PHOTOCYCLIZATION REACTIONS OF ETHYL 2-(8-OXO-5, 6, 7, 8-TETRAHYDRO-1-NAPHTHYLOXY)ACETATE and 8-OXO-5, 6, 7, 8-TETRAHYDRO-1-NAPHTHYLOXYACETONITRILE IN METHANOL

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Abstract: Photocyclization reactions were carried out on ethyl 2-(8-oxo-5, 6, 7, 8-tetrahydro-1-naphthyloxy)acetate and 8-oxo-5, 6, 7, 8-tetrahydro-1-naphthyloxyacetonitrile (six-membered ring ketones) 7a-b in Methanol. Irradiation of 7a-b gave cis- and trans-naphtho[1, 8-bc]furan derivatives 8a-b, cis- and trans-isomer of methanol incorporated naphtho[1, 8-bc]furan 12b and dehydrated naphtho[1, 8-bc]furan 11b. During irradiation of 7a, a methanol incorporated product (dihydroxy products) 9a and a diastereomeric derivative of meso- and dl-succinate (dimerization product) 10a were also isolated. The effect of polar protic solvent (methanol) on changing product distribution and reaction pathways of 6-membered cyclic ketones 7a-b are also discussed.

Introduction:
It is well-known that o-substituted aromatic carbonyl compounds which possess δ-hydrogen atoms undergo a very facile hydrogen abstraction under irradiation, called Norrish type II reaction. This reaction is useful in the synthesis of furan derivatives. Carbonyl compounds consist of benzaldehydes 1-3, acetophenones 2-6, benzophenones 4, 6-16, α-dicarbonyl compounds 17-20, benzoquinones 21-29 or cyclic ketones 1-2, 30-32. Among the compounds cyclic ketones have been studied from a view-point of reaction mechanisms and synthetic applications 30-31. In general, photocyclization reactions of carbonyl compounds 1 proceed via 1, 5-biradical intermediates 2 formed through δ-hydrogen abstraction by the excited carbonyl group as shown in Scheme 1 4, 6, 8-10, 12. Intramolecular cyclization of 2 gives cis- and trans-dihydrobenzofuranols 3. On the other hand if the irradiation was carried out in polar solvent like methanol the carbonyl group of 1* abstracts hydrogen from methanol to give a radical 4 which can give methanol incorporated product 5 16.

In this paper, we study the photochemistry of 6-membered cyclic ketones 7a-b in methanol (polar protic solvent) and we demonstrate the effect of substituent and solvent on changing product distribution and reaction pathways.
Results and Discussion:
Ethyl 2-(8-oxo-5, 6, 7, 8-tetrahydro-1-naphthyloxy)acetate and 8-oxo-5, 6, 7, 8-tetrahydro-1-naphthyloxyacetonitrile 7a-b for photocyclization reactions were prepared by the reaction of 8-hydroxy-1, 2, 3, 4-tetrahydro-1-naphthalenone 6 with ethyl bromoacetate and bromoacetonitrile in presence of a base the sequence of the reactions are outlined in Scheme 2.
Irradiation of 6-membered ring ketone 7a with high-pressure mercury lamp in methanol afforded cis- and trans-naphtho[1, 8-bc]furanol 8a (40% cis: trans ratio is 2.5:1), a diastereomeric products of meso- and dl-diethyl 2, 3-bis-(5, 6, 7, 8-tetrahydro-8-hydroxy-1-naphthyloxy)succinate 10a in 8% yield (Scheme 3, Table 1). The ratio between the two diastereoisomers was 1:2:1. During irradiation a methanol incorporated product (dihydroxy product) 9a was also obtained in 8% yield. The stereochemistry of the two isomers of naphtho[1, 8-bc]furanol 8a was assigned by considering an anisotropic effect of the methylene group at C3 for C2-H in the 1H nmr spectra. Generally, in dihydrobenzofuranol alkyl group at C3 shield C2-H at the cis position and deshield C2-H at the trans position, that is, in the cis-isomer the chemical shift of C2-H appears at a higher magnetic field than trans-isomer.

