Intramolecular Photoreactions of 4-(ω-Alkenyloxy)-6-methyl-2-pyrones

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Photoirradiations of 4-(ω-alkenyloxy)-2-pyrones **1** gave site- and regio-specific intramolecular [2+2]-cycloadducts **2** being oxatricyclic lactones, and/or Dewar-type valence-isomer derivatives **4**. The reaction path depended upon the alkenyl chain length. Namely the two or three carbon chain gave rise to intramolecular [2+2]-cycloaddition, while the four carbon chain caused both valence-isomerization and cycloaddition. Hydrolysis of the cycloadducts **2** gave oxabicycloalkanecarboxylic acids **7**.

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Recently intramolecular [2+2]-photocycloadditions of α,β-unsaturated ketones possessing alkenyl carbon chains have been widely utilized to synthesize a variety of stereocontrolled compounds including natural products [1]. On the other hand, from our interest in the intermolecular photocycloadditions of simple α,β:γ,δ-unsaturated carbonyl compounds, we have reported the reactions of 2-pyrones with various olefins and have clarified their nature related to peri-, site-, and regio-selectivities [2,3]. Such reactivities toward cycloaddition are not the same as those of α,β-unsaturated ketones, and are able to be controlled electronically.

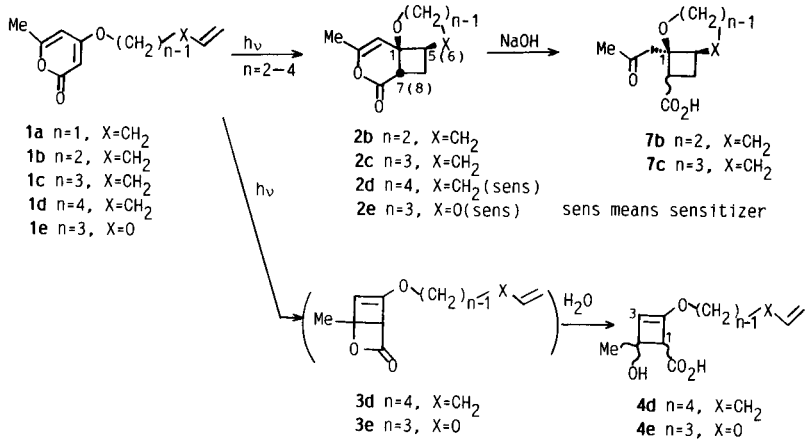
In this paper we report the intramolecular photochemical cycloadditions of 4-(ω-alkenyloxy)-6-methyl-2-pyrones **1a-d** and 4-(1,4-dioxa-5-hexenyl)-6-methyl-2-pyrone (**1e**) providing a simple route to mono- and dioxatricyclic lactones. Intramolecular reactivity of **1e** (X = O) is expected to be higher than that of **1c** (X = CH_2) because of the electrophilic property at 3,4-position of 2-pyrone ring in the excited state [2].

At first 2-pyrones, **1a-e**, were prepared by dehydrohalogenative coupling between 4-hydroxy-6-methyl-2-pyrone and halogenated olefins with base, in 30%, 42%, 81%, 74% and 84% yields, respectively.

Photoirradiation of a solution of **1b** (n = 2, X = CH_2) in acetone without benzophenone under nitrotgen at room temperature afforded a [2+2]-cycloadduct **2b** in quantitative yield. Similar photoirradiation of **1c** (n = 3, X = CH_2) gave also a [2+2]-cycloadduct **2c** quantitatively as shown in Scheme 1. Both of these reactions were found to be effectively sensitized by benzophenone. These results show that the intramolecular [2+2]-cycloadditions of **1** are site-, regio-, and stereo-specific, and proceed by way of triplet excited states of **1**. On the other hand, photoirradiations of **1d** (n = 4, X = CH_2) and **1e** (n = 3, X = O) without benzophenone gave cyclobutenecarboxylic acid **4d** (46% yield) and **4e**, respectively. Compound **4e** was labile and difficult to isolate, but it was detected by nmr spectroscopy. Sensitized photoirradiations of **1d** and **1e** with benzophenone or xanthone gave [2+2]-cycloadducts **2d** and **2e**, in 31% and 26% yields, respectively.

