Acid Catalysed *ipso* Photosubstitution of Alkoxy-substituted Benzenes in Aqueous Acid Solution

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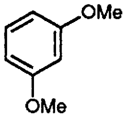
The first examples of acid catalysed *ipso* photosubstitution of alkoxy-substituted benzenes by solvent water, with observed quantum yields in the range 0.03—0.14 are reported, the mechanism of which is believed to involve initial photoprotonation of the aromatic ring in the excited singlet state.

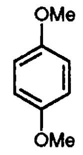
Numerous reports of fluorescence quenching of aromatic compounds by acid have appeared in the literature.[1—11] It has been reported that fluorescence quenching by protons of some benzenes and naphthalenes is associated with electrophilic attack of the proton on the aromatic ring in the excited state, resulting in overall proton exchange in some substrates.[1,4—7] For aromatic systems with photochemically reactive side chains, quenching by a proton has been interpreted as being due to assistance of the primary photochemical step by the proton.[8—11] We report here a new photochemical pathway available for alkoxy-substituted benzenes in the presence of acid: photosubstitution of the alkoxy group by solvent water, resulting in overall photochemical *ipso* substitution.

With an original interest in studying possible photochemical proton (deuteron) exchange of electron-rich benzenes, we photolysed 1,2-dimethoxybenzene (**1**) in 1:4 (v/v) MeCN–30% (w/w) D_2SO_4/D_2O or H_2SO_4/H_2O (10^{-2}—10^{-3} M substrate; Rayonet RPR 100 photochemical reactor; 254 nm; argon purged solutions; 5—20 min). To our surprise, (**1**) was quickly converted (after washing with H_2O) to (**2**), which was then photochemically converted to (**3**) on extended photolysis (Scheme 1). Deuterium incorporation in recovered (**1**) was also observed when photolysis was carried out in D_2SO_4/D_2O (as determined by GC-MS), and amounted to 40% monodeuteriation and 10% dideuteriation. It seems clear that an efficient photochemical substitution reaction is taking place in acid, competing with proton exchange since (**1**) was non-reactive to *ipso* substitution or proton exchange in the dark under otherwise identical conditions. When 20% ^{18}O-enriched water was used in the aq. H_2SO_4 acid portion, both (**2**) and (**3**) were found to be 20% enriched with ^{18}O at each OH group accordingly, indicative of a substitution mechanism and not a 'dealkylation' pathway, which would not have resulted in oxygen isotope incorporation in the products (Scheme 1). In addition, (**1**) showed increasing reactivity with increasing acidity, beginning at ~pH 2; in less acidic and neutral solution, (**1**) was photostable, even on prolonged photolysis. Photolysis of authentic (**3**) (natural abundance material) in 25% (w/w) H_2SO_4–MeOH gave (**2**) (48%) and (**1**) (9%), indicating that the *ipso* substitution process is not restricted to alkoxy groups, but works equally well for substitution of hydroxy on benzene rings.

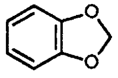
Exploratory studies showed that a variety of other alkoxy-substituted benzenes also react *via ipso* photosubstitution of the alkoxy group on photolysis in acid. For example, 1,2-benzodioxole† (**6**) gave exclusively (**3**) on photolysis in aqueous acid, as would be expected from a photosubstitution mechanism, since the product from the initial *ipso* photosubstitution of one of the alkoxy groups gives a hemi-acetal, which hydrolyses quickly to (**3**). Compound (**7**), on the other hand, gave a mixture of (**8**) and (**3**), also as expected, with (**8**) being the major product at low conversion. An interesting extension of these reactions is the overall ring opening of 1,2-dihydrobenzofuran (**12**) on photolysis in acid solution (Scheme 2), to give 2′-hydroxyphenethyl alcohol. Quantum yields for photochemical *ipso* substitution of some representative systems in 20% H_2SO_4 are given in Table 1. A range of reactivity, as measured by their quantum yields, was observed, with the *ortho*-substituted compounds showing significantly higher reactivity. For all reacting systems, acid was required to effect reaction; in solutions of pH >2, no reactions were observed with any of the compounds studied. Of interest is the fact that 1,3- and 1,4-dimethoxybenzenes [(**4**) and (**5**), respectively] did not undergo observable *ipso* photosubstitution (ϕ <0.001). However, photolysis of either (**4**) or (**5**) in 1:4 CH_3CN–(5—15%) D_2SO_4/D_2O resulted in significant (50—60%) incorporation of a single deuterium atom in the recovered substrate.‡