When 8-oxo-5, 6, 7, 8-tetrahydro-1-naphthyloxyacetonitrile 7b was irradiated in methanol, cis-2-cyano-2a-hydroxy-2a, 4, 5-tetrahydro-3H-naphtho[1, 8-bc]furan 8b was obtained in 25% yield, cis- and trans-isomer of methanol incorporated naphtho[1, 8-bc]furanol 8b was obtained in 38% yield, cis:trans ratio = 1:1.1 and dehydrated 4, 5-dihydro-3H-naphtho[1, 8-bc]furan-2-carbonitrile 11b in 3% yield (Scheme 4, Table 1). The stereochemistry of 8b was confirmed to be cis by direct comparison with the trans-isomer obtained by independent method using anisotropic effect.

Production of methanol incorporated naphtho[1, 8-bc]furan 12b was confirmed to be via the dehydrated naphtho[1, 8-bc]furan-2-carbonitrile 11b. Irradiation of 11b in methanol, afforded the methanol incorporated product 12b. The 1H nmr spectrum of the product in deuteriochloroform shows the protons signals of the methanol incorporated product of 12b along with other small signal of unidentified compound which is difficult to be separated.

Generally, photocyclization reaction of o-substituted carbonyl compounds in polar protic solvent such as methanol produces a mixture of cis- and trans-isomer of furan derivatives. In contrast to this result, photocyclization reaction of 7b in methanol produced one-isomer of cis-naphtho[1, 8-bc]furanol 8b selectively. The trans-isomer of 8b would be produced in the medium and undergo dehydration to afford 11b. The ease of dehydration of the trans-isomer of 8b than the cis-isomer of 8b would be attributed to the spatial direction of the hydroxyl group with regard to the hydrogen atom. In the case of trans-8b, the hydroxyl group and the hydrogen atom are arranged at the same direction and therefore, it can be easily dehydrated to give 11b which can undergo further photoreaction with methanol to give cis- and trans-isomer of methanol incorporated naphtho[1, 8-bc]furan 12b.
Photocyclization reactions of ethyl 2-(8-oxo-5,6,7,8-tetrahydro-1-naphthyloxy)acetate and 8-oxo-5,6,7,8-tetrahydro-1-naphthyloxyacetonitrile in methanol

Scheme 3

\[
\begin{align*}
\text{CH}_2\text{CO}_2\text{Et} & \overset{\text{hv} / \text{N}_2 \text{CH}_3\text{OH}}{\longrightarrow} \text{cis-8a} + \text{trans-8a} + \text{9a} \\
\end{align*}
\]

\[+ \]

\[
\begin{align*}
\text{meso- and dl-10a} \\
\end{align*}
\]

Scheme 4

\[
\begin{align*}
\text{CH}_2\text{CN} & \overset{\text{hv} / \text{N}_2 \text{CH}_3\text{OH}}{\longrightarrow} \text{cis-8b} + \text{11b} + \text{cis-12b} + \text{trans-12b} \\
\end{align*}
\]
It is noteworthy to report that, when \(7a-b\) was irradiated in acetonitrile \(^{30-31}\), products such as methanol incorporated products \(9a\), cis- and trans-isomers of \(12b\) and dimerization product \(10a\) were not isolated at all. The dramatic change on products distribution would be attributed to the effect of methanol (polar protic solvent) on changing reaction pathway \(^{1,16}\). Moreover, in the photoreaction of ethyl 2-(8-oxo-5, 6, 7, 8-tetrahydro-1-naphthyloxy)acetate \(7a\) and 8-oxo-5, 6, 7, 8-tetrahydro-1-naphthyloxy-acetonitrile \(7b\), rearranged products via spirocyclization of 1, 5-biradicals \(^2,4,30\) were not observed because the biradical \(13\) formed is stable by push-pull resonance \(^{37-39}\) between the electron withdrawing group (CO\(_2\)Et or CN group in \(7a\) or \(7b\), respectively) and the naphthyloxy oxygen atom.