The structures of **2b-e** were assigned as intramolecular [2+2]-cycloadducts from the spectroscopic evidence. For example, **2b**, 10-methyl-2, 9-dioxatricyclo[5.4.0.$0^{1,5}$] undec-10-en-8-one, showed a low field ^{1}H nmr signal (δ 4.92 ppm) of the olefinic proton, and also that (δ 3.28 ppm, dd, J = 8.0, 10.0 Hz) of 7-H. These are similar to the intermolecular [2+2]-adduct of 4,6-dimethyl-2-pyrone and ethyl vinyl ether [2]. The ring junction across the C_3-C_4 double bond in **1** could be deduced as cis-fused, since **2b** did not

Scheme 1



1a n=1, X=CH_2
1b n=2, X=CH_2
1c n=3, X=CH_2
1d n=4, X=CH_2
1e n=3, X=O

2b n=2, X=CH_2
2c n=3, X=CH_2
2d n=4, X=CH_2 (sens)
2e n=3, X=O (sens)

7b n=2, X=CH_2
7c n=3, X=CH_2

3d n=4, X=CH_2
3e n=3, X=O

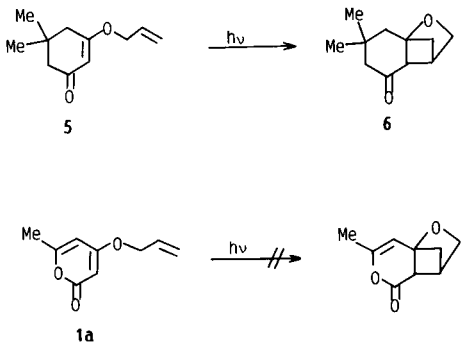
4d n=4, X=CH_2
4e n=3, X=O

change on treatment with basic alumina, which was used to infer the stereochemistry of ring junctions in photochemical [2+2]-cycloadducts [3]. And, it seemed reasonable to assume that the configuration between hydrogens at 5- and 7-positions is *trans*, because of the absence of long-range coupling between 5-H and 7-H [3]. Compound **4d**, which has been formed through the hydrolysis of bicyclolactone **3d**, was confirmed to be 2-(5-hexenyloxy)-4-hydroxy-4-methylcyclobut-2-ene-1-carboxylic acid from the ^{1}H nmr spectrum. Bicyclolactone **3d** could not be isolated for its lability.

The intramolecular photocycloreaction of **1b-c** occurred independent of the presence of sensitizer in other solvents, such as benzene, acetonitrile, and methanol, and the same products **2b-c** were obtained. Photoirradiation of **1a** (n = 1, X = CH_2) gave no product at the presence of benzophenone or not, and **1a** was recovered quantitatively.

On the basis of these results as shown in Scheme 1, photoreactions such as the intramolecular photochemical cycloaddition or valence-isomerization of **1** were found to be dependent on the alkenyl chain length. As the photoirradiation of **1a** gave no cycloadduct, the intramolecular cycloaddition of **1** was found to require the presence of at least more than two methylene units in the side chain of the chromophore. These observations were different from those of 3-(ω-alkenyloxy)-2-cycloalkenones in which photoreaction of **5** gave intramolecular cycloadduct **6** and "the rule of five" was effective [4,5]. This difference is thought to come from the fact **1** has a more rigid ring than **5**.

Scheme 2



We next investigated the hydrolysis of **2** leading to the formation of oxabicycloalkanecarboxylic acids. The hydrolysis of **2b-c** with 5% sodium hydroxide solution afforded **7b** and **7c**, in 60% and 65% yields, respectively. The structures of **7b** and **7c** were assigned from the spectral data.

EXPERIMENTAL

All the melting points were measured on a Yanagimoto Meltemp 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. The reported values for ir are cm^{-1} and ^{1}H nmr are δ (ppm). All the photoreactions were monitored by the use of gc, which was performed on a Yanagimoto G80 instrument using a column of Silicone SE-30 (10%) or by tlc on silica-gel plates.

4-(2-Propenyloxy)-**1a**, 4-(3-Butenyloxy)-**1b**, 4-(4-Pentenyloxy)-**1c**, 4-(5-Hexenyloxy)-6-methyl-2-pyrone (**1d**), and 4-(1,4-Dioxa-5-hexenyl)-6-methyl-2-pyrone (**1e**).

