

Chemistry of L-ascorbic acid. Part 3.¹ Photoreduction of quinones with 5,6-*O*-isopropylidene-L-ascorbic acid †

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Upon irradiation with UV light, instead of undergoing the Paternò-Büchi reaction, 5,6-*O*-isopropylidene-L-ascorbic acid reduced quinones quite efficiently and rapidly to the corresponding hydroquinones.

The biological and pharmacological activity as well as therapeutic potential of L-ascorbic acid and its derivatives have been studied extensively.² However, despite the fact that L-ascorbic acid possesses several interesting functional groups, its organic chemistry and synthetic potential has not been explored to any significant extent. The complex chemical properties²⁻⁴ of this 'mysterious small molecule' may have hindered developments in this regard.

Recently it has been shown¹ that the derivatives of L-ascorbic acid participate in a Paternò-Büchi reaction to furnish chiral oxetanes. In continuation of this work, it was of interest to study such an addition of L-ascorbic acid to quinones as they are known to participate⁵ in the Paternò-Büchi reaction, affording the corresponding oxetanes. However L-ascorbic acid is known to reduce different systems,⁶ including inorganic compounds,⁷ under photolytic conditions. L-Ascorbic acid is also reported⁸ to reduce quinones in a ground state reaction, albeit in a sluggish manner. Therefore, it was essential to check whether, under photolytic conditions, L-ascorbic acid would simply reduce the quinones to the corresponding hydroquinones or would undergo a Paternò-Büchi reaction to give the respective oxetanes. Results pertaining to the above investigation are described in the present communication.

In the initial phase of the work, a solution of 5,6-*O*-isopropylidene-2,3-di-*O*-methyl-L-ascorbic acid **1** and 2-hydroxy-1,4-naphthoquinone in acetone (0.1 molar solution) was irradiated with UV light (125 W lamp) using a pyrex filter at 25 °C in an immersion well photo-reactor. No appreciable reaction was observed even after prolonged period (>250 h) of irradiation. However, when an equimolar mixture of 5,6-*O*-isopropylidene-L-ascorbic acid⁹ **2** and 2-hydroxy-1,4-naphtho-

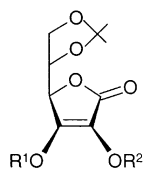
quinone by **2** in the dark was observed. This would imply that the photo-excited state of 2-hydroxy-1,4-naphthoquinone is reduced by **2**.

It was essential to check the possible involvement of acetone in the above reaction, either as a sensitizer or as a redox reagent, before exploring the scope of this reaction. The simplest way to check this could be to carry out the reaction in a photochemically inert solvent like dichloromethane or acetonitrile. However the L-ascorbic acid derivative **2** is insoluble in these solvents. But it was gratifying to observe that **2** had sufficiently good solubility in 1,2-dimethoxyethane (DME). Accordingly, a solution (0.1 molar solution) of an equimolar mixture of 5,6-*O*-isopropylidene-L-ascorbic acid **2** and 2-hydroxy-1,4-naphthoquinone in DME was irradiated with UV light (125 W lamp) using a pyrex filter at 25 °C in an immersion well photo-reactor. Under these conditions as well, reduction of 2-hydroxy-1,4-naphthoquinone to 1,2,4-trihydroxynaphthalene was over in 20 h. No difference in the outcome of the photoreaction, as compared to the reaction in acetone, was observed. This confirmed that acetone is not playing any other role, except that of a solvent, in the photochemical reaction.

In order to explore the generality of this observation, a series of quinones were irradiated with L-ascorbic acid derivative **2** in DME under the above reaction conditions. From the results obtained (Table 1) it is clear that, barring a few exceptions, most of the quinones undergo photo-reduction. Reduction of these quinones in the dark, under identical temperature and concentration conditions, was studied simultaneously. In general, naphthoquinones did not undergo reduction while benzoquinones were found to undergo reduction in the dark, though the rate was found to be quite slow (Table 1). Furthermore, the photoreduction of naphthoquinones and anthroquinones was found to be much slower than that of the benzoquinones. When the photoreduction of 2-hydroxy-1,4-naphthoquinone was carried out using 400 W UV lamp,¹¹ under otherwise identical reaction conditions, the reaction was complete in considerably reduced time (<5 h). Similarly, in the case of unsubstituted benzoquinone, the reduction was complete in a significantly shorter time (<30 min).