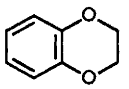
(**4**)



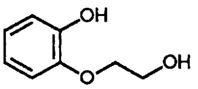
(**5**)



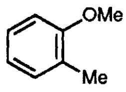
(**6**)



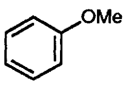
(**7**)



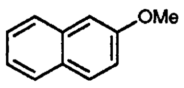
(**8**)



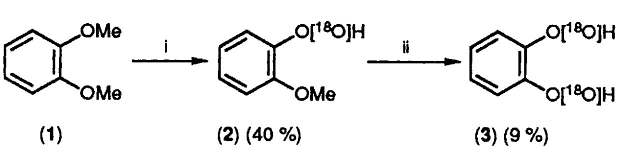
(**9**)



(**10**)



(**11**)



Scheme 1. *Reagents and conditions*: i, *hv*, 1:4 MeCN–30% (w/w) $D_2SO_4/H_2[^{18}O]$ or $H_2SO_4/H_2[^{18}O]$; ii, *hv*.

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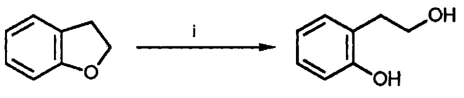
† The acetal linkage of (**6**) does not undergo thermal hydrolysis in the dark under the conditions of the experiment. Acetal groups of this kind are in general quite stable towards hydrolysis in acid, unlike simple acetals.

‡ The thermal ring proton exchange of 1,3-dimethoxybenzene (**4**) was sufficiently fast in acid solution of >15% D_2SO_4/D_2O that the photochemistry of this compound could not be studied at these higher acidities. However, thermal *ipso* substitution was not observed for (**4**) at any acid strength used (up to 40% H_2SO_4).



(12)

Scheme 2. *Reagents and conditions*: i, *hv*, 1:4 MeCN–30% (w/w) H_2SO_4.

Table 1. Quantum yields (ϕ) for photosubstitution in 1:4 (v/v) MeCN–20% (w/w) H_2SO_4.

Compound	ϕ	Compound	ϕ
(**1**)	0.10[a]	(**9**)	0.09
(**4**)	<0.001[b]	(**10**)	0.04[c]
(**5**)	<0.001[b]	(**11**)	<0.001[d]
(**6**)	0.04	(**12**)	≈0.03
(**7**)	0.09		

[a] ϕ = 0.036 and 0.14 in 5 and 30% H_2SO_4, respectively. Errors in measured quantum yields are ±20% of quoted value. [b] No detectable photoreaction by GC analysis. [c] Lodder and Havinga (ref. 7) have shown that this compound undergoes photochemical proton exchange of the aromatic protons in acid solution. [d] No detectable photoreaction by GC analysis. Shizuka and Tobita (ref. 4) have shown that this compound undergoes photochemical proton exchange of the aromatic protons in acid solution.

The fluorescence emissions of all of the above compounds are quenched by acid, beginning at about pH 2. In addition, fluorescence lifetimes (all first order decays, as measured by single-photon counting) decreased on going from pH 7 to more acidic solution. For example, for anisole (**10**), $\tau = 4.9$ ns in pH 7 and $\tau = 2.8$ ns in 10% H_2SO_4. This data, when taken with the observation of acid catalysis of *ipso* substitution, implies that the mechanism of photosubstitution probably involves initial photoprotonation of the aromatic ring in S_1. None of the compounds studied here are known to be significantly protonated in the ground state at the acidities used (*e.g.*, the pK_a for protonation of trimethoxybenzene ≈ −6).[12] Therefore, protonation prior to photoexcitation is unlikely. The photoprotonated intermediate may either undergo proton exchange or nucleophilic attack by water, resulting in photosubstitution. The different extent to which these compounds undergo *ipso* photosubstitution *vs.* simple proton exchange suggests that the sites of photoprotonation are highly dependent on the number and position of alkoxy substituents on the ring system. That is, protonation at the *ipso* position can result in substitution whereas protonation at a hydrogen site probably results in only proton (deuteron) exchange. A full understanding of the connection between photochemical proton exchange and the new *ipso* photosubstitution process described in this work will require additional studies, the results of which will provide new insights into the enhanced electrophilic reactivity of aromatic compounds in the excited singlet state previously unavailable.

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