Pergamon

Tetrahedron Letters, Vol. 37, No. 12, pp. 2027-2030, 1996
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0040-4039/96 $15.00 + 0.00

S0040-4039(96)00190-6

Acid Catalyzed Intramolecular Photochemical Reactions of 3-Alkenyloxyphenols

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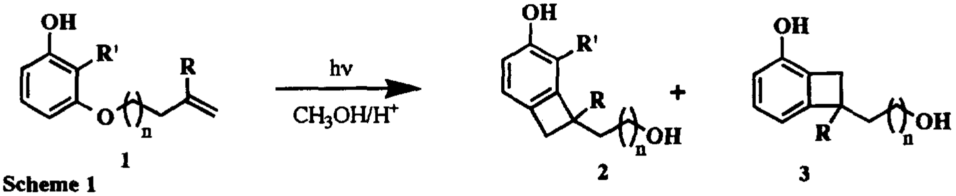
Abstract: Irradiation of 3-alkenyloxyphenols in a methanolic solution yields benzocyclobutenes. The efficiency increases if the reaction is carried out in the presence of acid. Formation of meta-alkylated phenols involving similar intramolecular [2+2] photocycloaddition intermediates is also observed when the olefinic double bond is substituted at the terminal position.

Photochemical cycloaddition reactions of alkenes to benzenic compounds have been frequently reported. Three types of cycloadditions [2+2], [2+3] and [2+4], are generally observed depending on the difference of redox potentials of the reaction partners.[1] In this context, intramolecular [2+2] cycloadditions have been reported to give unstable intermediates.[2] The primary cycloadducts are converted by further photochemical or thermal rearrangements to stable products, which have lost their aromatic character.

We have reported that the purity of the products and chemical yields of photolyses of salicylic derivatives (O-alk-3-enylsalicylic esters) are improved when small quantities of acid are added to the methanolic solution.[3] After excitation of the substrate and reversible thermal and photochemical rearrangements of the primary [2+2] cycloadduct, a tricyclic enolether intermediate is irreversily transformed to a mixed methyl acetal.

Based on this experience and wondering if addition of a strong acid to the reaction mixture might modify the relative redox potentials of the reaction partners, we decided to investigate the photochemical reactivity of alkenyloxyphenols under acidic conditions. Until now, little attention has been paid to the photochemistry of alkenylphenols. Few examples of intermolecular [2+3] photocycloadditions of alkenes to phenols are known[4]. Additionally, an intramolecular [2+2] photocycloaddition[5], photocyclization of allylphenols to benzodihydropyranes or benzodihydrofuranes and a photorearrangement di-π-methane[6], have been described. We report now that, in acidic conditions, intramolecular [2+2] photocycloaddition can be an efficient process for 3-alkenyloxyphenols.

When irradiated ($\lambda = 254$ nm) in methanol in the presence of H_2SO_4, **1a** yields two benzocyclobutenes **2a** and **3a** (50%), as a 9:1 mixture. Although the photoreaction can be observed in neutral solution, the reactivity is considerably improved when sulfuric acid is added in small amounts. Irradiation of terminal alkenyloxyphenols **1b**, **1d**, and **1e**, under the same conditions, led to similar results (Scheme 1, Table 1). We also noted a reduction of the rate of conversion for **1d** and **1e**, which might be due to steric hindrance, by substituting the ortho position ($R' = CH_3$) or the ethylenic carbon ($R = CH_3$). Furthermore, the reaction seems to be sensitive to the chain length of the starting material. Reactivity of **1b**, having an alkoxy link of 4 atoms, is not considerably modified, while no reaction is observed for **1c** with a link containing one more atom.