A study of the effect of the concentration and the temperature on the rate of the reduction was undertaken to confirm that the observed enhancement in the rate of the reductions of quinones is really a photochemical effect and not possibly due to the heating by the UV lamp. For this purpose the reduction of benzoquinone with the L-ascorbic acid derivative **2**, at different concentrations and temperatures, was conducted. Simultaneously, the effect of concentration and temperature on the dark reaction was studied as well. From the results of this study (Table 2) it is clear that the rate of the reduction, in the photochemical reaction, is independent of the concentration of the reacting species and the temperature. This confirms that the observed reduction of quinones with L-ascorbic acid derivative **2** is a photochemical reaction.

Under photolytic conditions, using wavelength >400 nm, quinones have been reported¹² to furnish addition products with electron rich olefins. Attempted reaction of 5,6-*O*-

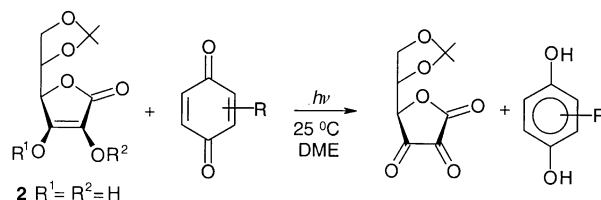


1 R¹ = R² = CH₃
2 R¹ = R² = H

quinone was irradiated in an identical manner, within 20 h, complete disappearance (TLC) of both the starting materials and concomitant formation of a single product was observed.^{10a,b} From the spectral data of the product, it was clear that L-ascorbic acid derivative **2** has effected reduction of 2-hydroxy-1,4-naphthoquinone to 1,2,4-trihydroxynaphthalene, rather than undergoing a Paternò-Büchi reaction. No reduction

† The IUPAC name for ascorbic acid is 5-(1,2-dimethylethyl)-3,4-dihydroxy-2,5-dihydrofuran-2-one.

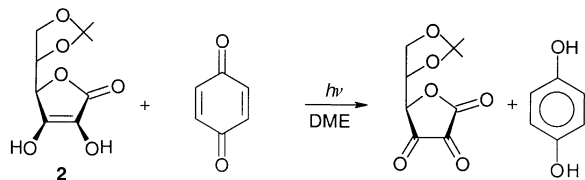
Table 1



Entry	Substrate ^{a,b}	Time/h		Yield ^c (%)	Mp/°C
		<i>hν</i>	Dark		
1	1,4-Benzoquinone	3	8	95	170–171 ^{18a}
2	2,5-Dimethyl-1,4-benzoquinone	20	40	56	213–214 ^{18b}
3	2,6-Dichloro-1,4-benzoquinone	25	40	87	164 ^{18c}
4	2,6-Di(<i>tert</i> -butyl)-1,4-benzoquinone	34	40	87	117–118 ^{18d}
5	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone	6	10	96	263 (decompose) ^{18e}
6	Tetrabromo-1,2-benzoquinone	8	10	83	191–192 ^{18f}
7	2-Methyl-1,4-naphthoquinone	80	NR ^d	42	166–167 ^{18g}
8	2-Hydroxy-1,4-naphthoquinone	20	NR ^d	35	154 ^{18h}
9	2,3-Dichloro-1,4-naphthoquinone	140	NR ^d	44	155–156 ¹⁸ⁱ
10	1,2-Naphthoquinone	4	20	62	108–109 ^{18j}
11	1,4-Naphthoquinone	NR ^d	NR ^d	NR ^d	NR ^d
12	9,10-Anthraquinone	NR ^d	NR ^d	NR ^d	NR ^d

^a Products were identified by the comparison of IR and NMR spectra and melting points with those of authentic samples. ^b Equimolar solutions of both the reactants were used. ^c Yield refers to the yield of pure isolated products from the photo-reaction. ^d No reaction starting material recovered.

