The photochemical oxidation of benzyl alcohols by the triplet excited state of coenzyme pyrroloquinolinequinone

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The first example of the photochemical reaction of coenzyme pyrroloquinolinequinone (PQQ) with benzyl alcohols is reported, where the triplet excited state of PQQ is the active species which oxidises alcohols to the corresponding aldehydes; the mechanism of the photochemical redox reaction between PQQ and benzyl alcohols is discussed.

PQQ **1** is a novel heterocyclic *o*-quinone cofactor that was first isolated and identified in 1979 from methanol dehydrogenase of methylotrophic bacteria.[1] Since then, much effort has been devoted not only to evaluate its biological and/or biomedical roles but also to understand its physicochemical properties and functions.[2] In contrast with intense research on photochemistry of ubiquitous coenzymes such as flavins and NAD(P)H,[3] very little attention has so far been focused on the photochemistry of coenzyme PQQ. Here we report the redox reactions of the photo-excited state of PQQ which is found to be a much stronger oxidant than flavins, providing valuable insight into the viability of PQQ as a photoreceptor.

Irradiation of a deaerated MeCN solution containing PQQTME (trimethyl ester of coenzyme PQQ)[4] **2** and *p*-methoxybenzyl alcohol ($ArCh_2OH$, Ar = *p*-$MeOC_6H_4$) with a xenon lamp at 25 °C results in formation of $PQQTMEH_2$ (reduced **2** in the quinol form) and the corresponding aldehyde (ArCHO) as shown in eqn. (1). Fig. 1 shows the UV–VIS

$$\mathbf{2} + ArCH_2OH \xrightarrow[MeCN]{h\nu} PQQTMEH_2 + ArCHO \qquad (1)$$

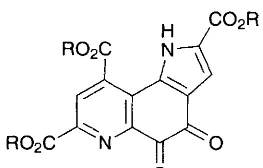
spectra observed in the photochemical reaction of **2** (5.1×10^{-5} mol dm^{-3}) with *p*-methoxybenzyl alcohol (3.2×10^{-2} mol dm^{-3}). The decrease in absorbance at λ_{max} = 356 nm due to the quinone is accompanied by the appearance of a new absorption band at λ_{max} = 326 nm due to the quinol with a clean isosbestic point at 342 nm.[4] The quantitative formation of $PQQTMEH_2$ and *p*-methoxybenzaldehyde in 1 : 1 ratio was confirmed by the ^1H NMR spectra of the products in CD_3CN.[4] The photoreduction of **2** also occurred with other benzyl alcohol derivatives [Ar = *p*-ClC_6H_4, C_6H_5, *p*-MeC_6H_4, 2,4-$(MeO)_2C_6H_3$]. In the dark, however, no thermal reaction occurred between **2** and $ArCH_2OH$.

The photoreduction of **2** by $ArCH_2OH$ is significantly retarded in the presence of dioxygen, which is a typical triplet quencher. The excitation of the absorption band (350 nm) of a MeCN solution of **2** results in no fluorescence.[5] Thus, the photochemical reaction of **2** may proceed *via* the triplet excited state rather than the singlet excited state. The triplet excited state of **2** was detected by laser flash photolysis. When **2** alone in deaerated MeCN was flashed with 355 nm laser light, a transient triplet–triplet (T–T) absorption spectrum having λ_{max} at around 400 and 570 nm and a broad shoulder above 600 nm was observed (Fig. 2). The decay of each absorption obeyed the first-order kinetics with the identical lifetime (τ) of 6.6 μs (see inset of Fig. 2). Such a first-order decay suggests that a T–T annihilation process is negligible under the present experimental conditions.

