Adduct Formation in the Photoreactions of Benzylic Ethers with Quinones

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Irradiation of 1,4-benzoquinone (BQ) in the presence of a series of benzylic ethers results in an adduct composed of one molecule of quinone and one molecule of the ether. In addition to the formation of this adduct, cleavage of the benzylic ether to the corresponding aldehyde and alcohol was observed. The amount of adduct formed was dramatically increased when the reaction was conducted in benzene. This is in contrast to the results of irradiation with 2,3-dichloro-5,6-dicyanoquinone (DDQ) where no adduct was isolable and only bond cleavage was observed. The major product of 2,5-dichloroquinone (DCQ) irradiation was bond cleavage of the benzylic ethers, but a small amount of adduct was observed as a reaction product. The formation of adducts in these quinone irradiations can be explained by the slower rate of adduct hydrolysis by lower potential quinones.

The reactions of quinones and dihydroquinones in biological systems continues to attract research interest.[1] During our studies of the reactions of 1,4-benzoquinone (BQ) with benzylic ethers, we observed a new photoproduct. This photoproduct was not observed in our previous studies of the photoreactions of DDQ with these same ethers, where bond cleavage of the benzylic ether was the exclusive product. We report here that changes in the quinone substituents result in a new photochemical reaction pathway for benzylic ether bond cleavages. Further, this reaction is a general reaction of low reduction potential quinones and a variety of benzylic ether functionalities.

The irradiation of BQ in the presence of benzyl phenyl ether (**1a**) is representative and is described to represent the general case. Irradiation of 0.05 M solutions of **1a** and BQ, followed by removal of solvent from the reaction mixture and silica gel column chromatography allowed the isolation of a new compound (i.e., **2a**) in addition to the expected products of bond cleavage (*i.e.*, benzaldehyde, **3a**, and phenol **4a**). This new compound was of only moderate stability. For example, the neat compound remained pure for less than 24 h. After this time, major amounts of the bond cleavage products (i.e., **3a** and **4a**) were observed. The new compound was most stable when stored in dilute solution (either CD_3CN or C_6D_6) at low temperature where 70–80% of the compound remained after 2 days.

The structure of **2a** was assigned based on the studies of its chemical reactivity and its ^1H NMR, ^{13}C NMR, and IR spectra. The compound was instantaneously cleaved by dilute HCl to afford the bond cleavage products **3a**, **4a**, and dihydroquinone (DHQ) in quantitative yield. On this basis, **2a** was assigned to be a 1:1 adduct of BQ and **1a**. Three adduct types of BQ compounds have been previously described in the literature. For all three adduct types, relevant spectral data have been reported. We refer to these structural types as Types I,[2] II,[3] and III[4] for ease of description of the structural assignment (see Scheme 1).

The assignment of the structure to be a phenolic ether adduct is based primarily on the lack of a carbonyl peak in the IR spectrum and no ^{13}C signals which could be attributed to a carbonyl group. The structure of **2a** was confirmed by X-ray analysis of the *p*-bromobenzoyl pyridinium chloride derivative **5**. This derivative was isolated by addition of the adduct (isolated by column chromatography) to a solution of the pyridinium chloride. The derivative structure is shown in Figure 1.[5a] Thus, there can be no doubt of the structure of **2a**.

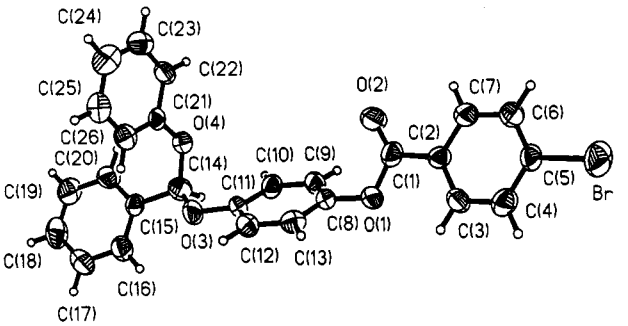
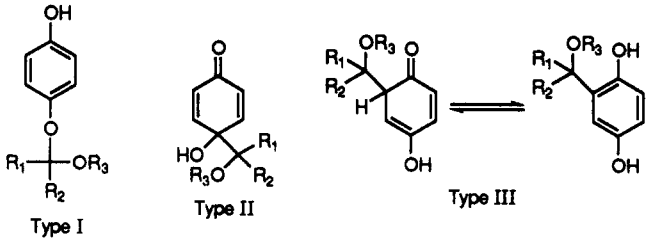


Figure 1. X-ray structure of **5**.