1) A solution of 4-hydroxy-6-methyl-2-pyrone (6.3 g, 50 mmoles), allyl bromide (6.1 g, 50 mmoles), and 1,8-diazabicyclo-[5.4.0]undec-7-ene (7.6 g, 50 mmoles) in acetonitrile (5 ml) was stirred for 18 hours at room temperature. After the solvent was removed, the residual oil was chromatographed on a silica gel column (Wakogel C-200) using benzene-acetone 3:1 v/v mixture as the eluent to give **1a** (2.53 g, 30%). 2) A similar solution of 2-pyrone (3.89 g, 31 mmoles), 4-bromo-1-butene (5.00 g, 37 mmoles), triethylamine (3.74 g, 37 mmoles), and acetonitrile (5 ml) was refluxed for 5 hours. The similar work up and chromatography using benzene-acetone 10:1 v/v mixture gave **1b** (2.33 g, 42%). 3) A similar solution of 2-pyrone (3.53 g, 31 mmoles), 5-bromo-1-pentene (5.00 g, 34 mmoles), triethylamine (3.44 g, 34 mmoles), and acetonitrile (5 ml) was refluxed for 5 hours. The similar work up gave **1c** (4.38 g, 81%). 4) A similar solution of 2-pyrone (3.24 g, 26 mmoles), 6-bromo-1-hexene (5.00 g, 31 mmoles), triethylamine (3.12 g, 31 mmoles), and acetonitrile (5 ml) was refluxed for 5 hours. The same work up gave **1d** (3.94 g, 74%). 5) A similar solution of 2-pyrone (1.60 g, 12.7 mmoles), 2-chloroethyl vinyl ether (2.04 g, 19.1 mmoles), 1,8-diazabicyclo-[5.4.0]undec-7-ene (2.90 g, 19.2 mmoles), and acetonitrile (5 ml) was refluxed for 5 hours. The similar work up gave **1e** (2.1 g, 84%). Compound **1a** was obtained as an oil; ir (neat): 1720, 1640, 1560 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.20 (s, 3H), 4.50 (bd, 2H), 5.34 (dd, 1H), 5.40 (d, 1H), 5.44 (dd, 1H), 5.80 (d, 1H), 5.96 (m, 1H); ms: m/z (relative intensity) 166 (M^+, 65), 41 (100).

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.66. Found: C, 65.21; H, 6.70.

Compound **1b** was obtained as an oil; ir (neat): 1720, 1650, 1565 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 2.17 (s, 3H), 2.51 (q, 2H), 3.97 (t, 2H), 5.12 (d, 1H), 5.16 (d, 1H), 5.38 (s, 1H), 5.78 (s, 1H), 5.82 (m, 1H); ms: m/z (relative intensity) 180 (M^+, 100).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.43; H, 6.63.

Compound **1c** was obtained as an oil; ir (neat): 1720, 1650, 1570 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.86 (m, 2H), 2.15 (m, 2H), 2.16 (s, 3H), 3.92 (t, 2H), 5.01 (d, 1H), 5.07 (d, 1H), 5.34 (s, 1H), 5.78 (m, 1H), 5.80 (s, 1H); ms: m/z (relative intensity) 194 (M^+, 14), 68 (100).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 67.86; H, 7.19.

Compound **1d** was obtained as an oil; ir (neat): 1730, 1650, 1570 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.51 (m, 2H), 1.78 (m, 2H), 2.11 (m, 2H), 2.18 (s, 3H), 3.93 (t, 2H), 4.98 (d, 1H), 5.03 (d, 1H), 5.39 (d, 1H), 5.77 (d, 1H), 5.80 (m, 1H); ms: m/z (relative intensity) 208 (M^+, 14), 82 (100).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.02; H, 7.73.

Compound **1e** was obtained as an oil; ir (neat): 1740, 1650, 1260 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 2.21 (s, 3H), 4.02 (m, 2H), 4.10 (dd, 1H), 4.17 (m, 2H), 4.24 (dd, 1H), 5.41 (d, 1H),

5.83 (d, 1H), 6.50 (dd, 1H); ms: m/z (relative intensity) 196 (M^+, 17.6%), 43 (100).

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.22, H, 6.16. Found: C, 61.11; H, 6.20.

10-Methyl-2,9-dioxatricyclo[5.4.0.0^{1,5}]undec-10-en-8-one (**2b**).

A solution of **1b** (n = 2, X = CH_2) (757 mg, 3.9 mmoles) in acetone (350 ml) was irradiated under nitrogen with a 400W high-pressure mercury lamp through a Pyrex tube for 4 hours at room temperature. The solvent was then removed under reduced pressure and the residue was chromatographed using benzene-acetone 15:1 v/v mixture to give product **2b** (491 mg, 70%), which formed quantitatively by gc analysis.

Compound **2b** had mp 72-74°; ir (potassium bromide): 1760, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ = 1.80-2.48 (m, 4H, 4-, 5-CH_2), 1.90 (s, 3H, Me), 2.74 (m, 1H, 5-H), 3.28 (dd, 1H, 7-H, J = 8.0, 10.0 Hz), 4.08 (m, 2H, OCH_2), 4.92 (s, 1H, =CH); ms: m/z (relative intensity) 180 (M^+, 3), 43 (100).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.59; H, 6.74.