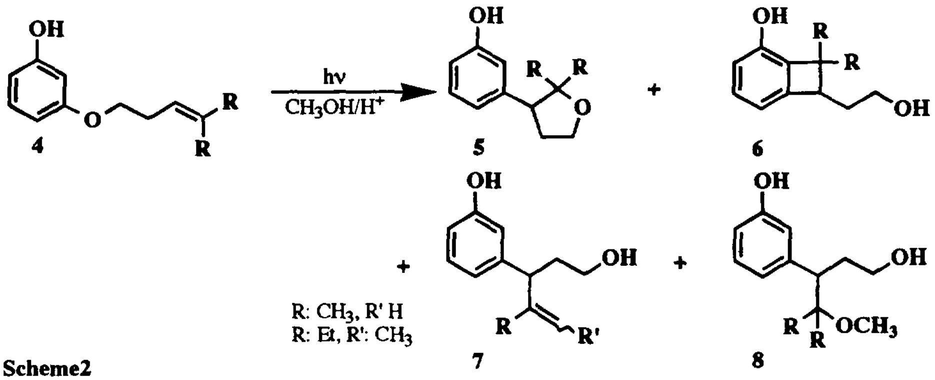


Scheme 1

Table 1

Entry	R	R'	n	Conversion	Yield (%) [1]	Ratio **2**/**3**
a	H	H	1	83	50	9/1
b	H	H	2	77	59	2/1
c	H	H	3	0	-	-
d	CH_3	H	1	50	60	5/1
e	H	CH_3	1	53	49	1/0

[1] based on conversion



Scheme2

Table 2

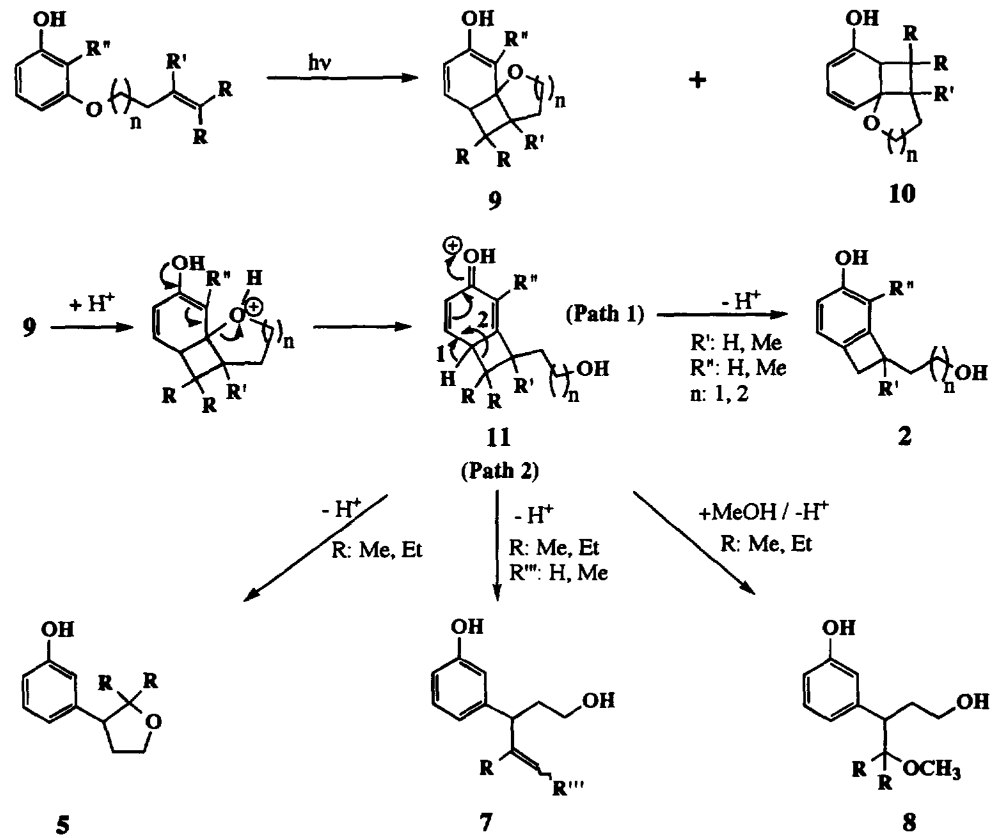
Entry	R	Conversion (%)	**5** (%)[1]	**6** (%)[1]	**7** (%)[1]	**8** (%)[1]	X (%)[5]
a	CH_3	73	10	13	10	37	2[2]
b	Et	86	20	11	40[4]	15	2[3]
c	i-Pr	0	-	-	-	-	-

[1] based on conversion, [2] in fraction **6**, [3] in fraction **5**, [4] cis/trans-ratio: 1.3/1
[5] unidentified product

When the terminal position is substituted by alkyl substituents, more complex mixtures are obtained (Scheme 2, Table 2). As an example, irradiation of **4a**, in acidic conditions, yields the alkylated products **5a**,

7a and **8a** besides the benzocyclobutene **6a**. Although similar reactivity is observed for **4b**, only slow decomposition of **4c** (R = iPr) occurred.

