide, were also used in reactions with quinoxaline: again the effect of the presence of TiO_2 was striking, and in addition the selectivity for radical formation in the case of dimethylforma-

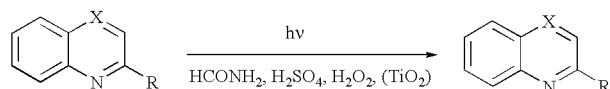
mide was more significantly shifted (with respect to the redox reactions) towards the abstraction of the hydrogen bonded to the methyl group *vs.* that bonded to the carbonyl group (see Scheme 2).

The yields and the ratios between the products were affected both by the amount of TiO₂ and the irradiation time, as is reported in Table 2.

What appears as an anomalous datum, the higher yield of (8) in the reaction without TiO_2 compared to that in the presence of 40 mg of TiO_2 , may be ascribed to a screening effect of the TiO_2 suspension. When the reaction was run with 10 mg of TiO_2 for 15 h (8) was obtained in 70% yield.

4-Ethylpyridine and 4-cyanopyridine did not react under the same experimental conditions in the presence or absence of TiO_2 . These bases instead react when the radicals are created via redox reactions.¹⁰

At this stage, we think it is premature to speculate on the mechanism, but some points may be stressed. The first regards the generation of the radicals and the second the re-oxidation of the intermediate formed *via* the attack of the radical R[•], whatever it is, on the base (see Fig. 1). H₂O₂ does not absorb sunlight and this means that no decomposition may occur *via* direct irradiation, we can instead consider its decomposition *via* electron transfer from the excited TiO₂ forming an OH⁻ and an OH[•]. This last species may in turn abstract the hydrogen from the amide.



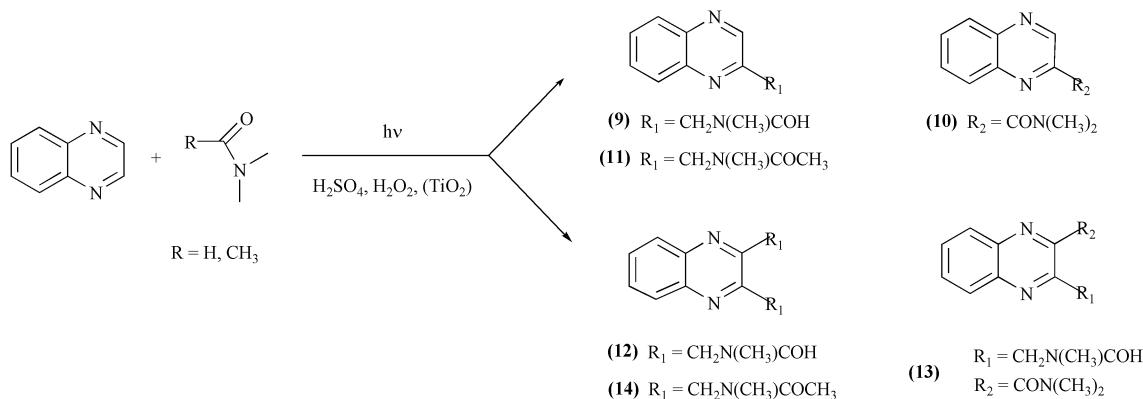
- | | |
|---|---|
| (1) X = CH, R = H
(2) X = CH, R = CH ₃
(3) X = C-CH ₃ , R = H
(4) X = N, R = H | (5) X = CH, R = CONH ₂
(6) X = C-CONH ₂ , R = CH ₃
(7) X = C-CH ₃ , R = CONH ₂
(8) X = N, R = CONH ₂ |
|---|---|

Scheme 1

Table 1 Comparison between reactions with and without TiO₂ for the different heterocyclic bases used^a

Base (1 mmol)	H ₂ SO ₄ /mmol	TiO ₂ /mg	Product	Yield (%)
Quinoline (1)	1	10	(5)	90
Quinoline (1)	1	no	—	0
Quinaldine (2)	1	10	(6)	100
Quinaldine (2)	1	no	(6)	30
Lepidine (3)	1	10	(7)	69
Lepidine (3)	1	no	(7)	38
Quinoxaline (4)	2	10	(8)	42
Quinoxaline (4)	2	no	(8)	19

^a The reactions were run irradiating 1 mmol of base, 4 mmol of H₂O₂ in 40 mL of formamide for 5 h.



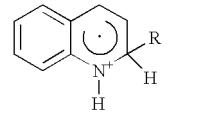
Scheme 2

The intermediate radical cation showed in Fig. 1 may be re-oxidised by H_2O_2 forming again OH^\cdot . Nevertheless, by following this hypothesis, it is not clear why a similar reaction did not occur when the pyridine derivative was used. Another possibility is the direct excitation of the heterocyclic base forming the radical from the amide, as already reported.¹¹ In this case the role of TiO_2 appears unclear unless a sensitisation of the substrate due to the presence of TiO_2 is hypothesised. Work

Table 2 Reactions between quinoxaline and dimethylacetamide or dimethylformamide. Yields and product distributions were dependent on the presence of TiO_2 and the irradiation time^a

Amide	Irradiation time/h	TiO_2/mg	Total yield (%)	Products and ratios
Formamide	5	40	45	(8)
Formamide	5	no	19	(8)
Formamide	15	40	56	(8)
Formamide	15	no	60	(8)
Dimethylacetamide	5	40	66	(11)/(14) = 4.5
Dimethylacetamide	5	no	26	(11)
Dimethylacetamide	15	40	100	(11)/(14) = 0.3
Dimethylacetamide	15	no	100	(11)/(14) = 1.4
Dimethylformamide	5	40	69	(9)/(10) = 12.5; (9)/(12) = 5.8; (9)/(13) = 12.5
Dimethylformamide	5	no	17	(9)/(10) = 24
Dimethylformamide	10	40	92	(9)/(10) = 26.0; (9)/(12) = 1.4; (9)/(13) = 6.5
Dimethylformamide	10	no	55	(9)/(10) = 24

^a The reactions were run irradiating 1 mmol of quinoxaline, 2 mmol of H_2SO_4 , 4 mmol of H_2O_2 dissolved in 40 mL of the appropriate amide.



$\text{R} = \text{amido or } \alpha\text{-N-amidoalkyl}$

Fig. 1

is in progress to establish a possible mechanism and to enlarge the finality of the reaction.

Notes and references

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