Photochemical Behavior of Allyl ethers of Vicinal Hydroxynaphthophenones

Kumaresan Murugesan, Sumathi Sowrirajan, Balasubramanian Kalpattu Kuppusamy

Abstract: *In this research work, hitherto unreported photochemical studies on allyl ethers of 1-hydroxy-2-naphthophenone, 2-hydroxy-1-naphthophenone and 3-hydroxy-2-naphthophenone are presented. While allyl ethers of 1-hydroxy-2-naphthophenone were photoactive at 330 nm and the other two ethers were photostable*

Keywords: *Photolysis, Claisen rearrangement, Hydroxynaphthophenones.*

I. INTRODUCTION

Ethers of aliphatic or aromatic hydroxyketones possessing δ-hydrogen, in general, are active in intramolecular 1,7-hydrogen abstraction and 1,5-biradical cyclisation reaction proceeding via $(n \to \pi)^3$ excited state. Alkenyl / alkynyl ethers of 2-hydroxybenzophenones possessing δ-hydrogen are the substrates where various possible competitive photochemical processes such as hydrogen abstraction-cyclisation, Paterno-Buchi reaction and cleavage (aryloxy-carbon bond) leading to photo-Claisen rearrangement product / 2-hydroxybenzophenone are possible. Especially, hydrogen abstraction reactions[1e] and hydrogen atom transfer reactions[1f] play a vital role in organic synthesis. While allyl phenyl ethers under photolysis conditions afford the photo-Claisen rearrangement product, 2-benzoyl / 2-acetyl substituted allyl phenyl ethers **1a-b**, undergo 1,7-H abstraction followed by 1,5-biradical coupling (Figure 1), providing 3-phenyl / 3-methyl substituted 2,3-dihydrobenzofuran-3-ols **2a-b**.[1a,b] The mechanism of this photochemical transformation has been studied in detail.[2] This photoreaction has been exploited in the synthesis of 2-alkyl-3-aryl-2,3-dihydrobenzofuran-3-ols and 2-alkyl-3-arylbenzofurans[3] and also in the synthesis of Afflatoxin.[1c] Interestingly, ether **1c**, led to only photochemical *cis-trans* isomerization.
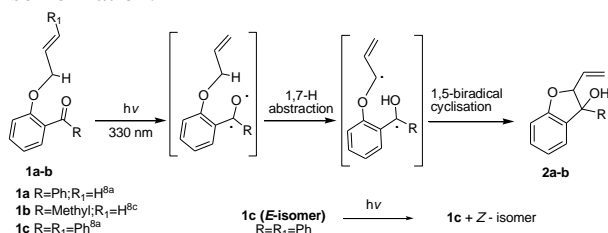

Fig.1 1,7-Hydrogen Abstraction In Ethers 1a-B

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II. EXPERIMENTAL

Most Extension of the above studies on vicinally substituted benzoylnaphthyl allyl ethers, the photosubstrates similar to ethers 1a-c is hitherto unreported. Also, many naphthalene derivatives such as naphthophenone, naphthaquinones and naphthopyrans, are known to exhibit significant biological potentials.[1d] In view of the above, the vicinally substituted benzoylnaphthyl allyl ethers **6**, **7**, **8** and analogous propargyl ether **9**, were synthesized and the photochemical behavior of vicinally substituted benzoylnaphthyl ethers **6a**, **6c** and **7-9** was investigated. (Figure 2). Ether **6b** was prepared as a reference compound for the cross-over experiment which will be discussed later. These ethers were prepared from the corresponding naphthols and were thoroughly characterized by NMR and HRMS spectral data**.**
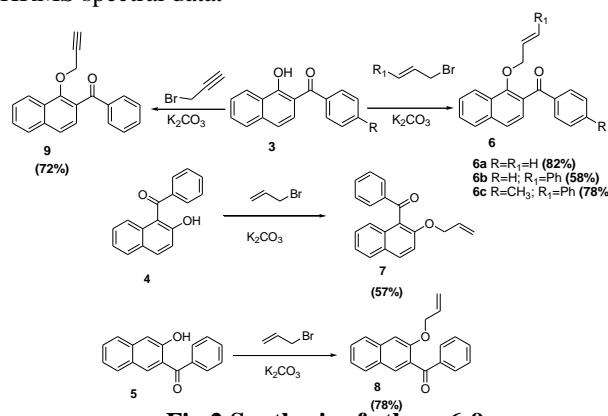

