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Enol Ether Formation by Disproportionation of the 1,5-Biradical Intermediate in the Photocyclization of o-Isopropoxybenzophenone

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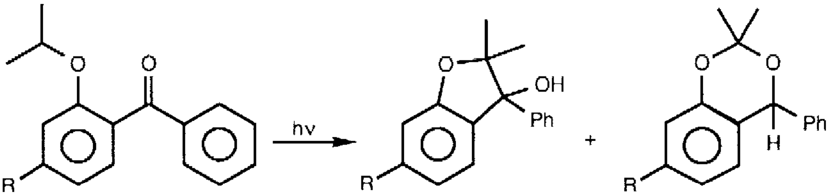
The 1,3-dioxane formed by uv irradiation of o-isopropoxybenzophenone is produced by intramolecular cyclization of a hydroxy enol ether, the disproportionation product of the 1,5-biradical formed by triplet state hydrogen abstraction. The enol ether is stable in the absence of acid.

In one of the original studies of the photocyclization of o-alkoxyphenyl ketones, it was noted that o-isopropoxy-p-methoxybenzophenone **1** gave not only the expected benzofuranol **2** but the 1,3-dioxane **3** [1] No mechanism was established for the formation of **3**; and to this day this sort of product formation has remained unique. We recently suggested[2] that the 1,5-biradical that cyclizes to **2** also disproportionates to a hydroxy enol ether, which then forms **3** by an internal ionic addition. We have now verified this supposition, demonstrated a new method to generate enol ethers, and found that the intramolecular addition of the hydroxy group to the enol ether occurs only upon acid catalysis.



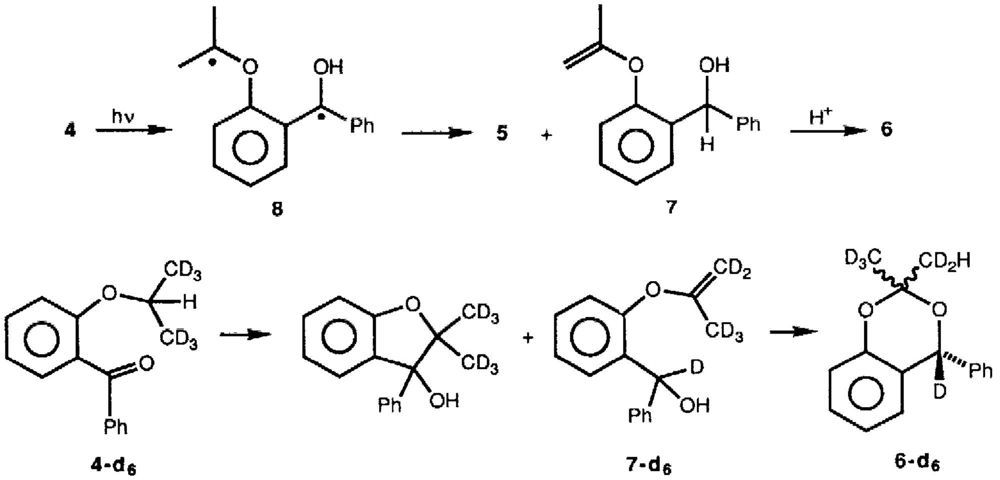
1 R = OCH_3
4 R = H

2: R = OCH_3
5 R = H

3 R = OCH_3
6 R = H

We have studied the parent o-isopropoxybenzophenone **4** and some deuterated derivatives UV irradiation of 0.02 M **4** in benzene produces **5** and **6** in a 2:1 yield as determined by gas chromatography, in agreement with the earlier work. The two products were separated by preparative TLC and characterized.[3,4] Quantum yields are 0.42 and 0.21 in benzene and 0 71 and 0 14 in methanol. When, however, we followed the reaction by NMR (benzene-d_6) we observed a 2 1 mixture of **5** and enol ether **7**.[5] Addition of one flake of naphthalenesulfonic acid to the NMR tube caused **7** to convert completely to **6** within minutes. The lifetime of **7** in "neutral" tubes depended on how the tubes had been cleaned; when they had undergone a final ammonia wash, **7** did not convert to **6** after several weeks. Thus **7** undergoes the expected acid-catalyzed addition of alcohol to enol ether, in a rare intramolecular fashion.

