Peri-selective Photocycloadditions of Methyl 2-Pyrone-5-carboxylate with Unsaturated Cyclic Ethers

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Photosensitized cycloaddition reaction of methyl 2-pyrone-5-carboxylate (**1**) with 2,3-dihydrofuran gave *cis*-exo- and *cis*-endo-[2+2] cycloadducts across the C_3-C_4 double bond in **1**, and a [4+2] cycloadduct which was different in addition-orientation from the Diels-Alder adducts. Each [2+2] cycloadduct was obtained by the use of sensitizers having different triplet energies. Photosensitized reactions of **1** with 3,4-dihydro-2*H*-pyrans afforded *cis*-endo-[2+2] cycloadducts, respectively. The photocycloaddition mechanism was also explained from the excited state of **1** calculated by means of MNDO-CI method.

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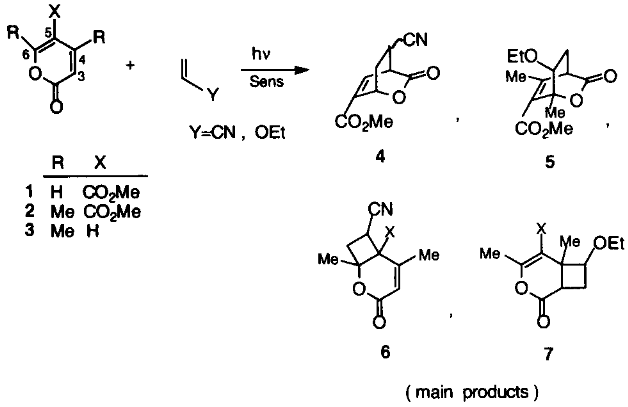
2-Pyrone has a basic heterocyclic skeleton containing an oxygen atom and is a conjugated dienone system in the form of a heterocyclic compound. Although much attention has been given to their thermal cycloaddition reactions [1], the investigation of the photochemical reactions has not been extended beyond our reports [2-5], except dimerizations and valence isomerizations [6,7]. Sensitized photoreactions of methyl 2-pyrone-5-carboxylate (**1**) with electron-deficient olefins gave mainly [4+2] cycloadducts **4** [3], while 4,6-dimethyl-2-pyrone (**3**) afforded [2+2] cycloadducts **6** across the C_5-C_6 double bond in **3** (Scheme 1). The investigation of the photocycloaddition reactions between **1** and electron-rich olefins has not been reported because of the preference of the Diels-Alder reactions [3,5].

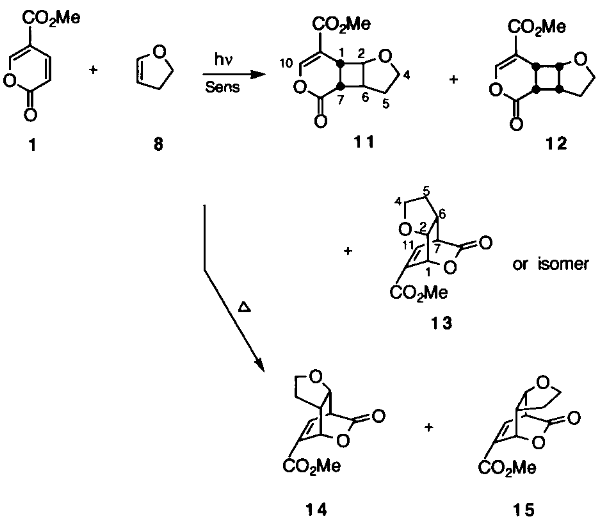
Scheme 1



We now report on sensitized photoreactions of **1** with some unsaturated cyclic ethers, which have low Diels-Alder reactivity compared with acyclic ethers because of their steric hindrance and/or ionic effects at the reaction points [8], in order to clarify the photoreactivity of **1** with electron-rich olefins.

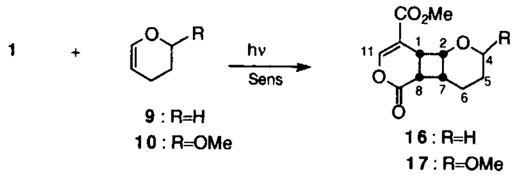
A solution of **1** and 2,3-dihydrofuran (**8**) in benzene in the presence of benzophenone (E_T = 69 kcal/mole) as a sensitizer was irradiated with 400W high-pressure mercury lamp through a Pyrex filter. The reaction was followed by gc. After removal of the solvent the residue was chromatographed on silica gel to afford a [2+2] cycloadduct **11** and a [4+2] cycloadduct **13** in 24% and 12% yields, respectively. By using 2-acetonaphthone (59 kcal/mole) as a sensitizer, the photoreaction gave another type of [2+2] cycloadduct **12** and a [4+2] cycloadduct **13** in 38% and 16% yields, respectively (Scheme 2). Photosensitized reactions of **1** with 3,4-dihydropyrans, **9** and **10**, by using 2-acetonaphthone gave only [2+2] cycloadducts, **16** and **17**, in 12% and 6% yields, respectively (Scheme 3). The same adducts were also obtained in the photoreactions by the use of benzophenone.