Fig.2 Synthesis of ethers 6-9

The UV absorption spectrum of **6a** showed λ_{max} at 254 nm (ε=27000), 330 nm (ε=2130) and 360 nm (ε=2500) in methanol. Although ethers of hydroxynaphthophenones have structural resemblance to ethers of hydroxybenzo- phenone, they differ in their excited states behaviour and consequently in their photophysical and photochemical behaviour. Upon irradiation, ethers of hydroxynaphtho- phenones are excited to $(\pi$-$\pi^*)^1$ state and hence, the most probable reactions of this exited state that can be expected are photo-Claisen rearrangement, and photocleavage. Photolysis experiments were done in a Rayonet type photoreactor and pyrex glass tube was used as the reaction vessel. Before photolysis, the solution of the photo- substrates was degassed with Nitrogen / Argon.

III. RESULTS AND DISCUSSION

Our initial investigation, began with irradiation of a 10^{-3} M solution of 1-allyloxy-2-naphthophenone **6a** in benzene as well as in acetonitrile at 254 nm in a

Rayonet type photoreactor, did not lead to any reaction. However, irradiation of ether **6a** in benzene at 330 nm and HPLC analysis of a sample after irradiation for 12 hours, revealed the presence of three products. It may be mentioned that unlike 2-allyloxybenzophenones which readily undergo 1,7-hydrogen abstraction and 1,5-biradical cyclisation under the above photolysis conditions[1-4](Figure 1), 1-allyloxy-2-naphthophenone **6a**, failed to furnish the corresponding 2,3-dihydro-3-phenylnaphtha[1,2-b]furan- 3-ol **11**. The spectral analysis of the photolyzed mass did not show any evidence for the formation of expected naphthofuranol **11**, but revealed the presence of photo-Claisen product **10a** (confirmed by comparing with the authentic sample prepared by thermal Claisen rearrangement), 1-hydroxy-2-naphtho-phenone **3a** due to photocleavage and starting material **6a** (Figure 3, Table 1). Workup yielded the photo-Claisen rearrangement product **10a**, 4-allyl-1-hydroxy-2-naphtho-phenone (24%), the starting material **6a** (12%) and the photocleavage product 1-hydroxynaphthophenone **3a** (36%). It is to be noted that whereas the hitherto unreported, thermal transformation of **6a** proceeding via a domino Claisen, Cope and enolisation, gave a single product, 4-allyl-1-hydroxy-2-naphthophenone **10a** in 65% yield, photolysis leads only to a mixture of **6a**, **10a** and **3a**.
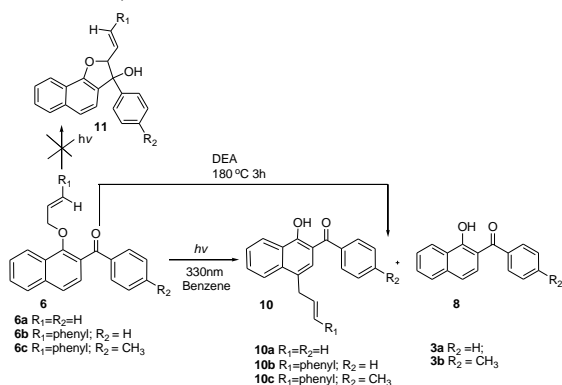

Fig.3 Photolysis of allyl ethers 6

Irradiation of the cinnamyl ether **6c** at 330 nm in benzene/acetonitrile (10⁻³ M) for 8 hours also led to a mixture of starting material, the photo-Claisen product **10c** and photocleavage product naphthol, **3b** as revealed by HPLC analysis (Table 1). This product **10c** was identified as 4-cinnamyl-2-(p-toluoyl)-1-naphthol, based on its NMR as well as by comparing it with an authentic sample prepared by thermal Claisen process. The structure was further confirmed by hydrogenating it to naphthol **12** (Figure 4).
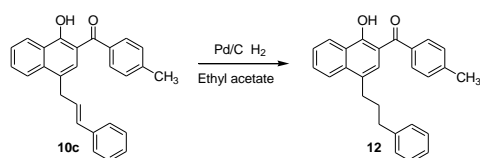