Table 2 Reactions of compound 2 with benzoquinone in DME



Entry	Molar Conc. ^a	Temp./°C	Time/h		Yield (%)
			<i>hν</i>	Dark	
1	0.0574	25	3	8	94
2	0.0287	25	3	8	95
3	0.0143	25	3	8	95
4	0.0069	25	3	8	90
5	0.0574	5	3	10	92
6	0.0287	5	3	10	90
7	0.0143	5	3	10	95
8	0.0069	5	3	10	90
9	0.0574	–12	3	14	92
10	0.0287	–12	3	14	91
11	0.0143	–12	3	14	95
12	0.0069	–12	3	14	90

^a Equimolar solutions of both the reactants were used.

isopropylidene-L-ascorbic acid with benzoquinone under these reaction conditions however did not give any product.

The failure of the reduction of quinones by **1** and their successful reduction by **2** indicates that free hydroxy groups at the 3 and/or 2 position in L-ascorbic acid are essential for the success of these reductions. This is evident from the fact that when the reduction of benzoquinone with a fully protected L-ascorbic acid derivative¹³ **1**, in the presence of an added external acid like trifluoroacetic acid (>1 equivalent), was attempted, no enhancement in the rate of reaction, as compared to that with just **1**, was observed. This implies that the reaction is proceeding by a photo-induced electron transfer between the L-ascorbic acid derivative **2** and the photoexcited state of quinone, leading to the formation of an ion–radical pair.¹⁴ The possibility of the formation of such an intermediate is supported by the fact that the free energy of activation for the photo-induced electron transfer between the L-ascorbic acid derivative **2** and the excited state of benzoquinone was computed to be $-19 \text{ kcal mol}^{-1}$ using the Rehm–Weller

equation.^{15,16} Application of these findings in synthesis is being actively explored.

Experimental

General

All solvents were distilled and dried before use. Dry DME was prepared by distillation from Na–benzophenone under nitrogen atmosphere. Dry acetone was prepared by refluxing over KMnO_4 till pink colour persisted (2 days). Then it was refluxed over K_2CO_3 for 4 h and distilled and stored over 4 Å molecular sieves. Quinones were purified by recrystallization and/or sublimation under reduced pressure. Silica gel (100–200 mesh) was used for column chromatography. IR spectra were recorded on Perkin-Elmer model 1600 series FT IR instrument. ¹H NMR spectra [ppm, TMS as internal standard] in CDCl_3 or DMSO were recorded on a JEOL FX 90Q instrument. Mps were obtained with a paraffin oil bath and are uncorrected.

General conditions for the photochemical reactions

A mixture of 5,6-*O*-isopropylidene-L-ascorbic acid **2** (5.00 g, 23 mmol) and quinone (23 mmol) was dissolved in dry DME (200 ml). This solution was purged with pure dry nitrogen gas for 5 min and then it was irradiated with UV light (125 W, medium pressure mercury lamp) in an immersion well photo-reactor under inert atmosphere of nitrogen. After the complete consumption of the quinone (TLC), the reaction mixture was concentrated under reduced pressure and the residue was chromatographed on a column of silica gel using hexane–ethyl acetate (7:1) solvent system. The pure compound obtained was crystallized and characterized by spectral methods.

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- 9 The L-ascorbic acid derivative **2** was found to have good solubility in acetone and was found to be insoluble in other normally used solvents. Hence acetone was used as the solvent for the reaction.
- 10 (a) Presumably, in the reaction the L-ascorbic acid derivative **2** is oxidized to dehydro-L-ascorbic acid which could not be isolated due to its instability; (b) irradiation of a solution of the quinone in acetone in the absence of L-ascorbic acid derivative **2** did not yield any reduced product, implying that acetone is not participating in the redox process and that the quinone is not reduced by any other species.
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