Photochemical Formation of 3-Methoxycyclohex-2-en-1-ones from 1,3-Cyclohexanedione and 2-Allyl-3-hydroxycyclohex-2-en-1-one in Methanol in the Presence of Quinones

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Irradiation of 1,3-cyclohexanedione and *p*-benzoquinone in methanol gave 3-methoxycyclohex-2-en-1-one. Allyl derivative of the 1,3-diketone was prepared as enol form and irradiated in methanol in the presence of *p*-benzoquinone to give the same type of photoproduct, *i.e.*, 2-allyl-3-methoxycyclohex-2-en-1-one. Allyldibenzoylmethane was synthesized and irradiated with *p*-benzoquinone in methanol but no remarkable amount of photoproduct was obtained.

key words: 1,3-cyclohexanedione, *p*-benzoquinone, electron transfer

INTRODUCTION

The photochemistry of 1,3-diketones has been a subject of extensive investigations [1]. Especially, the photocycloaddition reaction of the enol form of 1,3-diketones to alkenes is commonly referred to as the de Mayo reaction. The primary products are cyclobutanes. With 1,3-diketones, there is generally enough enolic tautomer in equilibrium with the parent diketone. The first reported example of the photocycloaddition of an enolized 1,3-diketone to an alkene was the addition of acetylacetone to cyclohexene, in which 1,5-diketone was obtained. The reactions can be used for the synthesis of six-membered rings by aldol cyclization. In addition, some photostable 1,3-diketones are known to protect harmful UV light from the sun, and also able to scavenge toxic free radicals produced in our body [2,3]. We reported that an acyclic 1,3-diketone such as dibenzoylmethane 1 added photochemically to p-benzoquinone to give 1,5-diketone 4 *via* 1:1 photoadduct 3 [4-6].

We recently found that irradiation of the cyclic 1,3-diketone 5 in methanol in the presence of various quinones gives 3-methoxycyclohex-2-en-1-one 6 as the major product. Its

Scheme 1.

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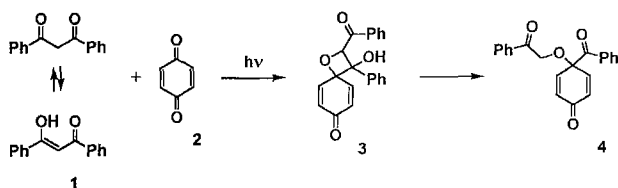
allyl derivative as enolic tautomer **8** was synthesized and irradiated under the similar condition to yield methoxy enone **9**.

MATERIALS AND METHODS

Materials. Methyl alcohol, ethyl alcohol, *n*-propyl alcohol and *i*-propyl alcohol were used after distillation. All chemicals were reagent grade materials purchased from Aldrich Chemical Co. and used without further purification. *n*-Hexane and ethyl acetate for column chromatography were used after distillation. Analytical thin layer chromatography (TLC) plates were purchased from Merck Co. as plastic sheets (20×20 cm) precoated with 0.25 mm silica gel together with fluorescent indicator.

Instruments. ^{1}H- and ^{13}C-NMR spectra were recorded on a 400 MHz Jeol JMN EX NMR spectrometer. Chemical shifts, δ, were reported as ppm downfield from internal tetramethylsilane (TMS) standard. Infrared (IR) spectra were recorded on a Nicolet 5-DX13 Fourier Transfrorm Spectrophotometer in KBr pellets. Ultraviolet (UV) spectra were obtained on Beckman DU 7500 spectrophotometer. Mass spectra were determined on a Hewlett Packard 5985A GC/MS system using electron impact method.

General Procedure for the Photoreactions of 1,3-Cyclohexanedione in the Presence of *p*-benzoquinone. Preparative photoreactions were conducted in a photoreactor composed of a water-cooled inner condenser and a Pyrex reaction vessel with 300 nm UV lamps (Rayonet Photochemical Reactor, Model RPR-208), after purging with dry nitrogen gas (purity: 99.9%) for 30 min. The reaction mixture was concentrated in vacuo and chromatographed over silica gel with n-hexane and ethyl acetate as the eluent (20:1 to 2:1, v/v).

Irradiation of 1,3-cyclohexanedione and *p*-benzoquinone.

