



Regio- and Stereo-Selective Formation of 2-Siloxy-2-Alkoxyoxetanes in the Photoreaction of Cyclic Ketene Silyl Acetals with 2-Naphthaldehyde and Their Transformation to Aldol-Type Adducts

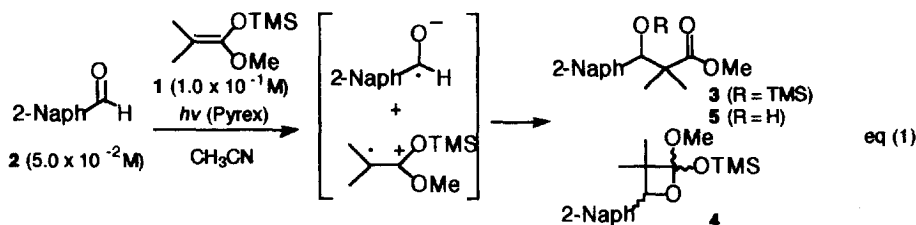
Manabu Abe*, Masayuki Ikeda, Yasuo Shirodai, and Masatomo Nojima

Department of Materials Chemistry, Faculty of Engineering, Osaka University, Suita, 565, Japan

Abstract: Regio- and stereo-selective formation of bicyclo 2-siloxy-2-alkoxyoxetanes **7**, **13**, **14** was achieved by the proper choice of the solvent and the silyl group in the photoreaction of the cyclic ketene silyl acetals **6**, **11**, **12** with 2-naphthaldehyde **2**, and their transformation to the aldol-type adducts **9**, **15**, **16** was easily accomplished under the neutral conditions.

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Among the oxetane derivatives, 2-alkoxyoxetanes possessing both the highly strained structure and the acetal moiety are worthy of study from the synthetic point of view.¹ However, in general, the preferential formation of 3-alkoxyoxetanes is observed in the Paterno-Büchi reactions² as expected from the stability of the involving 1,4-diradical intermediates.^{3,4} Turro has suggested that 2-alkoxyoxetanes, minor products in the photoreaction of vinyl ethers with carbonyl compounds, is derived from the radical-ion intermediates via electron transfer mechanism.^{3d,5} Recently, Fukuzumi and coworkers reported that in the photo-induced electron transfer reaction of β,β -dimethyl ketene silyl acetal **1**⁶ ($E_{ox} = 0.9$ V vs SCE) with 2-naphthaldehyde **2** ($E_{red}^{ex} = 0.9$ V vs SCE) in CH_3CN ,⁷ the regioselective carbon-carbon bond formation occurred to give only the silyl migration product **3** in a high yield.⁸ However, we have found the formation of the corresponding acid-labile 2-siloxy-2-alkoxy oxetane **4**, which leads to the ring-opened adduct **5** (71%) upon treatment with H_2O , as a major product together with **3** (17%) under the similar conditions as reported by Fukuzumi et al. (eq 1).⁹ The preferential formation of the 2-siloxy-2-alkoxy oxetanes is considered to be synthetically worthwhile.



We now report herein the regio- and stereo-selective formation of synthetically useful 2-siloxy-2-alkoxyoxetanes in the photoreaction with electron-rich cyclic ketene silyl acetals with 2-naphthaldehyde **2**, and also their chemical transformation to aldol-type adducts *under the neutral conditions*.

First of all, to establish the optimal conditions for the formation of 2-siloxy-2-alkoxy oxetanes **7**, the photoreactions of cyclic ketene silyl acetals **6**, which contains several types of silyl groups, with **2** were

carefully examined in degassed and dried solvents (eq 2 and Table 1). It was ascertained that the highly regio and stereo-selective formation of acid-labile bicyclic-oxetanes **7** was found in the reaction mixture. The formation of **7** was revealed by the NMR analysis, especially the peculiar ^{13}C NMR chemical-shift of the orthoester carbon.¹⁰ Their chemical transformation to the aldol-type adduct **9** was successfully performed upon treatment with H_2O . The major isomer of **7** was determined as anti-form by NOE measurement of the corresponding acetone **10** derived from **9**.¹¹ Neither **7** nor **8** was isomerized each other under the photolysis conditions.