Fig.4 Reduction of Claisen rearrangement product 10c

It is to be highlighted here that the other possible photo-Claisen product **13**, due to allylic rearrangement (Figure 5) could not be detected. Irradiation for a longer time did not lead to significant change in the photocleavage but led to the formation of more intangible mass, which may probably be due to extensive polymerization of the free radicals produced. The formation of all these products could be accounted for,

on the basis of the already established stepwise mechanism, involving a homolytic breakage of the C-O bond to form the 2-benzoyl-1-naphthoxy radical and allyl radical followed by recombination at carbon 4 of the naphthoxy moiety (Figure 9). The photo-Claisen product was found to be exclusively only the *E* isomer and no *Z* isome*r* **14** (Figure 5) was detected. Also, the recovered starting material was also found to be only the *E* isomer **6c** and no *Z* isomer could be observed. It is worth mentioning here that cinnamyl 2-benzoylphenyl ether exhibited a different behaviour under similar photolysis conditions leading to *cis -trans* isomerisation of the ether[1a] (Figure 3, **6c**)
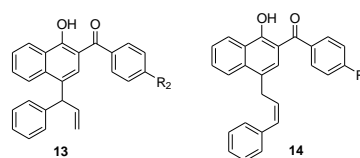

Fig.5 Possible photo-Claisen products

In order to understand the above photochemical outcome, it is essential to analyze the reports on photo- Claisen rearrangement on aryl allyl ethers. While thermal rearrangement of simple unsubstituted aryl allyl ether gives rise to the ortho-substituted phenol as single product,[5] photo-Claisen rearrangement of 3-substitutedphenyl (3-methyl-2-butenyl) ether[6], earlier reported by Carroll and Hammond,[6b] led to the formation of the respective phenol due to photo cleavage as well as ortho, para and meta photo-Claisen products (Figure 6).[6c] A remarkable product selectivity in favour of ortho was observed when photo-Claisen rearrangement of phenyl allyl ethers were carried out as solid complexes within zeolites[7a] and β-cyclodextrin[7b]. However, photo-Claisen reaction of 4-substitutedphenyl allyl ether furnished only a single product viz., 4-substituted-2-allylphenol.[6d,6e]
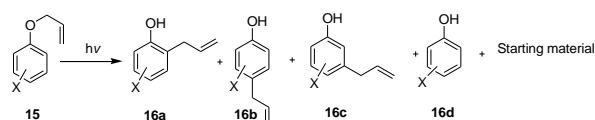

Fig.6 Photochemical reaction of phenyl allyl ether

The review by Francisco Galindo gives an excellent account of the literature development in this area up to 2005.[6i] The photo-Claisen rearrangement of substituted phenyl (3-methyl-2-butenyl) ether[6] **17** gives a complex mixture of products which can be explained only by a radical mechanism. Here, the primary process being the homolytic cleavage of the C-O bond[6f] followed by recombination of the radical pair at various positions of the aromatic ring with[6g] or without allylic inversion.[6h] This was supported by the findings from irradiation of isotopically labelled ethers. There are also a few reports on photo-Claisen rearrangement of naphthyl allyl ethers **18-19**[6g,8] (Figure 7).
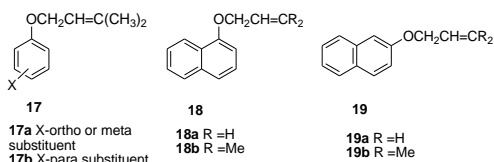
Fig.7 Rearrangement of Naphthyl Allyl Ethers

