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A PHOTOCHEMICAL ROUTE TO 2-ALKENYL- AND 2-ETHYNYLBENZOFURANS

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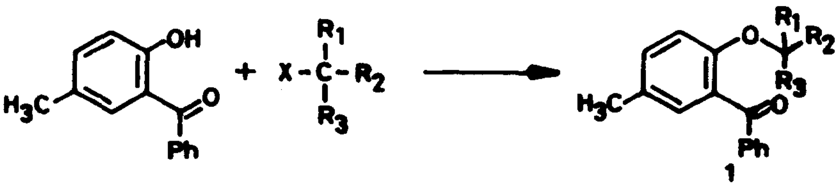
Abstract: Intramolecular cyclisation of 1,5-biradicals generated by irradiation of o-alkenyloxy and o-alkynyloxybenzophenones led to a facile synthesis of 2-alkenyl-3-phenyl and 2-ethynyl-3-phenylbenzofurans.

2-Alkenylbenzofurans have been used as dienes in the Diels-Alder route for the synthesis of naturally occuring dibenzofurans[1]. The chemistry of 2-alkenylbenzofurans and 2,3-dihydrobenzofurans has also received considerable attention in the recent past from chemical[1d] and physiological point of view[2b] as well as from pharmacological considerations[2c]. Though there are several methods for the construction of benzofuran system, none of these could be applied for a direct synthesis of 2-alkenylbenzofurans. These have been prepared by Vilsmeier-Haack formylation of appropriate benzofuran derivatives followed by Wittig reaction or by Palladium mediated vinylation of benzofuran[3] or by coupling of o-bromophenol with copper(I)alkenyl acetylide[1c]. In this communication, we report a facile synthesis of 2-alkenyl-3-phenylbenzofurans 3a, 3c and 2-ethynyl-3-phenylbenzofurans 3d based on cyclisation of 1,5-biradicals generated by irradiation of o-allyloxy and o-propargyloxybenzophenones. (SCHEME II)

The photosubstrates 1a-1f listed in Table-I were prepared as outlined in SCHEME I. These compounds have been thoroughly charatterised by spectral data and were purified by column chromatography prior to use.

SCHEME I



1

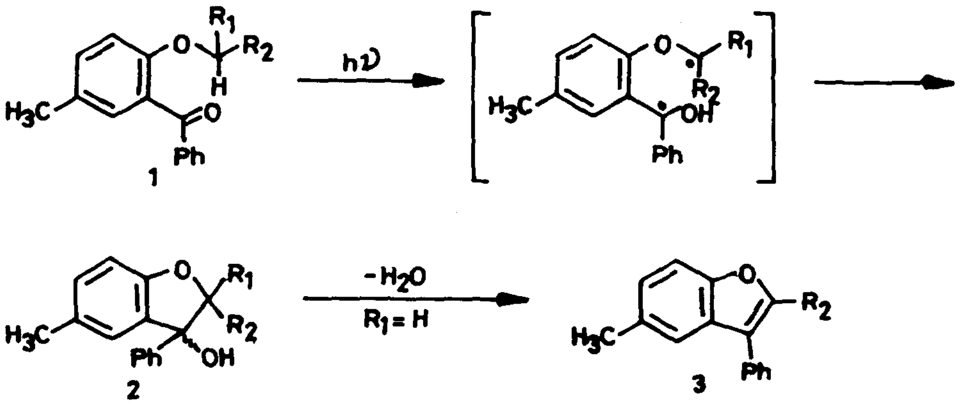
Table-I

o-Allyloxy and o-propargyloxybenzophenones

Compound	R_1	R_2	R_3	X	Base/ Solvent	Temp./ C (Time/h)	Yield(%)
1a	H	H	$CH=CH_2$	Br	KOH/EtOH	78 (36)	75
1b	H	H	CH=CHPh	Br	"	"	70
1d	H	H	C≡CH	Br	"	"	75
1c	H	H	$CH=CMe_2$	Br	NaOMe/DMF	80 (36)	60
1e	H	Me	C≡CH	OTs	NaH/THF	RT (48) + 60 (48)	40
1f	Me	Me	C≡CH	Cl	"	"	30