Irradiation of 5 (112 mg, 1 mmol) and *p*-benzoquinone 2 (108 mg, 1 mmol) in methanol (50 mL) with 300 nm UV light for 24 h yielded the enone 6 in 49% yield, along with 1:1 adduct 7 in 2% yield.

6: UV (MeOH), λ_{max} 250 nm; IR (KBr) 2945, 1666, 1608, 1003 cm⁻¹; ¹H-NMR (CDCl₃) δ5.29 (1H, s, =CH), 3.61 (3H, s, OCH₃), 2.33 (2H, t, CH₂), 2.27 (2H, t, CH2), 1.90 (2H, m, CH₂) ppm; ¹³C-NMR (CDCl₃) δ199.6 (C=O), 178.7 (C-O), 102.2 (-C=), 55.6 (OCH₃), 36.7 (CH₂), 28.7 (CH₂), 21.1 (CH2) ppm; Mass (EI) m/e 126 (M).

7: UV (MeOH), λ_{max} 305, 285, 275 nm; IR (KBr) 3375, 2958, 2925, 1729, 1461, 1266, 1125, 722 cm⁻¹; ¹H-NMR (CDCl₃) δ 9.58 (1H, s, OH), 7.15 (2H, d, 2CH′s), 6.97 (2H, d, 2CH′s), 6.45 (1H, s, CH), 3.02 (2H, t, CH₂), 2.64 (2H, t, CH₂), 2.36 (2H, m, CH₂); Mass (EI) m/e 220 (M).

Synthesis of 2-allyl-3-hydroxycyclohex-2-en-1-one. To a stirred suspension of sodium hydroxide (800 mg, 20 mmol) was added a methanol (10 mL) solution of 1,3-cyclohexanedione (2.242 g, 20 mmol) in small portions over a 20 min period as room temperature. To the mixture was added a methanol (5 mL) solution of allyl bromide (2.4 mL, 28 mmol) over a 30 min period. The reaction mixture was stirred for 7 days at room temperature and then poured into water (50 mL). The organic phase was washed with water/ethyl acetate (1:1, v/v) solution, dried with anhydrous magnesium sulfate and concentrated in vacuo. The residue was separated by silica gel column chromatography using *n*-hexane and ethyl acetate as eluents (1:1, v/v), and then recrystallized from ethyl acetate and hexane to give the final product 8 as white crystal (662 mg, 23%), along with diallylic derivative as liquid (10%).

8: UV (MeOH) λ_{max} 267, 261, 256 nm; IR (KBr) 3420, 2964, 1732, 1584, 1375, 1270, 1190, 1123, 1067, 987, 910, 732 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ5.83 (1H, m, =CH), 5.05 (1H, d, =CH₂, J=16.8Hz), 4.97 (1H, d, =CH₂, J=10Hz), 3.09 (2H, d, CH₂, J=5.6Hz), 2.49 (2×2H, t, CH₂, J=6.4Hz), 1.98 (2H, m, CH₂); ¹³C-NMR (100 MHz, CDCl₃) δ204.0 (C=O), 136.2 (CH=), 116.6 (C=), 114.5 (=CH2), 113.4 (=C-OH), 32.86 (CH₂CO, CH₂COH), 26.14 (CH₂), 20.81 (CH₂); Mass (EI) m/e 152 (M).

Synthesis of allyldibenzoylmethane. To a stirred suspension of sodium hydroxide (180 mg, 4.5 mmol) was added a methanol (10 mL) solution of dibenzoylmethane (448 mg, 2 mmol) in small portions over a 20 min period as room temperature. To the mixture was added a methanol (10 mL) solution of allyl bromide (0.2 mL, 2.3 mmol) over a 30 min period. The reaction mixture was stirred for 15 h at room temperature and then poured into water (50 mL). The organic phase was washed with water/ethyl acetate (1:1, v/v) solution, dried with anhydrous magnesium sulfate and concentrated in vacuo. The residue was separated by silica gel column chromatography using n-hexane and ethyl acetate as eluents (12:1, v/v), and then recrystallized from ethyl acetate and hexane to give the final product 10 as white crystal (332 mg, 63%).