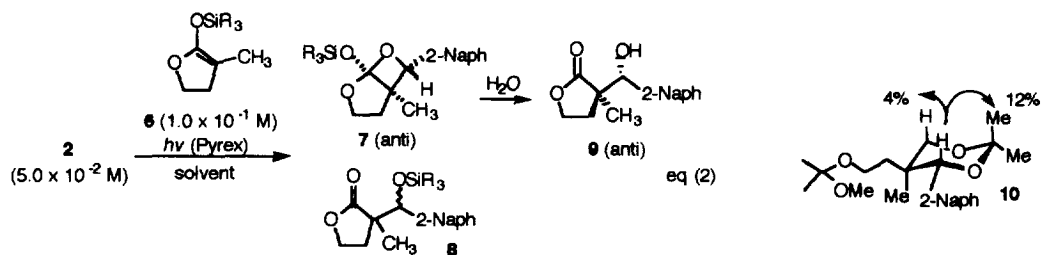


Table 1. The photoreactions of **6 with **2** under the various conditions.^a**

entry	6	SiR ₃	solvent (ϵ) ^b	Swain's value ^c		products and yields (%) ^{d, e}			diastereo ratios (anti : syn) ^e	
				A	B	7a (75)	8a (0)	7a (93 : 7)	7b (85 : 15)	8b (76 : 24)
1	6a	TBDMS	CH_3CN (37.5)	0.37	0.86	7a (75)	8a (0)	7a (93 : 7)		
2	6b	TMS	CH_3CN			7b (28)	8b (59)	7b (85 : 15)	8b (76 : 24)	
3	6c	TMEOS	CH_3CN			7c (20)	8c (48)	7c (81 : 19)	8c (62 : 38)	
4	6a	TBDMS	CH_2Cl_2 (8.93)	0.33	0.80	7a (75)	8a (0)	7a (90 : 10)		
5	6b	TMS	CH_2Cl_2			7b (73)	8b (0)	7b (91 : 9)		
6	6c	TMEOS	CH_2Cl_2			7c (55)	8c (22)	7c (92 : 8)	8c (44 : 56)	
7	6a	TBDMS	HMPA (29.6)	0.00	1.07	7a (73)	8a (0)	7a (87 : 13)		
8	6b	TMS	HMPA			7b (0)	8b (69)		8b (57 : 43)	

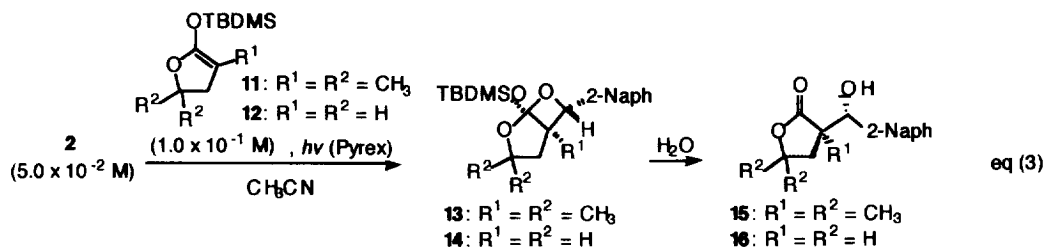
^a The photoreactions were performed in degassed and dried solvents through a Pyrex filter at 0 °C. ^b Dielectric constant. ^c Swain's A and B values express abilities to solvate anions and cations, respectively.¹² ^d Isolated yields based on used **2**. All new compounds **8** and **9** were characterized by both spectroscopic and elemental analysis. ^e Yields of **7** and their diastereo ratios were determined on the basis of the isolated **9** by ^1H NMR analysis after treatment with H_2O .

