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## Mechanistic Studies on the Photogenerated Dienol with α-Phenyl-*N-tert*-ButyInitrones

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The mechanism for the photochemical reactions of o-methyl-benzaldehyde (1), o-methyl-acetophenone (2) and o-methyl-benzophenone (3) in the presence of  $\alpha$ -phenyl-*N-tert*-butylnitrone (PBN) to the formation of stable nitroxyl radicals 4-6 is studied.

The nitroxyl radical product 6 can also be obtained by the thermolysis of benzocyclobutenol with PBN. Thus, the radical products were derived from a novel and regioselective 4+2 cycloaddition of the photogenerated dienol intermediate with PBN.

## INTRODUCTION

Dienol or o-quinodimethane intermediate is known to exist when o-methylbenzophenone or other o-methylphenyl carbonyl compounds are subject to photolysis.<sup>1</sup> The dienol intermediate can also be trapped chemically by cycloaddition with a dienolphile<sup>2</sup> (Equation 1).



Porter and Tchir<sup>3,4</sup> reported that five transients were detected when 2,4-dimethyl-benzophenone is photolyzed in cyclohexane. These transients include  $n\pi^*$  singlet state,  $n\pi^*$  triplet state, 1,4-biradical, and two long-lived dienol. Wilson and coworkers<sup>5</sup> have reported the comparison of conventional and laser-jet photochemistry of 2-methylbenzophenone and observed the formation of several dimers.

Nitrones such as  $\alpha$ -phenyl-*N*-tert-butylnitrones(PBN) and its derivatives have been used extensively as spin trapping reagents.<sup>6,7</sup> We have observed<sup>10</sup> a novel photoreaction between the excited o-methylbenzaldehyde (1), o-methylacetophenone (2), and o-methylbenzophenone (3) with PBN and its derivatives. As the mechanism for the generation of nitroxide radicals is still unknown, we would like to present some mechanistic studies on this novel reaction.

## EXPERIMENTAL SECTION

All the para or meta substituted PBN were prepared

from para- or meta-substituted benzaldehyde according to the published method.<sup>8,9</sup> Compounds 1-3 were obtained from Merck Co. and were recrystallized before use. The irradiations were made with a 450-W medium pressure mercury vapor lamp surrounded by a quartz water-cooling jacket or by a Rayonet photolysis apparatus equipped with 300 nm lamps.

The EPR spectrometer (Bruker EPR 300 X-band) was equipped with an ER 035M NMR gaussmeter, and the gvalue was measured with DPPH as internal standard. The EPR spectrometer was operated at a 100 KHz modulation frequency and a 9.76 GHz microwave. The EPR spectrometer was connected to a Perkin-Elmer HPLC with a silica gel column. A quartz cell with ca. 0.5 mm i.d. (internal diameter) and 3 cm long was set in the EPR sample cavity and was connected to the exit of the column with ca. 0.3 mm i.d. Teflon tubing. The microwave power was 12dB (6.3 mW). For HPLC-EPR, the magnetic field was fixed at the center peak maxima and the magnetic field modulations were applied at an amplitude of 7G to cover a wide range during the separation of radicals. Proton and Carbon-13 magnetic resonance spectra were recorded on a Bruker AM-300 FT-NMR and were reported in parts per million using CDCl3 as standard. A mass spectrometer (Finnagan) was operated at 70 or 20 eV ionization potential. Infrared spectra were recorded on a Perkin-Elmer 7000 spectrometer,

#### Photolysis of o-Methyl-benzaldebyde (1)

A solution of (1) (0.096 g, 0.2 M) in 4 mL in *n*-hexane was irradiated (254 nm) for 3.5 hours; the reaction mixture was evaporated under reduced pressure to give a slightly yellow viscous oil. The products (7) (0.039 g, 18.8%) and (8) (0.059 g, 28.9%) were obtained by column chromatogra-

Dedicated to Professor Yu-Shia Cheng on the occasion of her 65th birthday.

phy (*n*-Hexane : Ethyl acetate = 10 : 1,  $R_t = 0.48$  and 0.38). (7): <sup>1</sup>H NMR (CDCl<sub>3</sub>): 10.19 (s, 2H), 7.79 (d, 2H, J = 7.7 Hz), 7.39-7.26 (m, 6H), 3.10 (s, 4H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 192.7 (C=O), 142.1 (s), 137.2 (s), 133.8 (d), 132.8 (d), 131.5 (d), 126.9 (d), 34.9 (t). IR (KBr, cm<sup>-1</sup>): 2720, 1695. Mass (*m*/z relative intensity %): 238 (M<sup>+</sup>, 4.5), 220 (100), 119 (12.1). High resolution mass:  $C_{16}H_{14}O_2$ , Found: 238.1001, Cal: 238.0994.