From the results mentioned above, the plausible reaction pathways of photorection of \(7\) are shown in Scheme 5. Irradiation of \(7\) produces \((n, \pi^*)\) excited triplet state \(7^*\) after intersystem crossing process (ISC). The carbonyl group of \(7^*\) abstracts \(\delta\)-hydrogen to give 1, 5-biradicals \(13\) \(^4,6,8-10\). Intramolecular cyclization of \(13\) affords cis- and trans-isomers of dihydrobenzofuranols \(8a-b\). Production of methanol incorporated naptho[1, 8-bc]furan \(12b\) would occur via the dehydrated naptho[1, 8-bc]furan-2-carbonitrile \(11b\) and subsequent addition of a methanol molecule on the double bond of the furan ring in a nonstereoselective manner to give a mixture of cis- and trans-isomer of \(12b\). Formation of the dimerization product \(10a\) is not clear, however, it would be formed through the 1, 5-biradical intermediate \(13\) followed by dimerization and hydrogen abstraction from methanol. On the other hand, the carbonyl group of \(7^*\) abstracts hydrogen from methanol to give ketyl radicals \(14\) \(^{40-52}\) and hydroxymethyl radical (\(\cdot\)CH\(_2\)OH). Intermolecular coupling of \(14\) with hydroxymethyl radical gives dihydroxy products \(9a\).

From the above results, photocyclization reactions of 6-membered ring ketones \(7a-b\) are useful to prepare naptho[1, 8-bc]furan derivatives. Electron withdrawing group such as ethoxycarbonyl and cyano groups suppress spirocyclization reactions of the 1, 5-biradical intermediate. Polar protic solvent like methanol can change product distribution and reaction pathways via intermolecular hydrogen abstraction.

**Experimental:**

The melting points are uncorrected. Column chromatography was performed on silica gel (Wakogel C-200). Ether refers to diethyl ether. Methanol was used after distillation. Photoreactions were carried out with 400-W high-pressure mercury lamp (Riko UVL-400 HA) with Pyrex filter. The ir spectra were determined on a Hitachi Model 270-30 IR spectrometer. The \(^1\)H and \(^{13}\)C nmr spectra were determined at 200 MHz and 50 MHz on a Varian Gemini 200 FT NMR spectrometer, using tetramethylsilane as the internal standard.

**Synthesis of Starting Materials 7a-b:**

Starting compounds \(7a\) \(^{31}\) and \(7b\) \(^{30}\) were prepared according to Published procedures.

**General Procedure for Photoreactions of 7a-b:**

A methanol solution (500 ml) of the starting material (2.00 mmoles) was deoxygenated by bubbling nitrogen gas for 1 hour and then irradiated under monitoring by high performance liquid chromatography (hplc). The irradiation was stopped.
when the starting compounds almost disappeared. After irradiation the methanol was evaporated under reduced pressure below 40°. The residue was chromatographed and eluted with benzene-ether to give a variety of products.

Ethyl cis-2a-Hydroxy-2a, 3, 4, 5-tetrahydro-2H-naphtho[1,8-bc]furan-2-carboxylate cis-8a:

Compound cis-8a (29%) was obtained as colorless crystals from benzene, mp 122-122.5°. The 1H nmr and ir spectra of this compound is identical with authentic sample obtained by irradiation of 7a in acetonitrile 31.

Ethyl trans-2a-Hydroxy-2a, 3, 4, 5-tetrahydro-2H-naphtho[1,8-bc]furan-2-carboxylate trans-8a:

Compound trans-8a (11%) was obtained as colorless crystals from benzene, mp 106.5-107°. The 1H nmr and ir spectra of this compound is identical with authentic sample obtained by irradiation of 7a in acetonitrile 31.

