

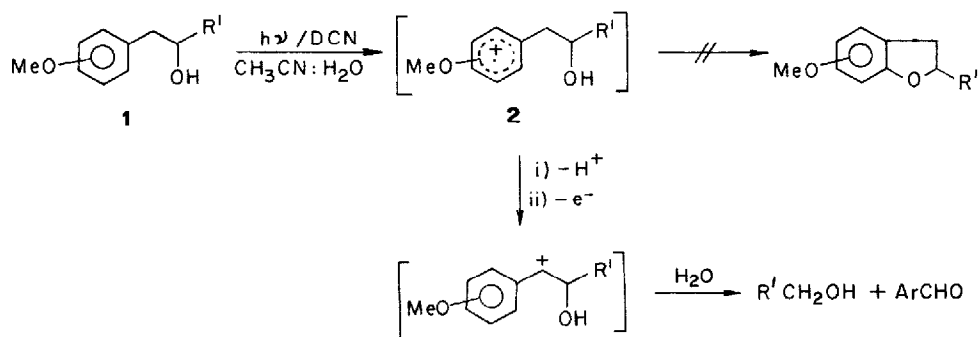
A ONE STEP SYNTHESIS OF 2-SUBSTITUTED BENZOFURANS FROM 2-ARYL-1-SUBSTITUTED ETHANE-1-ONES BY PHOTOINDUCED SET REACTIONS

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Abstract : An efficient one step synthesis of 2-substituted Benzofurans from the enolate of 2-Aryl-1-substituted ethane-1-ones by photoinduced SET has been reported.

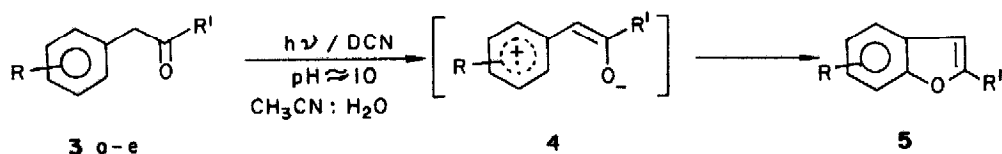
We have recently reported^{1,2} the intramolecular cyclization of arene radical cation, generated by photoinduced SET from excited singlet arenes to 1,4-dicyanonaphthalene (DCN) by carboxylate and hydroxyl nucleophiles to give coumarins¹ and precocenes². A number of hydroxy and methoxy substituted 2-alkyl or aryl benzofurans are known to be phytoalexins, associated with antifungal activity^{3,4}. Within the general context of inventing novel methods for the construction of 2-substituted benzofuran rings, there have been several reports recently⁵⁻¹⁰, but none of these represents the simple approach. Since 2-substituted benzofurans are common subunits of numerous biologically active polyoxygenated compounds, we envisioned to extend our methodology for the synthesis of 2-substituted benzofurans by intramolecular cyclization of arene radical cation of 2-aryl-1-alkyl ethane-1-ol(**1**). However, irradiation (> 280 nm) of a mixture of **1** (5 mmol) and DCN (0.25 mmol) in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (8:2) resulted only cleavage products¹¹ as shown in Scheme I.



SCHEME I

Formation of both radical or cationic species at benzylic position from arene radical cation due to proton or proton followed by electron loss have been reported from several groups¹². This has also been applied for the benzylic ether deprotection of alcohols by generating arene radical cation electrochemically¹³ and photochemically¹⁴.

The failure of the cyclization of **1** to benzofuran, led us to conceive the idea of utilizing the enolate ion intermediate **4** as probable nucleophile in the cyclization of arene radical cation of 2-aryl-1-substituted-ethane-1-ones (**3 a-e**). The central feature of this strategy entailed the blocking of benzylic position for possible proton loss. Cyclization of the enolate **4** to arene radical cation would then directly furnish the benzofurans **5**. Photolysis (pyrex filter, > 280 nm) of a mixture of **3 a-e** (2.9 mmol) and DCN (0.23 mmol) in 500 ml solution of acetonitrile:water (8:2) containing sodium hydroxide (pH \approx 10) using 125W mercury vapour lamp for 1-2 hr and usual work up gave corresponding benzofurans in 50-60% yield¹⁵ (Scheme II). Similar irradiation of **3a** without DCN or without alkali did not show any product.

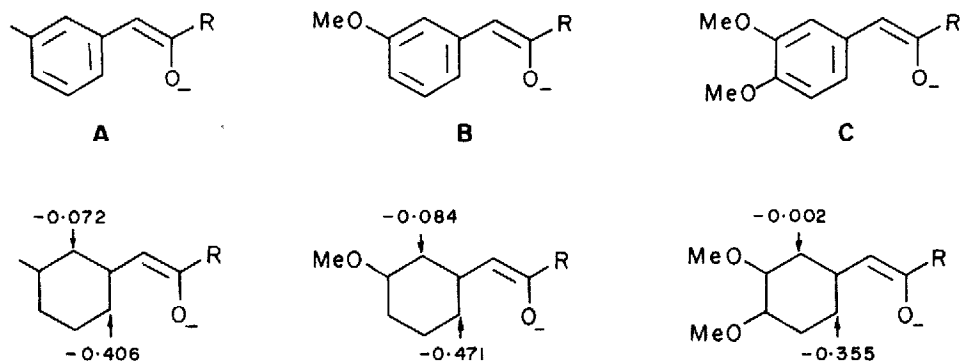


- a) R = 4' methoxy ; R' = methyl
- b) R = 4' methoxy ; R' = phenyl
- c) R = 2',5' dimethoxy ; R' = methyl
- d) R = 3',4' dimethoxy ; R' = methyl
- e) R = 3',4' methylenedioxy ; R' = methyl

SCHEME II

The regioselectivity of the cyclization can be explained from FMO theory. It is reasonable to assume that the HOMO of the radical cation (the singly occupied Π molecular orbital) should influence the position of attack at the aromatic ring. Huckel as well as MNDO calculations

on compound (A, B, C) show that the coefficients of the P-orbitals at the two carbon atoms on either side of the unsaturated substituents differ by very large magnitudes as shown in Scheme III. The larger coefficients are always found on the carbon that is found in the cyclization. Scope and detailed study of this reaction is in progress.



SCHEME III

Coefficients of the p-orbital on selected carbons in the
singly occupied II MOs of radical cations

Acknowledgement : The authors are thankful to Dr. A.V. Rama Rao, Director for his constant encouragement and to Dr. E.D. Jemmis, University of Hyderabad for theoretical calculations.

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15. Isolated yields. Yields are based on single experiment.

(Received in UK 30 January 1989)