Scheme 1



For all compounds reported in this study, similar chemistry and spectral data were observed (see Experimental Section and the supplementary material for spectral assignments and spectra). Data on the irradiation of these quinones in solutions containing **1** are gathered in Table 1. The yields of **2** and **3** are listed as a relative

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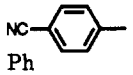
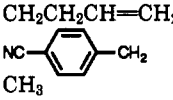
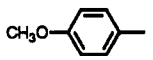
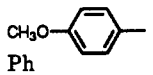
(5) (a) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. (b) Jones, G., II; Haney, W. A.; Phan, X. T. *J. Am. Chem. Soc.* **1988**, *110*, 1922.

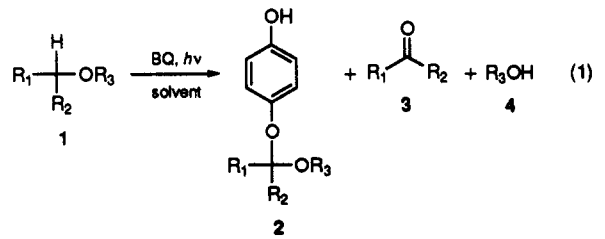
0022-3263/94/1959-3037$04.50/0

Table 1. Summary of Product Analysis for Irradiation of Quinones in the Presence of Various Ethers[a,b]

	substrate[c] (1)			light	time	conv	yield[e] (mol %)	
	R_1	R_2	R_3	source, nm	(h)	(%)	2	3
a	H	Ph	Ph	350[d]	23	21	52	48
				350	25	67	94	6
				>320	10	49	16	84
				sumlamp[d]	24	44	59	41
				sunlamp	21	51	85	15
b	H	Ph	$PhCH_2$	350[d]	27	79	53	47
				350	10	34	70	30
				sunlamp[d]	24	92	57	43
				sunlamp	21	63	94	6
				>320	48	50	67	33
c	Ph	Ph	Ph	350	35	42	77	23
				sunlamp[d]	24	19	48	52
				sunlamp	25	40	75	25
d	H	Ph	$CH_2CH_2CH{=}CH_2$	>320	11	98	69	31
e	H			sunlamp[d]	41	52	71	29
	H			sunlamp	56	25	100	0
f	H	Ph	CH_3	sunlamp	18	36	99	1
				sunlamp[d]	29	40	76	24
				350	26	46	96	4
				350[d]	22	37	76	24
g	H		Ph	sunlamp	21	43	70	30
h		Ph	CH_3	sunlamp	16	11	75	25
i[f]	H		Ph	sunlamp	13	25	10	90
j[f]	H	Ph	Ph	sunlamp	24	23	5	95

[a] 0.05 M of 1,4-benzoquinone was used as the sensitizer. [b] Benzene was used as the solvent unless otherwise noted. [c] 0.05 M in concentration unless otherwise noted. [d] CH_3CN as solvent. [e] Based on unreacted starting material. [f] 0.05 M of 2,5-dichloroquinone was used as the sensitizer; 0.01 M dibenzylamine added.

ratio such that their yields total 100%. However, this listing is somewhat arbitrary, since, in all cases, ≥95% mass balance was obtained. For **1d**, **1f**, and **1h** where **4** would be lost in the workup procedure, the closure of mass balance was completed by assuming that the yield of isolated **3** was equal to the yield of **4** produced in the reaction. Therefore, the results of irradiation of BQ in the presence of **1** can be described by eq 1.



(1)

A modest effort to optimize the conditions for formation of **2** was undertaken (Table 1). The effect of the light source had little effect on the reaction as shown by irradiation with either a 450-W Hanovia lamp equipped with a uranyl filter (listed in Table 1 as >320 nm), a 350-nm lamps from a Southern New England Ultraviolet irradiation device (350 nm in Table 1), or a sunlamp. Similar product distributions were observed when the reactions were run in the same solvent. In contrast, a solvent dependence on product yields was observed. The fraction of the reaction proceeding to adduct is dramatically increased in C_6H_6 when compared to the corresponding reaction in CH_3CN. This effect has been observed previously in the formation of adducts from chloranil and methyl arenes.[5b]

A second variable which has a modest effect upon the relative reaction yields is the presence of added base. Dibenzylamine was chosen as a base because it reacted more slowly with BQ* than did compounds **1**. By using dibenzylamine at low concentrations (0.01 M compared to 0.05 M for other reagents), its effect on the photoreactivity of the quinones and **1** could be kept to a minimum value. At the same time, its intrinsic basicity could be utilized to minimize the effects of acid-catalyzed hydrolysis in the reaction. For the reaction of **1a** with BQ, addition of 20 mol % dibenzylamine resulted in the ratio of **2**:**3** changing from 85:15 to 90:10. In fact, for the dichloroquinone adducts **1i** and **1j**, adduct isolation was only possible with the addition of a small amount of this base.