Ethyl 2-[8-Hydroxy-8-hydroxymethyl-5, 6, 7, 8-tetrahydro-l-naphthyloxy]acetates 9a:

Compound 9a (8%) was obtained as colorless crystals from ethyl acetate-hexane, mp 115-116°; ir (potassium bromide): 3460 (OH) and 1750 Cm" (CO2Et); nmr (deuteriochloroform): δ 1.32 (t, J = 7 Hz, 3H, CO2CH2CH3), 1.46-2.86 (m, 7H, 5-H, 6-H, and OH), 3.62 (d, J = 12 Hz, 1H, CH2OH), 4.30 (q, J = 7 Hz, 2H, CO2CH2CH3), 4.67 (s, 2H, OCH2), 4.93 (s, 1H, OH), 6.61 (d, J = 8 Hz, 1H, 2-H or 4-H), 6.80 (d, J = 8 Hz, 1H, 2-H or 4-H), 7.24 (dd, J = 8 and 8 Hz, 1H, 3-H); 13C nmr (deuteriochloroform): δ 14.1 (q), 20.0 (t), 30.6 (t), 32.5 (t), 61.8 (t), 65.5 (t). 66.9 (t), 74.3 (s), 109.5 (d), 123.5 (d), 127.8 (s), 128.1 (d), 140.8 (s), 156.3 (s), 168.5 (s).

C15 H20 O5 requires C, 64.29; H, 7.14. Found: C, 64.31; H, 7.14.

Meso- or dl-Diethyl 2, 3-bis-(5, 6, 7, 8-tetrahydro-8-hydroxy-1-naphthyloxy)succinate 10a:

These diastereoisomers 10a were obtained as colorless crystals from methanol in 16% yield and the ratio between them was 1.2:1. The first isomer had a mp = 159-160°; ir (potassium bromide): 3510 (OH) and 1750 Cm" (CO2Et) 1H nmr (deuteriochloroform): δ 1.32 (t, J = 7 Hz, 3H, CO2CH2CH3), 1.46-2.86 (m, 7H, 5-H2, 6-H2, 7-H2 and OH), 3.62 (d, J = 12 Hz, 1H, CH2OH), 3.97 (d, J = 12 Hz, 1H, CH2OH), 4.30 (q, J = 7 Hz, 2H, CO2CH2CH3), 4.67 (s, 2H, OCH2), 4.93 (s, 1H, OH), 6.61 (d, J = 8 Hz, 1H, 2-H or 4-H), 6.80 (d, J = 8 Hz, 1H, 2-H or 4-H), 7.24 (dd, J = 8 and 8 Hz, 1H, 3-H); 13C nmr (deuteriochloroform): δ 14.1 (q), 20.0 (t), 30.6 (t), 32.5 (t), 61.8 (t), 65.5 (t), 66.9 (t), 74.3 (s), 109.5 (d), 123.5 (d), 127.8 (s), 128.1 (d), 140.8 (s), 156.3 (s), 168.5 (s).

C28 H34 O8 requires C, 67.47; H, 6.83. Found: C, 67.45; H, 6.84.

The second isomer had a mp = 115-116°; ir (potassium bromide): 3510 (OH) and 1750 Cm" (CO2Et); 1H nmr (deuteriochloroform): δ 1.32 (t, J = 7 Hz, 3H, CO2CH2CH3), 1.46-2.86 (m, 7H, 5-H2, 6-H2, 7-H2 and OH), 3.62 (d, J = 12 Hz, 1H, CH2OH), 3.97 (d, J = 12 Hz, 1H, CH2OH), 4.30 (q, J = 7 Hz, 2H, CO2CH2CH3), 4.67 (s, 2H, OCH2), 4.93 (s, 1H, OH), 6.61 (d, J = 8 Hz, 1H, 2-H or 4-H), 6.69 (d, J = 8 Hz, 1H, 2-H or 4-H), 7.03 (dd, J = 8 and 8 Hz, 1H, 3-H); 13C nmr (deuteriochloroform): δ 14.1 (q), 21.0 (t), 31.6 (t), 36.3 (t), 61.3 (t), 65.3 (d), 82.5 (d), 109.6 (d), 122.4 (d), 127.1 (d), 128.6 (s), 143.3 (s), 157.7 (s), 168.3 (s).

