A BREAKTHROUGH FOR THE PHOTOCHEMICAL ARYLATION IN THE 3-(PHENYLMETHYL)-2(5*H*)-FURANONE SYSTEM LEADING TO THE TETRAHYDROINDENOFURANONE SYSTEM

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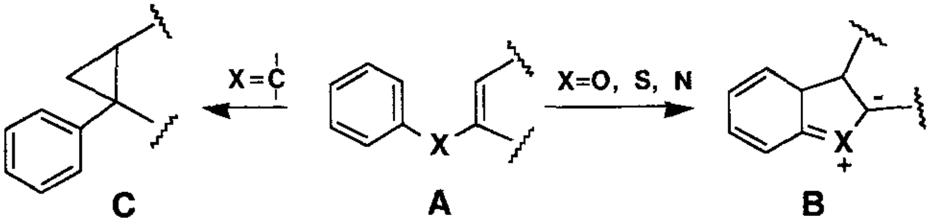
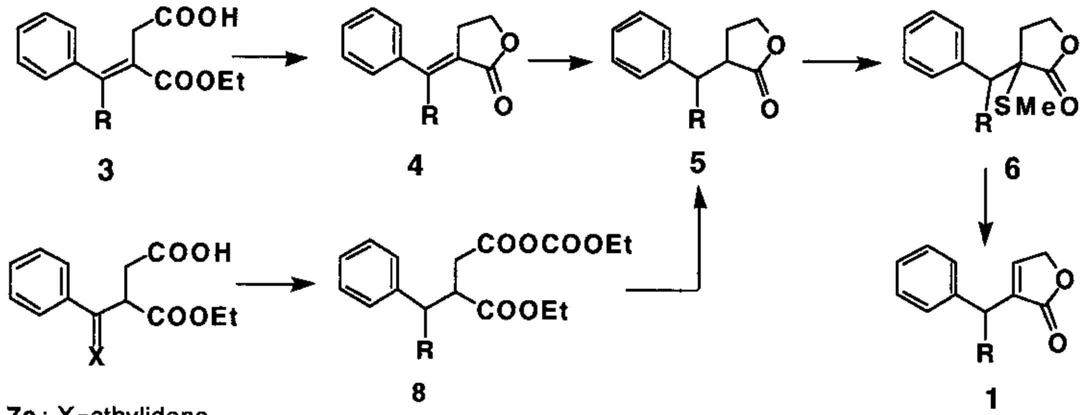
Abstract - The photochemistry of the 'central methane'-substituted 3-benzyl-2(5*H*)-furanone system (**1**) is described. Despite its di-π-methane structure, photochemical arylation was found to predominate in place of the di-π-methane rearrangement, and gave substituted tetrahydroindenofuranones (**2**) in good yields.

A variety of aryl vinyl heteroids based on the group VI elements (A; X=O or S) or on nitrogen (A; X=N) where the two π systems are in conjugation mediated by a lone-pair electron on the heteroatom are known to photo-cyclize to give aryl-annelated heterocycles (**B**).[1] The process is termed as heteroatom-directed photo-arylation and is characterized as photochemically initiated, electrocyclic reactions originating from arrangements of both an electron pair on a heteroatom and the electrons from at least one aromatic π-bond, and provides with a new aromatic ring substitution methodology for the synthesis of a variety of medicinally important natural products.[1,2] On the other hand, upon irradiation of the homogeneous version (**A**, X=C), another common photo-reaction, the di-π-methane rearrangement, is known to occur to afford cyclopropane derivatives (**C**).[3]



Previously we examined the photoreactivity of 3-(phenylmethyl)-2(5*H*)-furanone (**1a**), an example of the homogeneous version (**A**, X=$\overset{|}{\underset{|}{\mathrm{C}}}$) of the aryl-butenolidyl system, where no di-π-methane rearrangement was detected.[4] We have examined the photo-reactivity of the system (**1b**-**1f**) where the central methane is alkylated,[5] and have found that the introduction of appropriate substituents on the central methane leads to facile photo-arylation to afford functionalized tetrahydro-indenofuranones (**2**) in good yields.