Photolysis of allyl ether of 1-naphthol[8] was reported to yield both the 2-allyl and 4-allyl 1-naphthols. Pohlers et al. and others[6g] reported that while 3-methyl-2-butenyl naphthyl ethers[8] (Figure 7) exhibited fluorescence upon irradiation in methanol-d4 at 298 K, the methyl naphthyl ether analogues were inactive.[8] 1-Halo-2-naphthyl allyl ether and 2-halo-1-naphthyl allyl ether do not undergo photo-Claisen upon irradiation but leads to 2-halomethyl-2,3-dihydro-naphthofurans. In contrast, 3-halo-2-naphthyl allyl ether is photo stable and does not undergo any photoreaction.[9a] Substituent effects, Arrhenius activation parameters, and rate constants for the photo-Claisen rearrangement of allyl aryl ethers has also been studied.[9b] Photochemical rearrangement of benzyl vinyl ethers lead to 1,3-migration of the benzyl group in contrast to the 3,3 migration observed in thermal rearrangement.[9c] Influence of phenyl core substituent's and vision on orthogonality in the photo-Claisen rearrangement of allyl phenyl ether in micro-flow has recently been reported.[9d] In addition to the analysis on the above discussion, performing a cross over experiment, was thought to be helpful in getting some insight into the mechanism of the present photo-Claisen rearrangement**.** Thus, an equimolar mixture of the ethers **6a** and **6c** in benzene (10^{-3} M) was irradiated at 330 nm for 8 hours (Figure 8) and the reaction mixture was analyzed by HPLC. The anticipated products due to photo-Claisen rearrangement viz., **10a** and **10c** and the photo-Claisen products due to cross-over reactions viz., **10b** and **10d**, were separately prepared by thermal Claisen rearrangement of the respective ethers **6a, 6b, 6c** and **11e**. HPLC analysis of the photolysis mixture, revealed the absence of the expected cross-over products, **10b** and **10e** as well as the absence of the ethers **6b** and **11e** from cross over, arising out of recombination of the allylic radicals at ether oxygen center. Instead, the HPLC analysis revealed the presence of naphthols **3a** and **3b** (due to the cleavage of the respective naphthyl ether) and the respective starting materials **6a** and **6b** (Table 1 and Figure 8). The observed quenching of this photolysis reaction and failure to observe even the formation of the respective normal photo-Claisen products **10a** and **10c** in this attempted cross over experiment is difficult to explain.

Table 1 HPLC analysis of attempted Cross-over photolysis reaction mixture of ethers 6 and 6c.

Irradiation Time (h)	R	Conversion (% a/a by HPLC) *				
		6a	3a	6c	10c	3b
4	Allyl	31.91	5.35	18.51	-	9.93
8	Cinnamyl	28.95	9.87	14.59	0.38	13.25

* 10a, 10b, 10d – 0%

While triplet energy transfer, leading to *cis-trans* isomerization of the ether was reported in the photolysis of *cis* or *trans* isomer of cinnamyl ether of 1-hydroxybenzo-phenone, **6c**,[3a] no evidence could be obtained for such reaction in the photolysis of the cinnamyl ether **6c** of

1-hydroxynaphthophenone **3b** (Figure 3). It is presumed that the free radical intermediate has been quenched in singlet state itself. The absence of any product due to cross over reactions may be due to a faster recombination of the radical pair before they diffuse out of the solvent cage. The failure to observe product **13** due to allylic inversion, is also not understood. Examples are known in literature where photolysis of aryl ethers leads to all possible products arising out of homolytic breakage and recombination with and without allylic rearrangements.[6e] Recombination within the solvent cage without allylic rearrangement is also documented[6f].
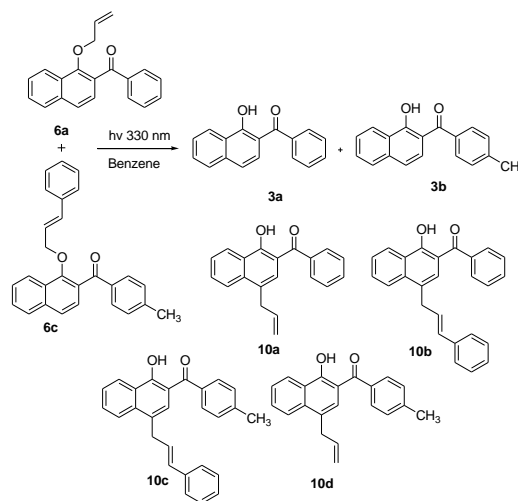

