Photocyclization of *o*-Phenoxybenzyl Alcohols in Aqueous Solution. A Simple Synthesis of 6*H*-Dibenzo[*b,d*]pyrans

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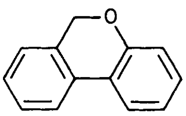
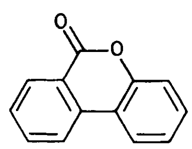
A new photochemical cyclization reaction of *o*-phenoxybenzyl alcohols is reported, which is observed only in aqueous solution, giving rise to 6*H*-dibenzo[*b,d*]pyrans in good yields.

The 6*H*-dibenzo[*b*,*d*]pyran ring system, as represented by the parent compound (**1**), has been of interest pharmacologically[1—3] and also because it is found in cannabinol, a constituent of cannabis.[4,5] Syntheses of (**1**) and related compounds have employed 2′-hydroxybiphenyl-2-carboxylic acid lactones in which the biphenyl fragment has already been assembled,[1] in addition to other cyclization procedures also taking advantage of a preassembled biphenyl ring system.[6,7] We are not aware of any photochemical routes to the 6*H*-dibenzo[*b*,*d*]pyran ring system apart from a report from Yang and co-workers[8] which also utilizes a preassembled biphenyl fragment in a synthesis of (**2**). We report here a new photochemical cyclization reaction which takes *o*-phenoxybenzyl alcohols to 6*H*-dibenzo[*b*,*d*]pyrans in good yields. The reaction is observed only in aqueous solution and is mechanistically unprecedented.

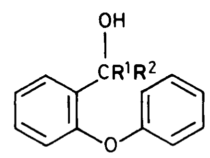
Our interest in the photochemistry of benzyl alcohols in aqueous medium have led us to explore a wide range of compounds, the results of which have been reported.[9—14] The present investigation stems from an interest in constructing the xanthene ring system *via* photodehydroxylation of *o*-phenoxybenzyl alcohol (**3**) as shown in Scheme 1. It was expected that carbocation photogeneration would be efficient (as observed for many other appropriately substituted benzyl alcohols),[9—14] and that a subsequent Friedel–Crafts alkylation might compete favourably with trapping by solvent water (which leads to starting material), and hence give xanthene (**6**). However, photolysis of (**3**) in aqueous acetonitrile [typically 70% (v/v) H_2O–MeCN; Rayonet RPR 100 photochemical reactor with 254 nm lamps; 100—400 mg in 200 ml solvent; photolysis time 30—120 min] gave 6*H*-dibenzo-[*b*,*d*]pyran (**1**) (Scheme 1) in good yields (typically > 50%)



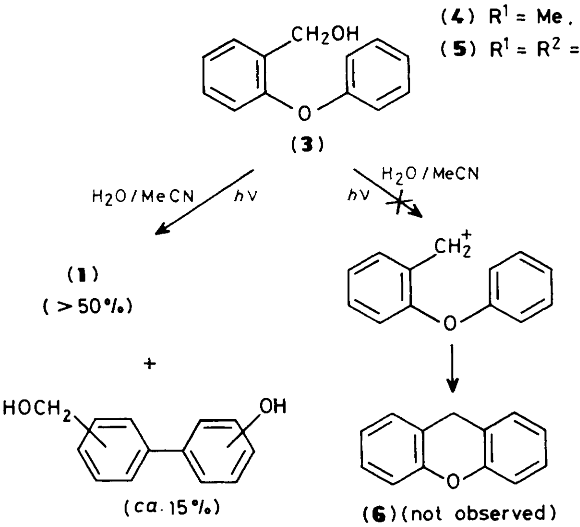
(1)



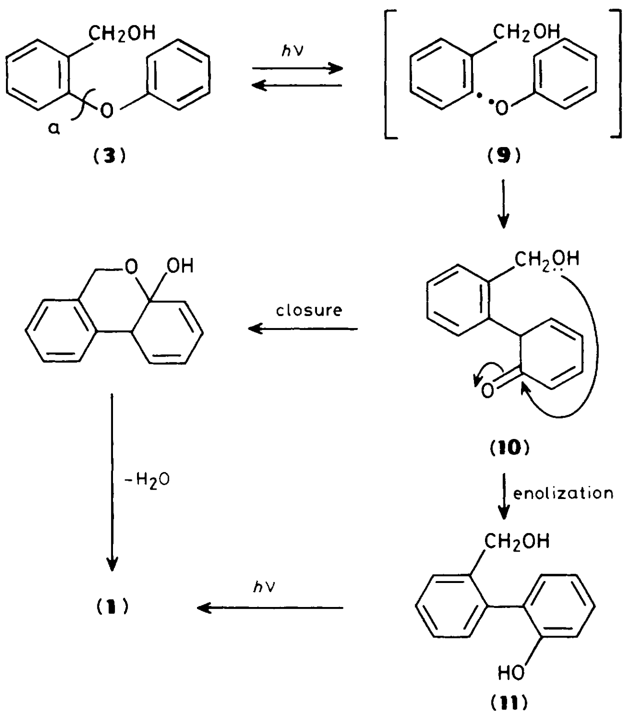
(2)