We believe that the isolation of adduct **2** in these systems is quite remarkable and represents a new synthetic route toward the synthesis of monobenzone derivatives. This class of compounds has been widely used as a depigmentor.[6] The isolation of these adducts is made more remarkable by the fact that their structures are really masked hemiacetals, since only an aryl bridging group separates the OH from the "acetal" carbon atom. Since the structure of **2** is essentially that of a hemiacetal, the solvent dependence for its formation is not at all surprising. More bond cleavage of **1** occurs in the relatively more polar CH_3CN than in nonpolar benzene. The observation of **2i** and **2j** is even more remarkable since the adduct was formed from dichloroquinone (DCQ). **2i** and **2j** were only isolable when base was added to the solution.

In summary, we report that adducts **2** are observable and isolable in the irradiation of low electron demand quinones BQ and DCQ. More adduct is isolable in the less-polar benzene than in CH_3CN. These results are in

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contrast to the higher potential quinones (i.e., DDQ) where no adducts are isolable.

Experimental Section

Gas-liquid chromatographic analyses were conducted on a Hewlett-Packard Model 5890A GLC equipped with a 10-m 5% phenylmethylsilicone column. Integration of the signals was performed by a Hewlett-Packard Model 3390A digital integrator. GC-MS were measured with a Hewlett-Packard Model 5980 mass spectrometer with a 5890 gas chromatograph equipped with a 25-m 5% phenylmethylsilicone column. IR spectra were recorded on a Midac Model or a Perkin-Elmer Model 1310 FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were measured in the indicated solvent on a JEOL GX-270 NMR spectrometer at room temperature. Chemical shifts are expressed in parts per million (ppm) upfield from $Si(CH_3)_4$.

Acetonitrile (from CaH_2) and benzene (from $LiAlH_4$) were freshly distilled immediately prior to use. Silica gel was purchased from Aldrich and was used as received. Unless otherwise indicated, all purchased chemicals originated from Aldrich Chemical Co. Benzyl phenyl ether was recrystallized from 95% ethanol. Dibenzyl ether was purified by flash chromatography (70–230 mesh of silica gel, 5% ethyl acetate in hexane). 4,4'-dicyanobenzyl ether[7] and diphenylmethyl phenyl ether[8] were synthesized by literature methods. Benzyl 4-butenyl ether, benzyl methyl ether, α-(cyclopropyl)benzyl methyl ether, and p-methoxybenzyl phenyl ether were synthesized by the method of Brewster and Theodore.[9]

General Photochemical Reaction Procedure. The substrates (0.05 M) were dissolved in the indicated solvent, i.e., benzene or acetonitrile, together with 1,4-benzoquinone (0.05 M) in reaction tubes, sealed with rubber septa, and degassed by bubbling with N_2 for 30 min prior to irradiation using the specified conditions. After irradiation, the solvent was removed and the resulting residues were separated by flash chromatography (silica gel 70–230 mesh, 5% ethyl acetate in hexane). For product distributions, see Table 1.

4-(Phenoxyphenylmethoxy)phenol (2a): IR (thin film) 3414, 1220, 1008, 820, 726, 697 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 4.83 (s, 1H, OH), 6.56 (s, 1H, CH), 6.66 (d, 2H, J = 8.97 Hz), 6.85 (d, 2H, J = 8.97 Hz), 6.99 (m, 3H), 7.25 (m, 2H), 7.38 (m, 3H), 7.59 (m, 2H); ^{13}C NMR (270 MHz, $CDCl_3$) δ 101.5, 116.0, 117.4, 119.4, 122.4, 126.7, 128.5, 129.1, 129.5, 137.4, 150.0, 150.9, 156.2.