11-Methyl-2,10-dioxatricyclo[6.4.0.0^{1,6}]dodec-11-en-9-one (**2c**).

A solution of **1c** (n = 3, X = CH_2) (985 mg, 5.1 mmoles) in acetone (500 ml) was similarly irradiated for 1.2 hours. After the solvent was removed *in vacuo*, the resulting solid was recrystallized from diethyl ether-hexane 1:1 v/v mixture to give **2c** (693 mg, 70%), which formed quantitatively by gc analysis.

Compound **2c** had mp 86-88°; ir (potassium bromide): 1760, 1690 cm^{-1}; ^1H nmr (deuteriochloroform): δ = 1.40-1.90 (m, 4H, 4-, 5-CH_2), 1.93 (s, 3H, Me), 2.10-2.35 (m, 3H, 6-H, 7-CH_2), 3.75 (m, 2H, OCH_2), 3.83 (dd, 1H, 8H, J = 3.0, 11.0 Hz), 4.94 (s, 1H, =CH); ms: m/z (relative intensity) 194 (M^+, 14), 68 (100).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 67.80; H, 7.22.

12-Methyl-2,10-dioxatricyclo[7.4.0.0^{1,7}]tridec-12-en-10-one (**2d**) and 2-(5-Hexenyloxy)-4-hydroxy-4-methylcyclobut-2-en-1-carboxylic Acid (**4d**).

1) A solution of **1d** (n = 4, X = CH_2) (360 mg, 1.7 mmoles) and benzophenone (72 mg) as a sensitizer in acetonitrile (120 ml) was irradiated for 5 hours. After the solvent was removed, the residue was chromatographed using benzene-acetone (10:1) to give **2d** (112 mg, 31%). 2) A similar solution of **1d** in acetonitrile without benzophenone was irradiated for 5 hours. The similar work up and chromatography using acetone gave cyclobutenecarboxylic acid **4d** (126 mg, 46%). Compound **2d** was obtained as an oil; ir (neat): 1760, 1695 cm^{-1}; ^1H nmr (deuteriochloroform): δ = 1.60-1.98 (m, 6H, 4-, 5-, 6-CH_2), 1.96 (s, 3H, Me), 2.24 (m, 3H, 7-H, 8-CH_2), 3.11 (t, 1H, 9-H, J = 10.0 Hz), 3.42 (ddd, 1H, 3-H, J = 5.0, 7.7, 12.8 Hz), 3.70 (ddd, 1H, 3-H', J = 3.2, 5.0, 12.8 Hz), 5.24 (s, 1H, =CH); ms: m/z (relative intensity) 208 (M^+, 13), 82 (100).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.40; H, 7.81.

Compound **4d** was obtained as an oil; ir (neat): 3200-2500, 1700 (broad) cm^{-1}; ^1H nmr (deuteriochloroform): δ = 1.49 (m, 2H, CH_2), 1.67 (m, 2H, CH_2), 2.01 (s, 3H, Me), 2.06 (m, 2H, CH_2), 3.14 (s, 1H, OH), 3.69 (s, 1H, 1-H), 4.12 (m, 2H, CH_2), 4.98 (d, 1H, =CH, J = 13.0 Hz), 5.05 (d, 1H, =CH, J = 18.0 Hz), 5.82 (m, 1H, CH=CH_2), 5.93 (s, 1H, 3-H), 9.1 (bs, 1H, CO_2H); ms: m/z (relative intensity) 226 (M^+, 2), 127 (100).

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.38; H, 7.89.

11-Methyl-2,5,10-trioxatricyclo[6.4.0.0^{1,6}]dodec-11-en-9-one (**2e**).