## Photolysis of o-Methyl-acetophenone (2)

A solution of (2) (0.107 g, 0.2 M) in 4 mL *n*-hexane was irradiated (254 nm) for 3.5 hours; the reaction mixture was evaporated under reduced pressure to give a slightly yellow viscous oil. The product (9) (0.059 g, 25.1%; recovered yield 83.8%) was obtained by column chromatography (*n*-Hexane : Ethyl acetate = 5 : 1,  $R_f = 0.57$ ) as white crystals. Recrystallization from hexane and chlorform gave colorless needles: mp 149-150 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): 7.65 (d, 2H, J = 7.8 Hz), 7.39-7.25 (m, 6H), 3.10 (s, 4H), 2.54 (s, 6H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 202.1 (C=O), 140.1 (s), 137.8 (s), 131.8 (d), 131.5 (d), 129.1 (d), 125.9 (d), 36.1 (t), 29.8 (q). IR (KBr, cm<sup>-1</sup>): 1668. Mass (*m*/z relative intensity %): 266 ( $M^*$ , 4.3), 251 (49), 248 (100), 133 (51). High resolution mass: C<sub>18</sub>H<sub>18</sub>O<sub>2</sub>, Found: 266.1313, Cal: 266.1307.

## **Quenching Experiments**

Compound 2 (0.107 g) and maleic anhydride (0.078 g) were dissolved in 4 mL *n*-hexane and placed in a quartz tube. PBN was added with a different concentration (0-1.0 M). The tubes were placed in a merry-go-round apparatus surrounding the 254 nm lamp. The tubes were irradiated for 3.5 hours. At the end of the irradiation, the internal standard was added to each tube. The relative yields of the radical product 5 (X=H) and the cycloaddition product 16 were analyzed by HPLC with a silica gel column.

### **RESULTS AND DISCUSSION**

An *n*-hexane solution of 1 (0.2 M) and *p*-Me-PBN (0.2 M) was photolyzed in the presence of oxygen with a medium pressure mercury lamp (or at 300 nm with a Rayonet lamp) for 3 hours. The solvent was then evaporated. The electron spin resonance spectrum taken in benzene solution indicated triplets of doublets consistent with splittings by a nitrogen (14.45G) and a hydrogen atom (2.43G) (Fig. 1). In the absence of oxygen, the photolyzed solution is not EPR active, however introduction of oxygen after the photolysis will give the same EPR spectrum. Similar EPR spectra (triplets of doublets) are obtained for compounds 2 and 3 when irradiation is carried out in the presence of PBN and its derivatives. The structure of the obtained radical products has been assigned<sup>10</sup> based on the infrared, mass, and also resolution enhancement analysis for the HPLC purified radical species. The reaction can be summarized as in Equation 2.



X = p-OMe, p-Me, p-CH(CH<sub>3</sub>)<sub>2</sub>, m-Me, H, p-F, m-OMe, p-Cl, p-Br, m-Cl, m-Br, p-CF<sub>3</sub>, m-CN, m-NO<sub>2</sub>, p-CN, p-NO<sub>2</sub>.

Based on chromatographic analysis, the reaction products from the irradiation of 1 and PBN include radical product (-35% yield for 4), oxazirane 11 (-5%), and the dimer product 7 (40%). The dimer 7 has been reported by a laser photolysis experiment among other products.<sup>5a</sup> Compound 8 has been reported.<sup>5b</sup> If compound 1 is irradiated in *n*-hexane without PBN, the reaction products include the dimer 7 (19%) and 8 (29%) (Equation 3). Irradiation of 2 and 3 in the absence of PBN gives dimers only (9 and 10). The oxazirane 11 is derived from the photoreaction of PBN itself<sup>8</sup> (Equation 4). The yields of the radical products (4-6) calculated from the HPLC for all the PBN derivatives are close to thirty five percent (based on the recovered starting material). At first glance, the radical products indicated regioselective trapping of the benzylic radical site, and it is interest-



Fig. 1. EPR spectrum from o-methyl-benzaldehyde (1) with p-Me-PBN after 3.5 hours of photolysis.



ing to compare this with the regioselective electron transfer<sup>11</sup> from the ketyl radical site of a photogenerated biradical to paraquat ( $PQ^{21}$ ) (Equation 5). However, the radical prod-

$$2 \xrightarrow{hv} (H_2^{\circ}, H_3^{\circ}) \xrightarrow{PQ^{2*}} (H_2^{\circ}, H_3^{\circ}) \xrightarrow{PQ^{2*}} (H_3^{\circ}) \xrightarrow{PQ^{2*}} (H$$

uct 5 (in less yield) can also be obtained by the thermolysis of benzocyclobutenol 12 with PBN at 120 °C (Equation 6). Thermolysis of 12 without PBN in toluene at 110 °C affords *o*-methyl-acetophenone 2 (30%) and the dimer 9 (-2% only) (Equation 7). It can be concluded that radical products (4-6)