Scheme 2



The structures of **11**, **12**, **16** and **17** were deduced as [2+2] cycloadducts across the C_3-C_4 double bond in **1**

Scheme 3



9 : R=H
10 : R=OMe
16 : R=H
17 : R=OMe

from the spectroscopic evidence. For instance, **11** and **12**, methyl 8-oxo-3,9-dioxatricyclo[5.4.0.0^{2,6}]undec-10-ene-11-carboxylates showed strong carbonyl absorptions at 1770 cm^{-1} in the ir spectra for a γ,δ-unsaturated lactone. The regiochemistry of the tetrahydrofuran ring was estimated from the relationship between 2-H and other protons in their ^{1}H nmr spectra. Since two isomers did not change on treatment with basic alumina, which was used to infer the stereochemistry of ring junctions in [2+2] cycloadducts [2,9], **11** and **12** could be assigned as *cis*-fused. The remarkable feature of the ^{1}H nmr spectrum of **11** was the coupling pattern of 1-H which occurred at δ 3.24 as a doublet-doublet-doublet ($J_{1,7}$ = 10.0, $J_{1,2}$ = 2.0, $J_{1,10}$ = 1.0 Hz). And, it seemed reasonable to assume that the stereochemistry of **11** and **12** are exo and endo configurations, respectively by noting the long range coupling between 2-H and 7-H (**11**: $J_{2,7}$ = 0 Hz, **12**: $J_{2,7}$ = 2.5 Hz) [10].

On the other hand, the structure of **13** was deduced as [4+2] cycloadduct from the spectral data and showing the nature of decomposition at 170°. The remarkable feature of the ^{1}H nmr spectrum of **13** was the coupling pattern of 1-H which occurred at δ 5.64 as a triplet ($J_{1,2}$ = $J_{1,11}$ = 3.0 Hz). The regiochemistry was confirmed as shown in Scheme 2 by showing different ^{1}H nmr spectrum to the Diels-Alder adducts, **14** and **15** [8], but the stereochemistry is unknown.

We now describe a MNDO-CI treatment of the photoreactions which leads to an understanding of the peri- and regioselectivities. The MNDO-CI method has become an increasingly powerful tool for the understanding of cycloaddition reactions [11]. It is reasonable to assume that these photocycloadditions proceed *via* biradical intermediates of **1** and olefins. The orbital energies and coefficients of triplet excited states (HSOMO and LSOMO) for **1** were obtained as follows: the optimized structure of the triplet excited state of **1** was calculated by using unrestricted Hartree-Fock wavefunction (UHF), and the energies and coefficients were estimated by CI calculation which was carried out by considering thirty six configurations of **1**. In the case of ethyl vinyl ether, the optimized structure of the ground state was calculated by restricted Hartree-Fock wavefunction (RHF), and the energies and coefficients were estimated by CI calculation which was performed by taking account of thirty six configurations of ethyl vinyl ether. It is reasonable to consider that the mechanism of the cycloadditions of **1** with unsaturated cyclic ethers is similar to that of reaction between **1** and ethyl vinyl ether. Figure 1 shows the estimated orbital energies and coefficients for **1** and ethyl vinyl ether by using MNDO-CI method [12].

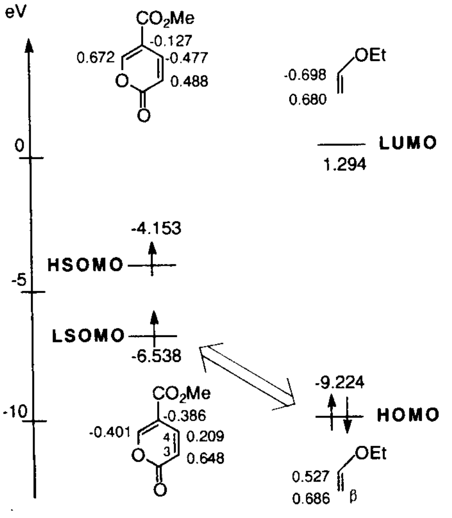
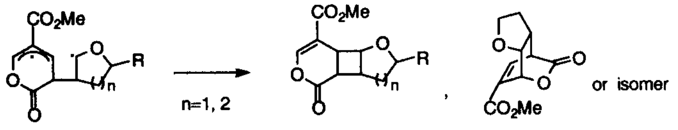