The quantum yields (Φ) for the photochemical redox reactions were determined from a decrease in absorbance due to **2** using a ferrioxalate actinometer with 360 nm irradiation.[6] The Φ value increases with an increase in [$ArCH_2OH$] to reach a limited value (Φ_∞). Such a saturated dependence of Φ on [$ArCH_2OH$] can be expressed by a double-reciprocal plot of Φ^{-1} *vs* $[ArCH_2OH]^{-1}$ according to eqn. (2), where K_{obs} is the

$$\Phi^{-1} = \Phi_\infty^{-1}\,\{1 + [K_{obs}(ArCH_2OH)]^{-1}\} \qquad (2)$$

observed quenching constant of the triplet excited state, $^3\mathbf{2}^*$. From the linear plots of Φ^{-1} *vs* $[ArCH_2OH])^{-1}$ are obtained the Φ_∞ and K_{obs} values. By using the τ value (6.6 μs) of $^3\mathbf{2}^*$, the observed rate constants (k_{obs}) can be obtained from the K_{obs} values using the relation, $K_{obs} = k_{obs} \times \tau$. These values are listed in Table 1 together with the one-electron oxidation potentials of $ArCH_2OH$.[7] The lifetime of the triplet–triplet absorption in Fig. 2 was shortened significantly by the presence



1 R = H: PQQ
2 R = Me: PQQTME

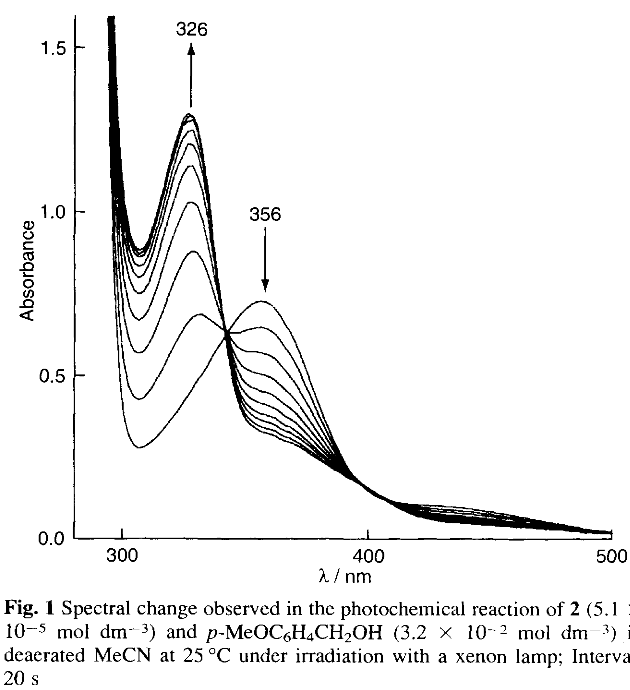


Fig. 1 Spectral change observed in the photochemical reaction of **2** (5.1×10^{-5} mol dm^{-3}) and *p*-$MeOC_6H_4CH_2OH$ (3.2×10^{-2} mol dm^{-3}) in deaerated MeCN at 25 °C under irradiation with a xenon lamp; Interval: 20 s

Table 1 Photochemical reaction of **2** with benzyl alcohols[a]

$ArCH_2OH$	E^0_{ox}[b]/ V	Φ_∞[c]	K_{obs}[c]/ $mol^{-1}\ dm^3$	k_{obs}[c]/ $mol^{-1}\ dm^3\ s^{-1}$	k_q[c,d]/ $mol^{-1}\ dm^3\ s^{-1}$
p-$ClC_6H_4CH_2OH$	2.01	1.6×10^{-2}	7.2×10^{-1}	1.1×10^5	[e]
$C_6H_5CH_2OH$	1.97	1.5×10^{-2}	8.3	1.3×10^6	[e]
$C_6D_5CD_2OH$	—	9.5×10^{-3}	8.8	1.3×10^6	[e]
p-$MeC_6H_4CH_2OH$	1.76	4.6×10^{-3}	31	4.7×10^6	[e]
p-$MeOC_6H_4CH_2OH$	1.46	4.7×10^{-2}	3.7×10^2	5.6×10^7	7.1×10^7
p-$MeOC_6H_4CD_2OH$	—	3.5×10^{-2}	3.7×10^2	5.6×10^7	[e]
$2,4$-$(MeO)_2C_6H_4CH_2OH$	0.99	2.1×10^{-2}	1.8×10^4	2.7×10^9	1.8×10^9

[a] [**2**] = 1.3×10^{-4} mol dm^{-3} in MeCN at 25 °C. [b] Determined using the SHACV method in MeCN containing 0.1 mol dm^{-3} TBAP.[7] [c] The experimental errors are within ±5%. [d] [**2**] = 3.5×10^{-5} mol dm^{-3} in MeCN at 25 °C. [e] High concentrations (*ca.* 1 mol dm^{-3}) required for the efficient quenching of ^{3}**2*** have precluded the accurate determination of the quenching rate constants.