1) A solution of **1e** (n = 3, X = O) (150 mg, 0.76 mmoles) and xanthone (150 mg) in acetone (120 ml) was irradiated for 1.5 hours. The similar work up and chromatography for **2d** using benzene-acetone gave **2e** (39 mg, 26%). 2) A similar solution of **1e** in acetone without xanthone was irradiated for 3 hours. In spite of the similar work up and chromatography, cyclobutenecarboxylic acid **4e**, which was detected by nmr spectroscopy, could not be isolated. Compound **2e** was obtained as an oil; ir (neat): 1760 cm^{-1}; ^1H nmr (deuteriochloroform): δ = 1.97 (d, 3H, Me), 2.00 (ddd, 1H, 7-H', J = 4.4, 9.5, 12.5 Hz), 2.14 (ddd, 1H, 7-H, J = 1.2, 10.1, 12.5 Hz), 3.57 (ddd, 1H, 3-H or 4-H, J = 2.2, 11.4, 12.1 Hz), 3.66 (ddd, 1H, 3-H' or 4-H', J = 1.1, 2.2, 11.4 Hz), 3.72 (ddd, 1H, 4-H or 3-H), 3.98 (ddd, 1H, 4-H' or 3-H'), 4.00 (dd, 1H, 8-H or 6-H, J = 9.5, 10.1 Hz), 4.04 (dd, 1H, 6-H or 8-H, J = 1.2, 4.4 Hz), 4.87 (q, 1H, =CH); ms: m/z (relative intensity) 196 (M^+, 100%).

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.40; H, 6.21.

1-Acetonyl-2-oxabicyclo[3.2.0]heptane-7-carboxylic Acid (**7b**) and 1-Acetonyl-2-oxabicyclo[4.2.0]octane-8-carboxylic Acid (**7c**).

1) A mixture of **2b** (200 mg, 1.1 mmoles) and 5% sodium hydroxide aqueous solution (3 ml) was stirred for 1 hour at room temperature. After neutralization of the solution with hydrochloric acid, the solution was extracted with diethyl ether to give **7b** (131 mg, 60%), which was a mixture of equal amount of stereoisomers. 2) A similar mixture of **2c** and 5% sodium hydroxide aqueous solution was stirred for 0.5 hour. The similar work up gave **7c** (50 mg, 50%).

Compound **7b** was obtained as an oil; ir (neat): 3200-2500, 1725, 1710 cm^{-1}; ^1H nmr (deuteriochloroform): δ = 1.72 (m, 2H, CH_2), 1.97 (m, 2H, CH_2), 2.15 (s, 3H, Me), 2.23 (s, 3H, Me), 2.80 (m, 1H, 5-H), 2.92, 3.08 (each d, 1H, CH_2COMe, J = 17.2 Hz), 3.18, 3.30 (each d, 1H, 7-H, J = 9.0 Hz), 3.9-4.2 (m, 2H, OCH_2), 10.2 (bs, 1H, CO_2H); ms: m/z (relative intensity) 198 (M^+, 10), 126 (100).

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.60; H, 7.12. Found: C, 60.53; H, 7.05.

Compound **7c** had mp 72-76°; ir (potassium bromide): 3200-2500, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ = 1.20-1.60 (m, 3H, 4-CH_2, 7-H), 1.90-2.08 (m, 3H, 5-CH_2, 7-H'), 2.18 (s, 3H, Me), 2.56 (m, 1H, 6-H), 2.75, 2.94 (each d, 1H, CH_2COMe, J = 15.0 Hz), 3.52 (t, 1H, 8-H, J = 8.0 Hz), 3.77 (t, 2H, OCH_2, J = 5.0 Hz), 10.14 (bs, 1H, CO_2H); ms: m/z (relative intensity) 212 (M^+, 1), 140 (100).

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.16; H, 7.64.

REFERENCES AND NOTES

[1] M. T. Crimmins, *Chem. Rev.*, **88**, 1453 (1988).

[2] T. Shimo, K. Somekawa and S. Kumamoto, *Nippon Kagaku Kaishi*, 394 (1983); *Chem. Abstr.*, **99**, 53539h (1983).

[3a] T. Shimo, K. Somekawa, Y. Wakikawa, H. Uemura, O. Tsuge, K. Imada and K. Tanabe, *Bull. Chem. Soc. Japan*, **60**, 621 (1987); [b] T. Suishu, T. Shimo, K. Somekawa and S. Tokita, 57th Annual Meeting of Japan Chemical Society, Abstracts II p 548 (1988).

[4] Y. Tamura, H. Ishibashi, M. Hirata, Y. Kita and M. Ikeda, *J. Org. Chem.*, **40**, 2702 (1975).

[5] An empirical rule called "the rule of five" means as follows: in

the 1,5-diene systems the preferred orientation is head-to-tail (cross addition) while the head-to-head addition (parallel addition) is favored in the 1,6-dienes. [a] T. Tamura, Y. Kita, H. Ishibashi and M. Ikeda, *J. Chem. Soc., Chem. Commun.*, 1167 (1971); [b] M. Ikeda, M. Takahashi, T. Uchino, K. Ohno, Y. Tamura and M. Kido, *J. Org. Chem.*, **48**, 4241 (1983) and references cited therein.