Figure 1 Estimated energies and coefficients of methyl 2-pyrone-5-carboxylate and ethyl vinyl ether

The energy gap between LSOMO(**1**)-HOMO(ethyl vinyl ether) is smaller than HSOMO(**1**)-LUMO(ethyl vinyl ether) and this frontier orbital interaction is much more important in the photocycloaddition. As the coefficient at C(3) in the LSOMO orbital of **1** and that at C(β) in the HOMO orbital of ethyl vinyl ether are larger than any other positions, the initial bond formation is inferred to occur at C(3)-C(β) to give a biradical intermediate **A** which may lead to the [2+2] and [4+2] cycloadducts (Scheme 4).

Scheme 4



A
11, 12, 16, 17
13

EXPERIMENTAL

All the melting points were measured on a Yanagimoto Mel-temp apparatus and are uncorrected. The ir, ^{1}H nmr and mass spectra were recorded on JASCO A-3, JEOL JNM-MH-100 (100 MHz) and JEOL JMSOISG spectrometers, respectively. The ^{1}H nmr spectra were recorded with TMS as an internal standard. All the photoreactions were monitored by the use of gc, which was performed on a Yanagimoto G80 instrument using a column of Silicon SE-30 (10%) or tlc on silica gel plates.

cis-exo-Methyl 8-Oxo-3,9-dioxatricyclo[5.4.0.0^{2,6}]undec-10-ene-11-

carboxylate (**11**), *cis*-endo-Methyl 8-Oxo-3,9-dioxatricyclo[5.4.0.-$0^{2,6}$]undec-10-ene-11-carboxylate (**12**) and Methyl 8-Oxo-3,9-dioxatricyclo[5.2.2.$0^{2,6}$]undec-10-ene-10-carboxylate (**13**).

A solution of methyl 2-pyrone-5-carboxylate (**1**) (3.0 g, 20 mmoles), 2,3-dihydrofuran (7.37 ml, 100 mmoles) and benzophenone (1.0 g, 5.5 mmoles) in benzene (200 ml) was irradiated under nitrogen for 24 hours at room temperature. The solvent was then removed under reduced pressure and the residue was chromatographed using benzene-acetone 10:1 v/v mixture to give **11** (1.07 g, 24%), **13** (0.54 g, 12%) and oxetane between benzophenone and 2,3-dihydrofuran (0.26 g, 19%, mp 144-146°) (lit [13], mp 141.5°).

Similar reaction of **1** (3.0 g, 20 mmoles) with 2,3-dihydrofuran (15.1 ml, 200 mmoles) in the presence of 2-acetonaphthone (2.2 g, 12.9 mmoles) as a sensitizer in benzene (200 ml) for 3.5 hours gave **12** (1.70 g, 38%) and **13** (0.71 g, 16%) by the same workup mentioned above.

Compound **11** had mp 118-121°; ir (potassium bromide): 1770, 1710, 1627 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.98 (m, 2H, 5-CH$_2$), 3.04 (dd, 1H, 7-H, $J_{7,1}$ = 10.0, $J_{7,6}$ = 5.0 Hz), 3.24 (ddd, 1H, 1-H, $J_{1,7}$ = 10.0, $J_{1,2}$ = 2.0, $J_{1,10}$ = 1 Hz), 3.40 (ddt, 1H, 6-H, $J_{6,2}$ = $J_{6,5'}$ = 6.0, $J_{6,7}$ = 5.0, $J_{6,5}$ = 2.0 Hz), 3.76 (s, 3H, Me), 4.10 (m, 2H, 4-CH$_2$), 4.34 (dd, 1H, 2-H, $J_{2,6}$ = 6.0, $J_{2,1}$ = 2.0 Hz), 7.50 (bs, 1H, 10-H); ms: m/z (relative intensity) 225 (M+1, 0.1), 70 (100).

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.89; H, 5.40. Found: C, 58.91; H, 5.54.

Compound **12** had mp 48-51°; ir (potassium bromide): 1771, 1722, 1658 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.98 (m, 2H, 5-CH$_2$), 3.68 (m, 3H, 1-, 6-, 7-H, $J_{1,2}$ = 4.0, $J_{1,7}$ = 10.5, $J_{6,7}$ = 10 Hz, The values of J were measured by adding Eu(dpm)$_3$ to **12** (Eu(dpm)$_3$/**12** = 1.57 mole/mole), 3.82 (s, 3H, Me), 3.88, 4.12 (each m, 1H, 4-CH$_2$), 4.78 (ddd, 1H, 2-H, $J_{2,1}$ = 4.0, $J_{2,6}$ = 7.0, $J_{2,7}$ = 2.5 Hz), 7.58 (d, 1H, 10-H, $J_{10,1}$ = 1.5 Hz); ms: m/z (relative intensity) 224 (M$^+$, 0.2%), 70 (100).