C28 H34 O8 requires C, 67.47; H, 6.83. Found: C, 67.45; H, 6.84.
Cis-2-Cyano-2a, 3, 4, 5-tetrahydro-2H-naphtho[1, 8-bc]furan-2a-ol cis-8b:

Compound cis-8b (29%) was obtained as colorless crystals from benzene-hexane, mp 113-114°. The $^1$H nmr and ir spectra of this compound is identical with authentic sample obtained by irradiation of 7a in acetonitrile.

4, 5-Dihydro-3H-naphtho[1, 8-bc]furan-2-carbonitrile 11b:

Compound 11b (3%) was obtained as a colorless oil. The $^1$H nmr and ir spectra of this compound is identical with authentic sample obtained by irradiation of 7b in acetonitrile.

Cis-2a-hydroxymethyl-2a, 3, 4, 5-tetrahydro-2H-naphtho[1, 8-bc]furan-2-carbonitrile cis-12b:

Compound cis-12b (18%) was obtained as colorless crystals from ethyl acetate-hexane, mp 169-170°; ir (potassium bromide): 3540 cm$^{-1}$ (OH); $^1$H nmr (deuteriochloroform): δ 1.22-2.67 (m, 7H, 3-H$_2$, 4-H$_2$, 5-H$_2$ and OH), 4.45 (d, J = 2 Hz, 2H, CH$_2$OH), 4.80 (s, 1H, 2-H), 6.64 (d, J = 8 Hz, 1H, 6-H), 6.82 (d, J = 8 Hz, 1H, 8-H), 7.10 (dd, J = 8 and 8 Hz, 1H, 7-H); $^{13}$C nmr (deuteriodimethylsulfoxide): δ 20.1 (t), 30.4 (t), 35.9 (t), 53.4 (s), 81.2 (t), 81.2 (s), 110.5 (d), 116.3 (s), 123.1 (d), 127.3 (d), 128.5 (d), 142.0 (s), 156.0 (s).

C$_{13}$H$_{13}$NO$_2$ requires C, 72.56; H, 6.04; N, 6.51. Found: C, 72.53; H, 6.01; N, 6.49.

Trans-2a-hydroxymethyl-2a, 3, 4, 5-tetrahydro-2H-naphtho[1, 8-bc]furan-2-carbonitrile trans-12b:

Compound trans-12b (20%) was obtained as colorless crystals from ethyl acetate-hexane, mp 196-197°; ir (potassium bromide): 3530 cm$^{-1}$ (OH); $^1$H nmr (deuteriochloroform): δ 1.24-1.82 (m, 5H, 3-H$_2$, 4-H$_2$ and OH), 2.46-2.84 (m, 2H, 5-H$_2$), 4.80 (d, J = 2 Hz, 2H, CH$_2$OH), 5.23 (s, 1H, 2-H), 6.83-6.27 (m, 3H, 6-H, 7H and 8-H); $^{13}$C nmr (deuteriodimethylsulfoxide): δ 19.2 (t), 30.6 (t), 37.6 (t), 54.7 (s), 78.8 (t), 78.9 (s), 112.2 (d), 116.3 (s), 124.3 (d), 127.4 (d), 130.3 (d), 141.0 (s), 155.7 (s).

C$_{13}$H$_{13}$NO$_2$ requires C, 72.56; H, 6.04; N, 6.51. Found: C, 72.55; H, 6.06; N, 6.53.

References:

Photocyclization reactions of ethyl 2-(8-oxo-5,6,7,8-tetrahydro-1-naphthyloxy)-acetate and 8-oxo-5,6,7,8-tetrahydro-1-naphthyloxyacetonitrile in methanol

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