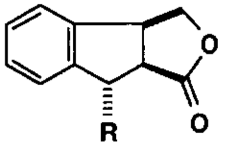


7a : X=ethylidene
7b : X=*n*-propylidene

a : R=H, **b** : R=Me, **c** : R=Et, **d** : R=*n*-Pr, **e** : R=c-Hex, **f** : R=*iso*-Pr

The 2(5*H*)-furanones (**1b**, **1e**, **1f**) were prepared as follows. The selective reduction of 1-ethyl 4-hydrogen 2-alkylidenesuccinates (**3**)[6] with borane-methyl sulfide complex followed by acid-catalyzed lactonization of the resulting hydroxy esters afforded 3-alkylidenedihydro-2(3*H*)-furanones (**4**), which were subjected to catalytic hydrogenation over palladium on carbon in glacial acetic acid to give dihydro-2(3*H*)-furanones (**5**). Sulfenylation of **5** according to the Trost's method[7] gave the corresponding α-methylthiodihydro-2(3*H*)-furanones (**6**) in good yields. The sodium metaperiodate oxidation of **6** in aqueous tetrahydrofuran at 50°C followed by heating at 120°C (neat) or in boiling toluene afforded the desired 2(5*H*)-furanones (**1b**, **1e**, **1f**) in 31-40 % overall yields from **3**. The furanone with an ethyl or *n*-propyl substituent (**1c** or **1d**)[6] was prepared from 1-ethyl 4-hydrogen 2-(1-phenyl-1-alkenyl)succinate (**7a** or **7b**), the regio-isomer of **3**. The mixed anhydride (**8**) obtained by hydrogenation of **7** and subsequent treatment with ethyl chloroformate was reduced by sodium borohydride, and acid-catalyzed lactonization of the reduction product gave the common intermediate (**5c** or **5d**) for the synthesis of **1**.

Photo-irradiation[8] of **1b**-**1f** in methanol through a Pyrex filter afforded mainly the corresponding photo-cyclized products, 3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-*c*]furan-1-one (**2b**-**2f**),[9] with concomitant formation of the photo-reduced products (**5**)[10] and methanol adducts (**9**).[11] The product distributions were shown in Table 1.



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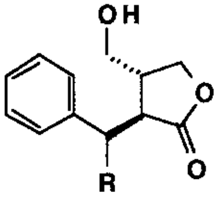

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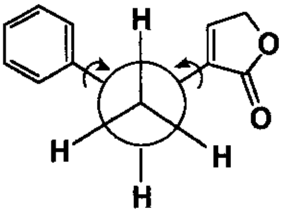
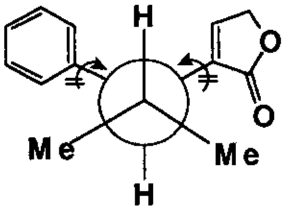
Table 1

substrate 1	R	reaction time(h)	products (isolated yield %) 2	9	5
a	H	23	8	20	20
b	Me	19	42	10	4
c	Et	19	50	10	3
d	*n*-Pr	19	64	10	3
e	c-Hex	5	78	trace	2
f	*iso*-Pr	14	80	7	2

Predominant photochemical arylation encountered in the irradiation of **1** would be attributable to facile formation of a radical at the β position in the enone system.[12] It is interesting to note that the efficiency of the cyclization in **1** is increased with the bulkiness of the substituents on the 'central carbon'. Inspection of the Newman projection of **1f** suggests that the phenyl and butenolidyl π planes on the 'central methane' are highly restricted in free rotation by the isopropyl methyls and are forced to get close to each other to result in facile photo-coupling into the indenofuranone system. The present case is a rare example of photocyclization in the di-π-methane system, and provides with a new route to the tetrahydroindenofuranone skeleton.



1b



1f

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6. Prepared from diethyl succinate by the Stobbe condensation with the corresponding ketones in the presence of sodium hydride. For preparation of **3b**, see, G. H. Daub and W. S. Johnson, *J. Am. Chem. Soc.*, 1948, **70**, 418.

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8. The photo-irradiation was carried out in an immersion apparatus fitted with an Ishii UV-HT 200W high pressure mercury lamp under a nitrogen atmosphere.

9. Compound **2e**: mp 136-137°C (colorless needles from *n*-hexane-acetone). Ir ($CHCl_3$) cm^{-1}; 1763. ^{1}H-Nmr ($CDCl_3$) δ; 0.94-1.32 (5H, m), 1.42-1.48 (1H, m), 1.60-1.82 (5H, m), 3.14 (1H, dd, *J*=8.0, 1.0), 3.49 (1H, dd, *J*=5.0, 1.0), 3.99 (1H, ddd, *J*=8.0, 7.0, 1.0), 4.46 (1H, dd, *J*=9.5, 1.0), 4.64 (dd, *J*=9.5, 7.0), 7.20-7.30 (4H, m). Ms *m/z* (%); 256 (M^+, 34), 129 (100). The stereochemistry of the products was determined on the basis of the NOE experiments.

10. The physical and spectroscopic properties of the photo-products (**5**) were completely in accordance with those of authentic specimens obtained in the synthetic pathway to **1**.

11. The stereochemistry was determined on the basis of the NOE experiments.

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