10: UV (MeOH) λ_{max} 325, 284, 248 nm; IR (KBr) 3469, 2927,

1701, 1596, 1449, 1270, 744, 695 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ7.95 (4H, d, Ph), 7.56 (2H, t, Ph), 7.45 (4H, t, Ph), 5.93-5.83 (1H, m, CH=), 5.31 (1H, t, CH, J=6.8, 6.4Hz), 5.10 (1H, dd, =CH₂, J=15.2, 1.6Hz), 5.03 (1H, d, =CH₂, J=10Hz), 2.87 (2H, t, CH₂, J=6.8, 6.4Hz); ¹³C-NMR (100 MHz, CDCl₃) δ195.3, 135.8, 134.9, 133.4, 128.8, 128.4, 117.1, 56.72, 33.61 ppm; Mass (EI) m/e 264 (M).

Photoreaction of allyl derivative as enol with *p*-benzoquinone. Irradiation of 8 (153 mg, 1 mmol) and *p*-benzoquinone 2 (108 mg, 1 mmol) in methanol (50 mL) with 300 nm UV light for 6 days yielded the enone 9 in 41% yield.

9: UV (MeOH) λ_{max} 266 nm; IR (KBr) 3086, 2945, 1649, 1615, 1434, 1380, 1239, 1199, 1172, 1118, 1038, 917 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ5.82-5.75 (1H, m, =CH), 4.97 (1H, dd, =CH₂, J=16.8, 1.6 Hz), 4.88 (1H, d, =CH₂, J=9.6Hz), 3.81 (3H, s, OCH₃), 3.01 (2H, d, CH₂, J=6.0Hz), 2.59 (2H, t, CH₂, J=6.4Hz), 2.34 (2H, t, CH₂CO, J=6.8, 6.4Hz), 2.00 (2H, m, CH₂); ¹³C-NMR (100 MHz, CDCl₃) δ197.4 (C=O), 172.2 (C-O), 136.2 (CH=), 116.9 (=C), 113.6 (=CH₂), 55.14 (OCH₃), 36.2 (CH₂), 26.18 (CH₂);, 24.79 (CH₂), 20.76 (CH₂) Mass (EI) m/e 166 (M).

RESULTS AND DISCUSSION

In order to compare the photochemical reactivity of cyclic 1,3-diketones with acyclic 1,3-diketones, the photoreactions of 1,3-cyclohexanedione and its allyl derivative with *p*-benzoquinone in methanol were investigated using 300 nm UV light. As described before, it was reported that dibenzoylmethane 1 added photochemically to p-benzoquinone 2 to give 1:1 photoadduct 3 which subsequently underwent retro-aldol type cleavage to yield 1,5-diketone 4, as shown in Scheme 1 [4-6].

Interestingly, irradiation of cyclic 1,3-diketones 5 and *p*-benzoquinone 2 in methanol gave rise to 3-methoxycyclo-hex-2-en-1-one 6 in 60% yield as the major product. On the other hand, the expected product 7 as 1:1 photoadduct, was isolated in only 2% yield. Whereas irradiation of diben-zoylmethane 1 and *p*-benzoquinone 2 in methanol did not yield same type of photoproducts.

Several alkoxy enones, like 6, could also be isolated in the photochemical reactions of 1,3-cyclohexanedione 5 (1mmol) with *p*-benzoquinone 2 (1 mmol) in ethyl alcohol, *n*-propyl alcohol and *i*-propyl alcohol in 47%, 31%, and 37 % yield, respectively. The structure of the products were character-
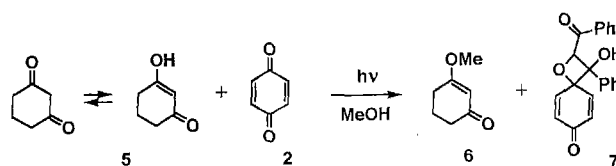
Scheme 2.

ized by some spectral data such as IR, NMR, and mass spectra. Vinyl protons were observed at δ5.33, 5.31, and 5.34 ppm, respectively, in ^{1}H-NMR spectrum taken in chloroform-d. The carbon signals for those bearing alkoxy groups were found at 177, 179 and 170 ppm in ^{13}C-NMR spectrum (CDCl$_3$). Mass spectrum (EI) also showed the molecular ion peaks at m/e 140, 154 and 154, respectively. The 1,3-diketone 5 was also irradietd with some other p-quinones such as tetrachloro- and tetrabromo-1,4-benzoquinone, 1,4-naphthoquinone, and anthraquinone in methanol, in which 3-methoxyenone 6 was isolated in 50 to 58% yields. o-Quinones, such as tetrachloro-1,2-benzoquinone and acenaphthenequinone, were also irradiated in the similar condition where 6 was isolated in ca. 46-49% yields, whereas it was found that phenanthrenequinone was not effective.