4-[(Phenyl)(phenylmethyl)methoxy]phenol (2b): IR (thin film) 3415, 1211, 820, 725, 696 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 4.65 (s, 2H, CH_2), 5.40 (s, 1H, OH), 6.12 (s, 1H, CH), 6.70 (d, 2H, J = 9.2 Hz), 6.88 (d, 2H, J = 9.2 Hz), 7.23–7.55 (m, 10H); ^{13}C NMR (270 MHz, $CDCl_3$) δ 151.9, 150.7, 150.6, 137.4, 128.8, 128.4, 127.9, 127.7, 126.7, 118.9, 118.5, 115.9, 101.4, 67.3.

4-(Diphenylphenoxymethoxy)phenol (2c): IR (thin film) 3407, 1220, 820, 729, 701 cm^{-1}; ^1H NMR (270 MHz, CD_3CN) δ 6.54 (d, 2H, J = 9.3 Hz), 6.57 (s, 1H, OH), 6.98 (d, 2H, J = 9.3 Hz); 7.1–7.73 (m, 15H, Ph); ^{13}C NMR (270 MHz, CD_3CN) δ 106.1, 116.3, 120.7, 122.2, 123.2, 127.7, 128.8, 129.2, 130.1, 143.5, 148.2, 153.1, 155.4.

4-(3-Butenoxyphenylmethoxy)phenol (2d): IR (thin film) 3407, 1548, 1255, 819, 728, 698 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.35 (qt, 2H, J = 6.7, 1.3 Hz, $CH_2CH{=}CH_2$), 3.60 (dt, 1H, J = 9.2, 6.7 Hz, CH_2O), 3.68 (dt, 1H, J = 9.2, 6.7 Hz, CH_2O), 4.84 (s, 1H, OH), 5.02 (ddt, 1H, J = 10.3, 1.9, 1.3 Hz, $CH_2{=}$), 5.07 (ddt, 1H, J = 17.1, 1.9, 1.3 Hz, $CH_2{=}$), 5.79 (ddt, 1H, J = 17.2, 10.3, 6.7 Hz, CH=), 6.05 (s, 1H, OCHO), 6.72 (d, 2H, J = 9.2 Hz), 6.93 (d, 2H, J = 9.2 Hz), 7.25–7.55 (m, 5H, Ph); ^{13}C NMR (270 MHz, CD_3CN) δ 34.8, 66.9, 103.6, 116.7, 116.9, 120.1, 127.6, 129.2, 129.7, 136.5, 139.8, 151.1, 153.0.

4-[[(4-Cyanophenyl)methoxy](4-cyanophenyl)methoxy]phenol (2e): IR (thin film) 3406, 2232, 1508, 1211, 1121, 1036 cm^{-1}; ^1H NMR (270 MHz, CD_3CN) δ 4.72 (s, 2H, CH_2), 6.25 (s, 1H, OH), 6.64 (s, 1H, CH), 6.71 (d, 2H, J = 9.3 Hz), 6.90 (d, 2H, J = 9.3 Hz), 7.43 (d, 2H, J = 8.4 Hz), 7.67 (d, 2H, J = 8.4 Hz), 7.74 (m, 4H); ^{13}C NMR (270 MHz, CD_3CN) δ 68.2, 102.2, 116.7, 116.8, 119.4, 119.6, 120.3, 128.6, 129.0, 133.2, 133.4, 1444.0, 144.2, 150.4, 150.9, 153.4.

4-(Methoxyphenylmethoxy)phenol (2f): IR (thin film) 3410, 1510, 1212, 1100, 1090, 1010 cm^{-1}; ^1H NMR (270 MHz, CD_3CN) δ 3.37 (s, 3H, OCH_3), 5.97 (s, 1H, CH), 6.68 (s, 1H, OH), 6.71 (d, 2H, J = 8.97 Hz), 6.89 (d, 2H, J = 8.97 Hz), 7.32–7.53 (m, 5H); ^{13}C NMR (270 MHz, CD_3CN) δ 54.1, 104.2, 116.7, 120.0, 127.6, 129.3, 129.7, 139.4, 151.1, 153.0.

4-[(4-Methoxyphenyl)phenoxymethoxy]phenol (2g): IR (thin film) 3412, 2054, 1612, 1508, 1235, 1199, 1174, 1028, 829, 755, 692 cm^{-1}; ^1H NMR (270 MHz, CD_3CN); δ 3.77 (s, 3H, CH_3), 6.67 (s, 1H, CH), 6.68 (d, 2H, J = 9.1 Hz), 6.72 (s, 1H, OH), 6.85 (d, 2H, J = 9.1 Hz), 6.94 (d, 2H, J = 8.8 Hz), 6.99 (m, 3H), 7.26 (m, 2H), 7.53 (d, 2H, J = 8.8 Hz); ^{13}C NMR (270 MHz, CD_3CN); δ 55.9, 101.6, 114.7 116.7, 118.1, 120.1, 123.3, 129.1, 130.5, 130.9, 150.3, 153.3, 157.2, 161.2.