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.89; H, 5.40. Found: C, 59.10; H, 5.62.

Compound **13** had mp 124-128° (>170° dec); ir (potassium bromide); 1770, 1710, 1627 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.78, 2.10 (each m, 1H, 5-CH$_2$), 2.64 (m, 1H, 6-H), 4.02 (m, 2H, 4-CH$_2$), 4.24 (dd, 1H, 2-H, $J_{2,6}$ = 8.0, $J_{2,1}$ = 3.0 Hz), 5.64 (t, 1H, 1-H, $J_{1,2}$ = $J_{1,11}$ = 3.0 Hz), 7.28 (dd, 1H, 10-H, $J_{10,7}$ = 6.0, $J_{11,1}$ = 3.0 Hz); ms: m/z (relative intensity) 225 (M+1, 0.3), 70 (100).

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.89; H, 5.40. Found: C, 58.75; H, 5.47.

cis-endo-Methyl 9-Oxo-3,10-dioxatricyclo[5.5.0.$0^{2,7}$]dodec-11-ene-12-carboxylate (**16**).

A solution of **1** (3.0 g, 20 mmoles), 3,4-dihydro-2*H*-pyran (17 ml, 200 mmoles) and benzophenone (1.0 g, 5.5 mmoles) in acetonitrile (200 ml) was irradiated for 5 hours and the solvent was then removed under reduced pressure. The resulting solid was filtered to give two types of [4+2] dimers of **1** [7] (0.74 g, 24%) and the filtrate was chromatographed using benzene-acetone 10:1 v/v mixture to give **16** (0.30 g, 6.3%). The same photoreaction by using 2-acetonaphthone as a sensitizer afforded 12% of **16** and 15% of [4+2] dimers of **1**.

Compound **16** had mp 102-104°; ir (potassium bromide): 1765, 1720, 1656 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.60-2.06 (m, 4H, 5-, 6-CH$_2$), 3.06 (m, 1H, 7-H), 3.32 (m, 2H, 4-, 8-H), 3.60 (ddt, 1H, 1-H, $J_{1,2}$ = 6.0, $J_{1,8}$ = 10.0, $J_{1,7}$ = $J_{1,11}$ = 2.0 Hz), 3.76 (s, 3H, Me), 3.88 (m, 1H, 4'-H), 4.24 (td, 1H, 2-H, $J_{2,1}$ = $J_{2,7}$ = 4.5, $J_{2,8}$ = 2.0 Hz), 7.67 (bs, 1H, 11-H); ms: m/z (relative intensity) 207 (M-OMe), 84 (100).

Anal. Calcd. for $C_{12}H_{14}O_5$: C, 60.53; H, 5.88. Found: C, 60.25; H, 6.00.

cis-endo-Methyl 4-Methoxy-9-oxo-3,10-dioxatricyclo[5.5.0.$0^{2,7}$]dodec-11-ene-12-carboxylate (**17**).

A solution of **1** (3.0 g, 20 mmoles), 3,4-dihydro-2-methoxy-2*H*-pyran (24 ml, 200 mmoles) and 2-acetonaphthone (2.2 g, 12.9 mmoles) in acetonitrile (200 ml) was irradiated for 7 hours. The same workup described for **16** afforded **17** (0.32 g, 6%) in addition with 35% of [4+2] dimers of **1**.

Compound **17** had mp 151-153°; ir (potassium bromide): 1765, 1706, 1654 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.44 (m, 1H, 5-H), 1.76 (m, 3H, 5'-H, 6-CH$_2$), 3.01 (m, 1H, 7-H), 3.33, 3.76 (each s, 3H, Me), 3.34 (ddd, 1H, 8-H, $J_{8,1}$ = 10.0, $J_{8,7}$ = 8.0, $J_{8,2}$ = 2.0 Hz), 3.66 (ddt, 1H, 1-H, $J_{1,2}$ = 5.0, $J_{1,7}$ = $J_{1,11}$ = 2.0, $J_{1,8}$ = 10.0 Hz), 4.31 (td, 1H, 2-H, $J_{2,1}$ = $J_{2,7}$ = 5.0, $J_{2,8}$ = 2.0 Hz), 4.70 (t, 1H, 4-H, $J_{4,5}$ = 3.0 Hz), 7.60 (bs, 1H, 11-H); ms: m/z (relative intensity) 237 (M-OMe, 5), 57 (100).

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.23; H, 5.97. Found: C, 58.20; H, 6.07.

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