Irradiation[6] of o-allyloxybenzophenone 1a (λ_{max}^{MeOH} = 250nm, 330nm) in benzene(10^{-3}M) at room temperature in argon atmosphere at 350nm for one hour resulted in complete consumption of the starting material. Work up afforded a solid product (90%) which was found to be a mixture consisting mostly of 2,3-dihydro-3-phenyl-2-vinylbenzofuran-3-ol 2a[7] with a minor amount of 3-phenyl-2-vinylbenzofuran 3a[8]. Refluxing this crude product with anhydrous Copper sulphate in benzene for two hours completely converted it to 3a. Extension of this method for the keto ethers 1c and 1d afforded the benzofurans 3c and 3d respectively in 90% yield through 2c and 2d[9].

SCHEME II



2a R_1 = H, R_2 = $CH{=}CH_2$
2c R_1 = H, R_2 = $CH{=}CMe_2$
2d R_1 = H, R_2 = $C\equiv CH$
2e R_1 = Me, R_2 = $C\equiv CH$

3a R_2 = $CH{=}CH_2$
3c R_2 = $CH{=}CMe_2$
3d R_2 = $C\equiv CH$

Presence of substituents at 1 and 3 positions of alkenyloxy or alkynyloxy moiety has been found to have a significant retarding effect on the rate of cyclisation. Thus, while keto ethers 1a and 1d underwent photocyclisation within one hour, keto ethers 1c and 1e required longer time (3-4 hours). Surprisingly, the cinnamyl ether 1b failed to undergo this photocyclisation even upon prolonged irradiation.

It was of interest to study the photochemical outcome of 1,1-dimethylprop-2-ynyloxybenzophenone 1f which has no 'δ' hydrogens but possesses 'ε' hydrogens. However, irradiation of this keto ether 1f led only to ether cleavage yielding 2-hydroxy-5-methylbenzophenone. No evidence could be seen for the formation of any benzopyranyl product arising by 'ε' hydrogen abstraction[10] and cyclisation, findings which are in accordance with the earlier reports on the photocyclisation of α-(o-(benzyloxy)phenyl)acetophenone[11]. Irradiation of the keto ether 1e afforded only the 2,3-dihydrobenzofuranol 2e (80%). Products arising out of internal redox photorearrangement were not observed[12]. We could not detect any product due to intramolecular Paterno-Buchi reaction in these cases. Irradiation of the keto ether 1a at shorter wavelength led to recovery of the starting material.

To our knowledge there are only two other photochemical routes for building the benzofuran ring system which involves the photochemical six electron cyclisation of phenyl vinyl ethers to dihydrobenzofurans[13] or photochemical ring closure of o-allylphenols, though a somewhat related example to ours in the aliphatic system is known in literature[14]. Although Wagner et al., had envisaged that 1,5-biradical cyclisation could offer untapped potential from a synthetic viewpoint[15], it has not been explored till now. Our present work provides a simple and direct entry for the synthesis of 3-aryl-2-vinyl and 3-aryl-2-ethynylbenzofurans[16-18], which are potential synthons and not easily accessible by the available methods.

We are currently investigating the application of this route for the synthesis of spirobenzofuran systems present in antifungal agents like Griesefulvin [2c].

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6. Irradiations were carried out in a Rayonet photoreactor (Model RPR208) using pyrex vessel.
7. The stereochemistry of benzofuranol is being looked into.
8. The products were characterised by IR, NMR, UV and Mass spectral data. HPLC analysis shows that the product ratio of 2a to 3a decreases with increase in irradiation time, which may possibly be due to thermal dehydration.
9. In all these cases, the parent 2-hydroxy-5-methylbenzophenone was isolated in 10% as side product due to photochemical ether cleavage.
10. For 'ε' hydrogen abstraction and cyclisation of 1,6-biradicals to pyran derivatives see H.A.J.Carless and G.K.Fekarurhobo, Tetrahedron Lett., 25, 5943 (1984).
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