Allyl derivatives were synthesized from allyl bromide and 1,3-diketones using sodium hydroxide in methanol. In the case of 1,3-cyclohexanedione, the final product isolated was not 1,3-diketone but the enolic tautomer 8 of the diketone. Irradiation of 8 and p-benzoquinone 2 in methanol also gave rise to the same type of methoxy enone 9 in 41% yield. On the other hands, irradiation of allyldibenzoylmethane 10, prepared from allyl bromide and dibenzoylmethane 1, and p-benzoquinone 2 in methanol did not yield any noticable photoproducts.
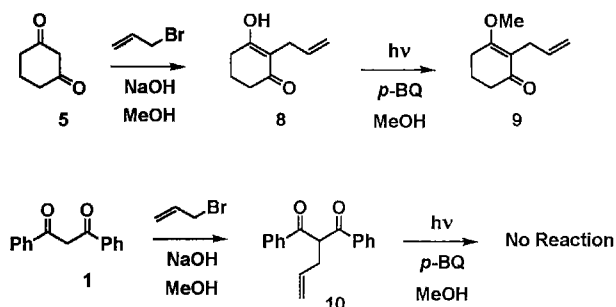
Scheme 3.

The formation of 3-alkoxycyclohex-2-en-1-ones is supported for the involvement of enolic tautomer of 1,3-cyclohexanedione 5 in this electron transfer reactions. The first step may be the formation of a charge transfer complex, followed by the electron transfer. Nucleophilic attack of the cation radical by methanol generates a radical species as a hemiacetal. The electron which was initially accepted by p-benzoquinone is returned to the newly formed radical, converting it into a carbanion which is then protonated by alcohol. Finally, dehydration of hemiacetal results in 3-methoxycyclohex-2-en-1-one 6, as shown in Scheme 4. The enone 6 was also isolated in 27% yield when irradiated 5 and N, N-dimethylaniline as a donor molecule.

Photochemical syntheses of ethers from alkenes or photoisomerization of alkenes have been carried out by using
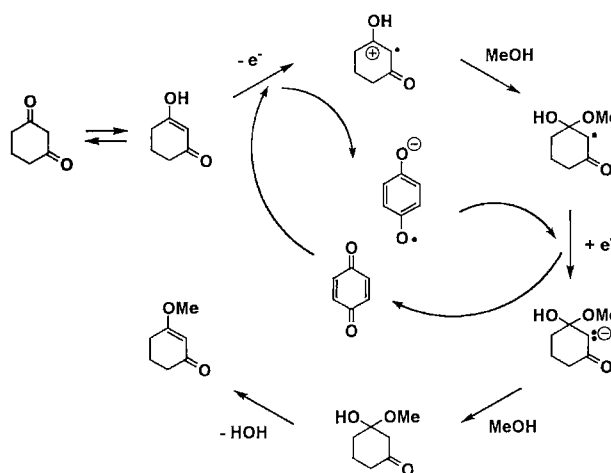
Scheme 4. Proposed mechanism for the formation of 3-methoxycyclohex-2-en-1-one.

electron acceptors such as dicyanobenzene, dicyanonaphthalene, or chloranil. Many cyanoaromatic compounds have been useful in generating cation radicals from organic molecules via single-electron transfer complex [7]. The synthetic significance of photoaddition reactions has been expanded since the development of electron transfer reactions [8]. It is noteworthy that the 3-methoxyenones 6 and 9 are easily produced when they exposed to UV light in methanol in the presence of quinones. The formation of 3-methoxyenones in neutral condition may be significant in the one-pot syntheses of various bicyclic or tricyclic compounds using the intramolecular photocycloaddition reactions of the 3-substituted enones produced from the cyclic 1,3-diketone and alcohols [1, 8]. Extension of the syntheses of polycyclic compounds from the photoreactions of 1,3-diketones with a variety of alcohols will be investigated.

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