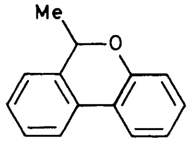
(3) $R^1 = R^2 = H$
(4) $R^1 = Me, R^2 = H$
(5) $R^1 = R^2 = Me$



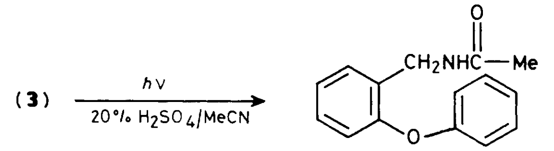
Scheme 1



Scheme 2



(7)



along with a mixture of hydroxybiphenyls (*ca.* 15%) (which were characterized by ^{1}H n.m.r. of the mixture and by g.c./m.s.), along with recovered substrate. Separation of (**1**) from starting material and the hydroxybiphenyl products was accomplished readily by chromatography thanks to the large difference in retention times between (**1**) and any of the side products or the starting alcohol (**3**). The estimated quantum yield for formation of (**1**) is *ca.* 0.01 which is relatively low, but the chemical yields are high. Photolysis of xanthene (**6**) under similar conditions to those described above results in negligible photochemistry and proves that (**1**) is not a secondary photoproduct of (**6**) under the reaction conditions. The formation of (**1**) is therefore mechanistically interesting and additional studies were carried out.

Photolysis of (**4**) in aqueous solution gave 6-methyl-6*H*-dibenzo[*b*,*d*]pyran (**7**) as the corresponding cyclization product, while a similar photolysis of (**5**) resulted in mostly recovered starting material; the corresponding pyran product was formed only in trace amounts. Interestingly, the photocyclization of both (**3**) and (**4**) requires the presence of water in the medium since photolysis in any of the commonly available organic solvents (*e.g.*, MeOH, EtOH, pure MeCN, *etc.*) gave no trace of the corresponding pyran and only modest lost (<10%) of substrate. Upon addition of water, the yield of the pyran (as well as extent of conversion of reaction) increases with increasing water content. Photolysis of (**3**) in a mixture of 70% (v/v) of 20% H_2SO_4–MeCN gave only the acetamide (**8**). When MeOH is used instead of MeCN as the cosolvent, only the corresponding methyl ether is formed. No reaction is observed in the dark. Thus in the presence of acid, the photodehydroxylation (solvolysis) pathway is observed, to give the *o*-phenoxybenzyl carbocation, which is trapped by MeCN or MeOH to give the above-mentioned observed products. The expected Friedel–Crafts alkylation to give (**6**) is not observed. Carbocation formation is not important in neutral solution, and an alternative reaction pathway operates.

The above results indicate that photochemistry of appropriately substituted diaryl ethers can give unexpected products if photolyses are carried out in neutral aqueous solution. Previous studies of diaryl ether photochemistry[15—17] have shown that aryl–oxygen bond cleavage is the primary photochemical process, to give a radical pair. Recombination of the radical pair leads to isomeric hydroxybiphenyls *via* an overall photo-Claisen type rearrangement.[15—17] In addition, the photocyclization of some diaryl ethers to dibenzofurans has also been reported.[18,19] The observation of hydroxybiphenyl products in the present reactions would argue for a mechanism involving initial aryl–oxygen bond homolysis (Scheme 2), to generate a radical pair [*e.g.*, (**9**)]. What is exceptional about (**3**) and (**4**) is that in the absence of water, the compound is relatively inert; that is, the majority of the radical pairs must recombine to give starting material. In the presence of water, it is suggested that the radical pair (**9**) recombine to give predominantly the *ortho*-coupling product (**10**), which can lead to pyran (**1**) *via* cyclization or give hydroxybiphenyl (**11**) on enolization. We have found that photolysis of an authentic sample of (**11**) in aqueous MeCN gives (**1**) as the exclusive product in high yield. Thus, either reaction pathway of (**10**) would ultimately give (**1**). Additional studies are warranted to explain why bond 'a' (Scheme 2) is preferentially broken in the primary photochemical step and why water is so essential for recombination of (**9**) to give (**10**), although it is reasonable that the high polarity of water may favour the formation of (**10**) [as opposed to recombination to give back (**3**)] because of stabilization *via* H-bonding and solvation of the incipient polar carbonyl group in this product.

We are grateful to the Natural Sciences and Engineering Research Council (N.S.E.R.C.) of Canada for support of this research. Additional support from the University of Victoria in the form of a graduate fellowship to C. G. H. is also acknowledged.

Received, 9th May 1988; Com. 8/01790E

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