$$\begin{array}{c} & OH \\ CH_3 + PBN & 110^{\circ}C \end{array} + 5 (X=H) \end{array}$$
(6)

$$12 \frac{110^{\circ}C}{110^{\circ}C} 2 + 9$$
(7)

were derived from a regioselective 4+2 cycloaddition of PBN with the photogenerated dienol intermediate (Equation 8). In order to confirm that the reaction is derived from the dienol intermediate,<sup>12</sup> we have prepared 2-trimethylsiloxy-4-methyl-2,4-pentadiene 13 by thermal or photochemical reaction of 2-methyl-2-penten-4-one with silylating reagents.<sup>13</sup>

The compound 13 is the precursor of dienol anion 14, which formed from the reaction with potassium fluoride. When compound 13 is heated with potassium fluoride in the presence of PBN, the reaction product is paramagnetic, and the EPR spectrum recorded in toluene solution is as shown in Fig. 2. The triplets of doublets spectrum is consistent with a hyperfine coupling constant of 13.79G from one nitrogen atom and 2.02G from one proton coupling (g =



2.0020).<sup>14</sup> The infrared spectra for the reaction product indicated the NO stretch at around 1300-1000 cm<sup>-1</sup> and conjugated carbonyl (C=O) stretched at 1680 cm<sup>-1</sup>. The structure of the radical product is assigned as 15 in Equation 9.



The radical yields based on the EPR spectrum analysis were also weaker than these in the photolysis reaction. However, we have demonstrated that thermally prepared dienol anion 14 can also react with PBN through 4+2 cycloaddition to generate the nitroxide radical 15.



Fig. 2. EPR spectrum from the reaction of 2-trimethylsiloxy-4-methyl-2,4-pentadiene (13) with potassium fluoride and PBN.

The photogenerated dienol intermediate is responsible for the formation of the nitroxide radical formation. The quenching experiment of the Diels-Alder product 16 (with maleic anhydride) with different concentration of PBN is indicated in Fig. 3, in which the relative yield of product 16 formation is quenched by adding the PBN into the reaction mixture. The extent of quenching is proportional to the concentration of PBN. The relative yield of the radical product 5 (X=H), measured by EPR intensity, is proportinate to the PBN concentration (Equation 10). From Fig. 3, it was estimated that the rate of reaction of PBN with the dienol intermediate is three times faster than the rate of the Diels-Alder reaction of the dienol intermediate with maleic anhydride.



The quenching experiment with constant PBN concentration (0.5 M) and variations in maleic anhydride concentrations (0-1 M) was unsuccessful because the dienol intermediate is more reactive with PBN.

It is possible to measure the relative rate of the substituted PBN (X-PBN) with the photogenerated dienol by the HPLC-EPR method. The relative rate can be obtained by using two equal concentrations of different PBN derivatives



Fig. 3. Plot of PBN concentration (M) vs. the relative concentration of the dienophile trapping product (16) and the nitroxide radical (5).

in the same reaction mixture with the starting material (1-3). If  $K_x$  represents the rate constant of X-PBN and  $K_y$  represents the rate constant of Y-PBN, the relative rate can be obtained from Equation 11. [X]<sub>o</sub> and [Y]<sub>o</sub> represent the radical product concentrations from the reaction of the dienol with X-PBN and Y-PBN, respectively, and they are measured at low conversion of the PBN. Since an equal amount of PBN derivates were used ( $K_x/K_y$  is equal to [X]<sub>o</sub>/[Y]<sub>o</sub>), the ratio [X]<sub>o</sub>/[Y]<sub>o</sub> can be obtained by measuring the relative intensities of the HPLC-EPR chromatogram. The ratio is independent of the irradiation time. The relative rates (ratio of two radical concentrations) are from 0.96 to 1.13. It is conclude that there is no substituent effect for the reaction of the dienol intermediate with PBN derivatives.

$$\frac{K_{\chi}}{K_{Y}} = \frac{[Y-PBN][X]_{o}}{[X-PBN][Y]_{o}}$$
(11)

#### CONCLUSIONS

Novel nitroxide radicals 4-6 were obtained by the photolysis of 1-3 with sixteen PBN derivatives. The nitroxide radical can also be obtained by the thermal reaction of PBN with benzocyclobutenol. The reaction of 2-trimethylsiloxy-4-methyl-2,4-pentadiene with potassium fluoride in the presence of PBN can also generate a similar nitroxide radical. Thus, the nitroxide radicals are obtained from the photo-generated dienol intermediate with PBN through a regioselective 4+2 cycloaddition followed by oxidation.

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#### **Key Words**

Photolysis; o-Methylacylbenzene; PBN.

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