4-(Cyclopropylmethoxyphenylmethoxy)phenol (2h): IR (thin film) 3385, 1507, 1448, 1212, 1087, 991, 914, 831, 758, 702 cm^{-1}; ^1H NMR (270 MHz, CD_3CN) δ 0.24 (m, 1H), 0.40 (m, 2H), 0.59 (m, 1H), 1.09 (m, 1H), 3.38 (s, 3H, OCH_3), 6.62 (d, 2H, J = 9.2 Hz), 6.63 (s, 1H, OH), 6.90 (d, 2H, J = 9.2 Hz), 7.31 (m, 3H), 7.50 (m, 2H); ^{13}C NMR (270 MHz, CD_3CN) δ 12, 21, 50.5, 105.5, 116.1, 116.7, 123, 128.1, 128.7, 142.2, 150.4, 153.

2,5-Dichloro-4-[(4-methoxyphenyl)phenoxymethoxy]phenol (2i): IR (thin film) 3517, 3071, 1613, 1589, 1470, 1251, 1174, 1029, 988, 829, 755, 692 cm^{-1}; ^1H NMR (270 MHz, CD_3CN) δ 3.77 (s, 3H, CH_3), 6.74 (s, 1H, CH), 6.78 (s, 1H, OH), 6.95 (d, 2H, J = 8.6 Hz), 6.95–7.04 (m, 3H), 6.99 (s, 1H), 7.17(s, 1H), 7.20–7.29 (m, 2H), 7.56 (d, 2H, J = 8.6 Hz); ^{13}C NMR (270 MHz, CD_3CN) δ 56.0, 102, 114.7, 118.2, 118.4, 119.6, 121.4, 123.7, 124.5, 129.3, 129.7, 130.6, 145.8, 149.2, 156.9, 161.4.

2,5-Dichloro-4-(phenoxyphenylmethoxy)phenol (2j): IR (thin film) 3516, 3064, 1588, 1478, 1222, 1188, 1076, 989, 754, 694 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 5.30 (s, 1H, OH), 6.62 (s, 1H, CH), 7.02–7.05 (m, 2H), 7.03 (s, 1H), 7.20 (s, 1H), 7.23–7.28 (m, 3H), 7.38–7.41 (m, 3H), 7.63–7.66 (m, 2H); ^{13}C NMR (270 MHz, $CDCl_3$) δ 102.2, 117.3, 120.7, 120.8, 122.8, 125.1, 126.6, 126.7, 128.5, 129.3, 129.5, 136.4, 145.3, 147.4, 155.9.

Synthesis of 4-(Phenoxyphenylmethoxy)phenyl p-Bromobenzoate (5). 5 was synthesized using a general method for the synthesis of acid anhydrides.[10] p-Bromobenzoyl chloride (87 mg, 0.40 mmol) was mixed with 1 mL of freshly dried benzene and pyridine (60 mg, 0.76 mmol) under nitrogen. A white precipitate was observed after stirring for 5 min, indicating the formation of the reactive acyl halide–pyridinium complex. The reaction vessel was placed in a cold water bath at 5 °C and a solution of adduct **2a** in 1 mL of dried benzene was added all at once. Stirring was continued for 30 min at 5 °C and the pyridinium chloride was removed by suction filtration. After solvent removal in vacuo, the residue was triturated with hexane to give crude **6**, which was recrystallized from 5% ethyl acetate/hexane to give colorless crystals with a melting point of 117–118 °C: IR (deposited film) 1734, 1588, 1504, 1264, 1187, 1702, 1010, 750, 695 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 6.67 (s, 1H, CH), 7.00–7.07 (m, 7H), 7.25–7.31 (m, 2H), 7.41–7.48 (m 3H), 7.61–7.63 (m, 2H), 7.64 (d, 2H, J = 8.8 Hz), 8.03 (d, 2H, J = 8.8 Hz); ^{13}C NMR (270 MHz, $CDCl_3$) δ 100.6, 117.3, 118.3, 122.4, 122.5, 126.7, 128.3, 128.6, 128.8, 129.3, 129.5, 131.5, 131.9, 137.1, 145.5, 153.8, 156.0, 164.6.

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Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra of **2a–2j** (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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