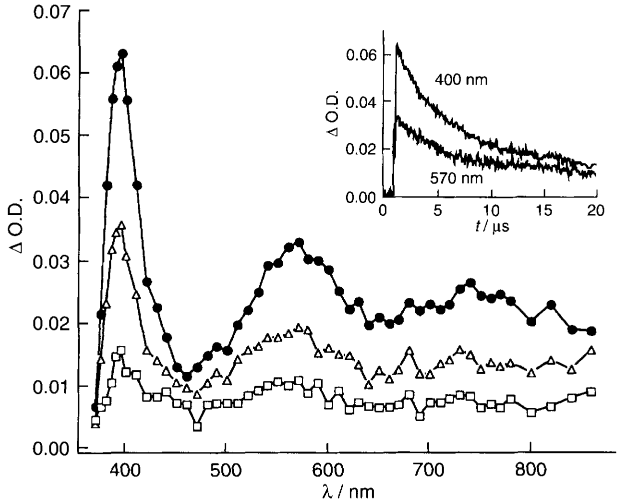


Fig 2 Triplet–triplet absorption spectra of **2** obtained in the laser flash photolysis of a deaerated MeCN solution of **2** (5.0×10^{-5} mol dm^{-3}) at 25 °C. Inset: Kinetic trace for the **2** triplet state decay at 400 and 570 nm.

of $ArCH_2OH$. From the quenching experiments of the triplet–triplet absorption were determined the quenching rate constants (k_q). The k_q values with p-$MeOC_6H_4CH_2OH$ and $2,4$-$(MeO)_2C_6H_3CH_2OH$ are also listed in Table 1, where the k_q values agree well with the observed rate constants (k_{obs}). Such an agreement between k_q and k_{obs} strongly indicates the involvement of ^{3}**2*** as the active species in the photochemical reaction of **2**.

The kinetic deuterium isotope effects for the photochemical reaction of **2** with $ArCH_2OH$ were also determined using p-$MeOC_6H_4CH_2OH$ and p-$MeOC_6H_4CD_2OH$. The results are listed in Table 1. No kinetic isotope effect is observed on the k_{obs} value (1.0 ± 0.05). However, the appreciable kinetic isotope effect (1.3 ± 0.05) is observed on Φ_∞. With $PhCH_2OH$ the kinetic isotope effect is observed on the Φ_∞ value (1.6 ± 0.05) but none on the k_{obs} value (1.0 ± 0.05). As shown in Table 1, the k_{obs} value increases with a decrease in the E^0_{ox} value. Such a dependence of k_{obs} on E^0_{ox} as well as the absence of the kinetic isotope effect on k_{obs} strongly indicates that the reaction of ^{3}**2*** with the alcohol proceeds *via* electron transfer followed by proton transfer rather than direct hydrogen atom transfer. The coupling of electron- and proton-transfer is a well-established alternative for the formal hydrogen atom transfer in organic photochemical systems,[8] particularly in the photoreduction of flavins.[3] Albini *et al.* have also recently reported that electron transfer occurs in the photochemical reactions between aromatic ketones and benzylsilane and stannane derivatives.[9]

The Φ_∞ values being much smaller than unity and the observation of the kinetic isotope effect on Φ_∞ (Table 1) indicate a competition between the back electron transfer to the ground state reactant pair and a transfer of a benzylic proton to oxygen to form the radical pair, followed by the facile transfer of the second hydrogen atom to yield the final products.

No photochemical reduction of flavins by benzyl alcohols has occurred in the absence of a catalyst.[3,10] Thus, the present study has revealed that a relatively new *o*-quinone cofactor PQQ is a much more reactive photoreceptor than a well known biological photoreceptor, *i.e.* flavins.

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