In order to explain the observed reactivity, we propose the mechanism presented in scheme 3.



Scheme 3

After excitation, the compounds **1** and **4** undergo intramolecular [2+2] photocycloaddition, to yield the tricyclic intermediates **9** and **10**. The [2+3] cycloaddition process, which is frequently observed during irradiation of similar substrates[1] cannot be detected under these conditions. The subsequent ring opening, occurring in acidic conditions and similar to the elimination of an alcohol from β-alkoxy ketones, yields the quinoid intermediate **11**. Depending on the nature of the substituents on **11**, different paths can be followed to restore the aromaticity. When R is hydrogen, enolization by loss of the proton in the para position relative to the hydroxyl group, yields to **2** (path 1). In the presence of gem-dialkyl substituents on the cyclobutane moiety, a CC bond cleavage can become competitive (path 2). The tertiary carbocation, which is formed in this process, reacts immediately in a characteristic manner: intramolecular trapping of **11** leads to the tetrahyrofuranyl derivative **5**; intermolecular trapping of the intermediate by solvent molecules, leads to **8** and finally, release of a proton from the substituent R gives the hydroxyalkene **7**. Although the minor regioisomer

10 could react in the same way as **9**, in all the investigated compounds **1** and **4**, only proton abstraction at the ring junction, perhaps assisted by the ortho hydroxy function, leading to **3** and **6** occurrs. Such rearomatization processes are common in the literature for related cyclohexa-2,5-diones in the presence of Broensted or Lewis acids.[7] The presence of ionizing conditions indicated that the reaction products might be in equilibrium. To test if the reaction mixture was obtained under kinetic conditions or not, we submitted **5a** - **8a** to the irradiation conditions. These products were recovered almost unchanged and no interconversion between the products could be detected, indicating their kinetic origin.

In the absence of acid in the methanolic solution and as already indicated, the conversion is very slow[8]. In non-hydroxylic solvents such as acetonitrile, only slow decomposition and complex mixtures of products can be observed, whether the reaction is carried out in the presence or absence of acid. The starting products are recovered quantitatively when submitted to the same reaction conditions but without irradiation.

Experimental Conditions

In a typical experiment, a methanolic solution (16 ml) containing 3-alkenyloxyphenol (about 0.5 mmol) and H_2SO_4 (0.1 mmol), was irradiated under argon at $\lambda = 254$ nm (Rayonet, $T = 30$ °C). After 14 h, the reaction was stopped and $NaHCO_3$ was added to the solution. After evaporation of the solvent, the residue was subjected to flash chromatography.[9]

References and Notes

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8. The origin of the acid catalysis is still unknown and is subject of present studies to decide between several mechanisms of the photochemical step.
9. NMR Data for **2a**: ^1H NMR (CD_3OD): $\delta = 6.81$ (d/d, $J = 8/0.7$ Hz 1H), 6.51 - 6.64 (m, 2 H), 3.70 (t, $J = 6.5$ Hz, 2H), 3.44 (d/d/t, $J = 2.5/5/8$ Hz, 1H), 3.19 (d/d, $J = 5/13$ Hz, 1H), 2.61 (d/d, $J = 2/13$ Hz, 1H), 1.87 (d/t, $J = 8/7.5$ Hz, 2H) ppm; ^{13}C NMR (CD_3OD): $\delta = 157.59$, 151.01, 134.30, 124.50, 115.20, 110.38, 61.39, 40.25, 38.50, 35.50 ppm.

(*Received in France* 18 *December* 1995; *accepted* 29 *January* 1996)