Three facts should be noted in the photoreactions: (1) the exclusive and stereoselective formation of **7a** in high yields was observed in all the solvents (entries 1,4,7), whereas in the reaction of **6b** (SiR₃ = TMS) and **6c** (SiR₃ = trimethoxysilyl (TMEOS)), **7** and/or **8** were obtained depending upon the used solvent; (2) the product ratios **7b/8b** and **7c/8c** increased with both the decrease of Swain's B value¹² (HMPA > CH_3CN > CH_2Cl_2) which expresses the ability to solvate cations and the increase of the A value which expresses the ability to solvate anions (entries 2,3,5,6,8), and furthermore the ratio increased in the low ϵ solvent (CH_2Cl_2); (3) the ratios of stereoisomers of oxetanes **7** were higher than those of **8** (entries 2,3,6). In this regard, the exclusive and anti-selective formation of oxetanes **7**, which can be easily led to the aldol-type adduct **8** while retaining the stereochemistry, can be achieved by the proper choice of both the solvent and the silyl group.

The electron transfer from **6** to the excited state of **2** seems to be important step in the photoreactions. The reductive-quenching experiments of the excited state of **2** by oxidizing agents were performed in the

presence of **6a**. In the case of using DABCO ($E_{\text{OX}} = 0.64$ V vs SCE,¹³ 1 eq relative to **6a**) the formation of oxetanes **7a** was effectively suppressed to give **9** (17% yield, anti : syn = 91 : 9) after treatment with H_2O . The solvent effects on the product distribution of **7/8** (Table 1) suggest that the oxetanes **7** may be formed from the structurally fixed exciplex¹⁴ or the contact radical-ion pair, whereas the silyl-migration adducts **8** mainly come from the radical-radical coupling of the solvent separated radical-ion pair. This mechanistic consideration is also supported by the fact that the diastereo ratios of **7** were higher than those of **8** (entries 2,3,6). The high silyl migrating ability of TMEOS (entry 5) can be explained by the higher positive-charge density on the silicon atom of 6c^{*+} .¹⁵ On the other hand, the exclusive formation of oxetane **7a** ($\text{SiR}_3 = \text{TBDMS}$) was obtained in all the solvents (entry 1,4,7). The results suggest that both the solvation of the cationic site, which is mainly localized at silicon,¹⁵ and the nucleophilic addition toward the silicon by 2^{*-} are suppressed by the bulky substituents at silicon.¹⁶

To gain the preliminary information regarding the stereochemical outcome, dimethyl substituted **11** and non-substituted **12** were used for the photoreactions with **2** (eq 3). In the case of **11**, completely anti-selective formation of oxetane **13** was observed to afford the aldol-type adduct **15** in 75% yield after treatment with H_2O . With **12**, the aldol-type adduct **16** (39%) was obtained in almost the same diastereoselectivity (anti : syn = 84 : 16) as **7a**. Thus, the steric repulsion between the naphthyl group and the tetrahydrofuran ring system is probably an important factor to control the stereochemistry of the photoproducts.



Finally, in order to evaluate the synthetic utility of our photoreaction, Mukaiyama-Aldol reactions of **6a** with **2** were performed under the typical conditions¹⁷ (Table 2). Consequently, the aldol-type adducts **8a** and **9** were obtained in low stereoselectivities. These observations form a remarkable contrast to our photo-aldol reactions which lead to high diastereoselectivities (eqs 2 and 3, Table 1).

Table 2. Mukaiyama-Aldol Reactions of 6a with 2 in CH_2Cl_2 at -78 °C.

entry	Lewis acid	products and yields (%)		diastereo ratios	
				(anti : syn)	
1	$\text{BF}_3 \cdot \text{OEt}_2$	8a (51)	9 (36)	8a (59 : 41)	9 (47 : 53)
2	TiCl_4	8a (16)	9 (76)	8a (44 : 56)	9 (57 : 43)

In summary, by the proper choice of the solvent and the silyl substituent, the exclusive and anti-selective formation of 2-siloxy-2-alkoxyoxetanes **7**, **13**, **14**, which can be easily led to the aldol-type adducts **9**, **15**, **16**, was accomplished in the photoreaction of the cyclic ketene silyl acetals **5**, **10**, **11** with 2-naphthaldehyde **2**. Further synthetic studies on the use of the stereo-controlled 2-siloxy-2-alkoxyoxetane as a key intermediate and the mechanistic investigation are now in progress.

References and Notes

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