Fig.8 Cross Over Reaction Of Ethers 6a And 6c

As the polarity of the solvent plays an important role in stabilizing the radicals and their life-time and hence, in changing the course of the reaction, photolysis of ether **6** was carried out in various solvents, listed in Table 2. As expected, factors that stabilize the free radicals in solution, such as solvent polarity (entry 2 and 4) or substitution at the olefinic linkage (entry 8 and 9) tend to promote reactions due to photocleavage leading to 1-hydroxy-2-naphtho- phenone **3a** and polymerization that lead to the formation of intangible mass. Carroll and Hammond have reported that 3-methyl-1-phenoxybut-2-ene, when irradiated at 254 nm either in cyclohexane ($\Phi=0.55$) or in isopropanol ($\Phi=0.75$) leads to the formation of six different products. Here, in both the solvents, the sum of the individual quantum yields of the six products was found to be less than the overall quantum yield and probable reason for this observation was ascribed to polymerization.[6b] In gas phase photolysis of 3-methyl-1-phenoxybut-2-ene[10] it was suggested that the products are formed via dissociation-radical recombination mechanism and not by a concerted process. In yet another study, photo-Claisen rearrangement of allyl aryl ethers, were reported to involve radical pair intermediates.[6e] Based on all these literature reports, the photochemical outcome of the irradiation of allyl ethers of 1-hydroxy-2-naphthophenone may be explained as outlined in Figure 9**.**

Table 2 Photolysis of ethers 6a and 6c

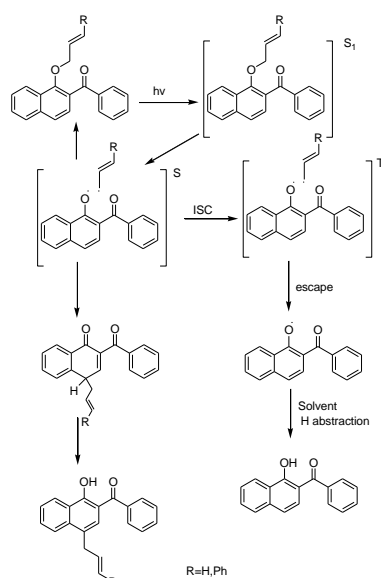| Entry	Ether	Solvent	Time (h)	Conversion (%, a/a by HPLC)		
				11	**10a**	**8**
1		Benzene	12	10.38	29.94	39.75
2		CH₃CN	12	18.43	9.88	19.50
3		CH₃CN-H₂O	8	11.13	2.93	76.38
4	6a	Acetone	8	4.98	1.7	66.43
5		Benzene-BF₃.Et₂O	12	-	-	94.90
6		Benzene, TEA	12	-	-	96.20
7		Silica gel Slurry		No reaction		
8	6c	Benzene	4	19.26	1.30	36.80
9		Benzene	8	21.04	1.05	26.26

Fig.9 Mechanism of photo-Claisen rearrangement of ethers 6

The photo-Claisen rearrangement undergone by 2-benzoyl-1-naphthyl allyl ethers **6a, 6b and 6c** prompted us to study the photolysis of isomeric ethers **7** and **8**. Although, the UV spectra of these ethers exhibited maxima at 310 nm (ε = 1759) and 330 nm (ε = 2686), similar to those of the ethers **6,** both the ethers were found to be stable under photolysis conditions. Irradiation of ether **7** or **8** in benzene at 330 nm for 10 hours did not lead to any reaction and only starting material was could be isolated. Irradiation of the propargyl ether **9** also did not lead to any clean product. Only the 1-hydroxy-2-naphthophenone, from the photo cleavage was isolated from this photolysis experiment.

IV. CONCLUSION

Allyl ether of 1-hydroxy-2-naphthophenone upon UV exposure led to photo-Claisen rearrangement product and photocleavage (3:4). In the studied examples, photo-Claisen rearrangement is more facile in non-polar solvent and polar solvent promotes more photocleavage. Cinnamyl ether of 1-hydroxy-2-naphthophenone underwent predominantly photocleavage upon UV exposure in a shorter time. Whereas the allyl ethers of 2-hydroxy-1-naphthophenone and 3-hydroxy-2-napthophenone were photochemically inert.

ACKNOWLEDGMENT

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