Scheme 1

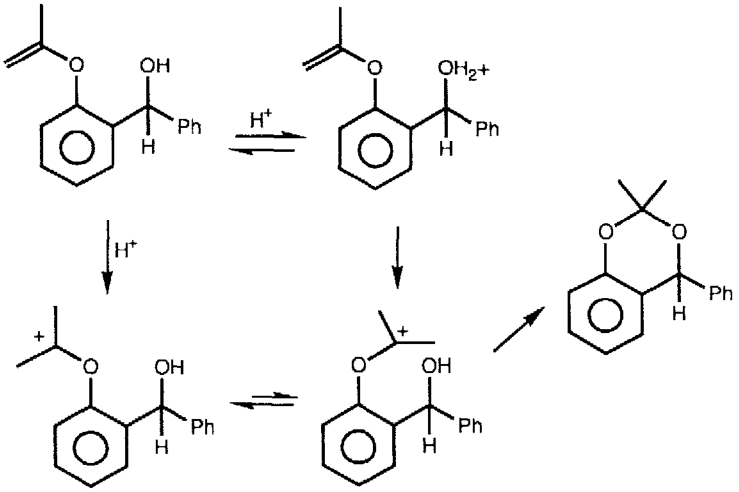


When **4-d$_6$** was irradiated, the **5**/**7** ratio was 3.1. The absence of a benzylic proton signal at 6 07 ppm in **7-d$_6$** and at 5.75 ppm in **6-d$_6$** indicated that a deuterium had shifted to this position from one of the isopropyl methyls. Thus **7** is concluded to be formed by disproportionation of intermediate biradical **8**, with a kinetic isotope effect k_H/k_D of 1.5. There are now several examples of such disproportionation of bis-tertiary biradicals;[6-8] its occurrence here adds support to our earlier suggested mechanism for the rearrangement of o-_tert_-butylacetophenone to 1-(o-isobutenylphenyl)ethanol.[7] It is interesting that the isotope effect is relatively small. Disproportionation of hydroxybiradicals to ketones, which involves O-H bond breaking, also shows a small primary isotope effect,[9] whereas disproportionation to enols, which involves breaking of a C-H bond, shows larger isotope effects.[2,10] Both forms of disproportionation are quite exothermic. The very different isotope effects presumably indicate a much earlier transition state for disproportionation at O–H relative to C–H. Since both forms of biradical disproportionation involve 1,6-hydrogen transfers, it is very unusual that disproportionation to an unsaturated alcohol competes so well with disproportionation back to starting ketone. The original workers actually speculated that the triplet ketone abstracted hydrogen from a methyl group and that the 1,6-biradical disproportionated to enol ether.[1] The deuterium labelling rules out this unlikely possibility.

These findings allow a rare look at the intramolecular reactions of an enol ether. The indefinite stability of **7** in benzene in the absence of added acid strongly suggests that no uncatalyzed addition of the alcohol to the enol ether can take place. The ^{1}H-NMR spectrum of **6-d$_6$** indicates that the two methyl groups are equally protonated. It is very likely in these nonpolar solvents that the hydroxy group is first protonated and that rate-determining[11] intramolecular protonation of the double bond then occurs. In that case a stereospecific *syn* addition would be one mechanistic possibility;[12] models make it clear that there is a single favored conformation for intramolecular proton transfer from oxygen to carbon. However, since specific protonation does not occur, it is impossible to tell whether the double bond is protonated inter- or intramolecularly Intermolecular protonation of the favored *anti* conformation of the enol ether must lead to random stereochemistry. In the case of intramolecular protonation, the intermediate carbocation is sufficiently stable that free rotation might still occur before what must be quite rapid nucleophilic attack by the hydroxyl group.

We are exploring whether this reaction can be adapted as a method of protecting secondary alcohols for eventual site specific photooxidation and for studying the kinetics of intramolecular addition of alcohols to enol ethers.[13]

Scheme 2



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(3) Compound **5**: ^{1}H-NMR (CDCl$_3$) δ 0.87 (s, 3H), 1.60 (s, 3H) 2.14 (br s, 1 H) 6.91 (d, J = 8.2 Hz, 1 H) 6.96 (t, J = 7.5 Hz, 1 H) 7.24 (d, J = 6.6 Hz, 1 H) 7.30 (t, J = 7.4 Hz, 1 H) 7.33-7.40 (m, 3 H) 7.49 (dd, J = 8.0, 1.7 Hz, 2 H); ^{13}C-NMR (CDCl$_3$) δ 20.3, 25.9, 85.2, 92.8, 111.1, 120.8, 125.6, 127.2, 127.7, 128.0, 130.5, 132.1, 140.1, 159.2, IR 3450 cm^{-1}.

(4) Compound **6**: ^{1}H-NMR (C$_6$D$_6$) δ 1.39 (s,3H), 1.60 (s, 3H), 5.75 (s,1H), 6.64 (m, 2 H) 7.05-7.20 (m, 5 H) 7.31 (d, J = 7 Hz, 2 H), (CDCl$_3$) δ 1.63 (s, 3 H) 1.65 (s, 3 H) 5.87 (s, 1 H) 6.63 (d, J = 6 Hz, 1 H) 6.78 (t, J = 7.5 Hz, 1 H) 6.85 (d, J = 8.5 Hz, 1 H) 7.15 (t, J = 8 Hz, 1 H) 7.3-7.4 (m, 5 H); ^{13}C-NMR (CDCl$_3$) δ 22.1, 28.4, 73.6, 100.1, 116.9, 120.3, 123.3, 126.7, 128.3, 128.46, 128.54, 128.6, 140.6, 151.0; IR, no peaks above 3025 cm^{-1}; m.p. 70°. NOE analysis indicates that the methyl group at 1.39 ppm is cis to the benzylic proton.

(5) Compound **7**: ^{1}H-NMR (C$_6$D$_6$) δ 1.70 (d, J = 0.9 Hz, 3H), 3.94 (d, J = 1.5 Hz, 1H), 3.96 (d of quart, J = 1.5, 0.9 Hz, 1H), 6.07 (s, 1H), 6.7-7.8 (m, 9H).

(6) Kirmse, W. unpublished results, for which we thank him.

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