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EFFICIENT PHOTOCHEMICAL OXETANE FORMATION FROM 2-PYRONES AND BENZOPHENONES IN THE SOLID STATE

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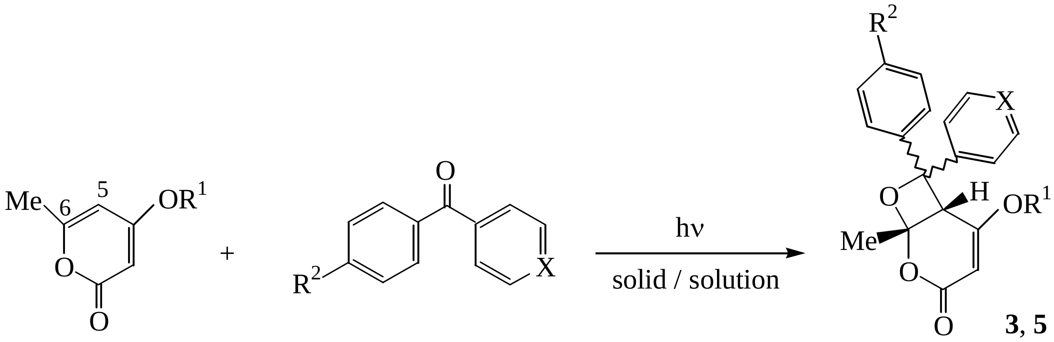
Abstract – Solid-state photocycloaddition reactions of 2-pyrones (**1**, **4**) with benzophenone derivatives (**2a-c**, **f**) afforded highly site- and regioselective oxetanes (**3a**, **3b**, **3c**, **3f**, **5a**, **5b**, **5c**, **5f**) across the C5-C6 double bond in **1** or **4** *via* the triplet excited state of **2**. The site- and regioselectivities were explained by MO calculations.

Photochemical reactions of two-component organic crystals or solid mixtures give us much attention from the viewpoint of controlling the selectivities of the reactions because of the tight and regular arrangement of the molecules in the crystals using a non-covalent interaction in the environment.[1–4] In our recent papers,[5-7] we have described a high selective [2+2] cycloaddition reaction with high efficiency by irradiation to 1:1 complex crystals between 2-pyrones, possessing a cyclic dienoate ring structure, and maleimide even by irradiation to the grinding mixtures. Since only limited investigation of oxetane formation has been reported in the solid state,[8,9] we report here an efficient photocycloaddition reaction of 2-pyrones with benzophenone derivatives affording oxetanes with high site- and regioselectivities as a part of our continuing solid-state photoreaction program.

A mixture of crystals of **1** (1.0 mmol) and **2a** (1.0 mmol) in a mortar was ground for 10 min with a pestle. The powder was sandwiched with two Pyrex glass plates and photolyzed for 24 h with a 400 W high-pressure mercury lamp under nitrogen atmosphere at room temperature. The reaction mixture was chromatographed by silica gel using ethyl acetate – hexane (1:5 v/v) as eluent to give **3a** in 86% yield by NMR spectral analysis (Scheme 1). The results of the similar photoreactions of **1** and **4** with **2** were summarized in Table 1. The structure of **3a** was established by X-Ray crystallographic analysis (Figure 1),[10] which had been previously reported[11] without X-Ray structure analysis, showing



2

1: R^1=Me
4: R^1=$CH_2C_6H_4Me$(*p*)

a: R^2=H, X=CH
b: R^2=Me, X=CMe
c: R^2=H, X=C-OMe
d: R^2=H, X=C-NO_2
e: R^2=OMe, X=C-OMe
f: R^2=H, X=N

3a: R^1=Me, R^2=H, X=CH
3b: R^1=R^2=Me, X=CMe
3c: R^1=Me, R^2=H, X=C-OMe
3f: R^1=Me, R^2=H, X=N
5a: R^1=$CH_2C_6H_4Me$(*p*), R^2=H, X=CH
5b: R^1=$CH_2C_6H_4Me$(*p*), R^2=Me, X=CMe
5c: R^1=$CH_2C_6H_4Me$(*p*), R^2=H, X=C-OMe
5f: R^1=$CH_2C_6H_4Me$(*p*), R^2=H, X=N

Scheme 1

Table 1 Photoreactions of 2-Pyrones (**1**,**4**) with Benzophenones (**2a-f**) in the Solid State[a] and in Solution.[b]

		yield(%)[c] in the solid state		yield(%)[c] in solution
2-pyrone	benzophenone	oxetane	recovered	
		3	**2**	**3**[d]
1	**2a**	86(**3a**)	14	19
	2b	60(**3b**)	40	6
	2c	28(**3c**)	72	13
	2d	0	100	0
	2e	0	100	0
	2f	42(**3f**)	58	24
4	**2a**	84(**5a**)	16	41
	2b	80(**5b**)	20	20
	2c	42(**5c**)	58	21
	2d	0	100	0
	2e	0	100	0
	2f	58(**5f**)	42	29

[a] Equimolar mixture of **1** and **2** was irradiated for 24 h. [b] Equimolar solution of 2-pyrone (**1** or **4**) and **2** was irradiated for 24 h. [c] Estimated from NMR spectral analyses based on total integral between **2** and oxetanes. [d] Calculated yield using internal standard (pyrazine) in acetonitrile solution (25 mM).

high site- and regioselective oxetane ring fused at the C5-C6 double bond of the 2-pyrone. The assignment of the same structure (**3** and **5**) to other oxetanes were based on their ^{1}H NMR, IR and MS spectra that were analogous to those of **3a**.[12] The oxetanes (**3c**, **3f**, **5c**, and **5f**) were found to be 1:1 mixtures of two stereoisomers from the NMR spectral

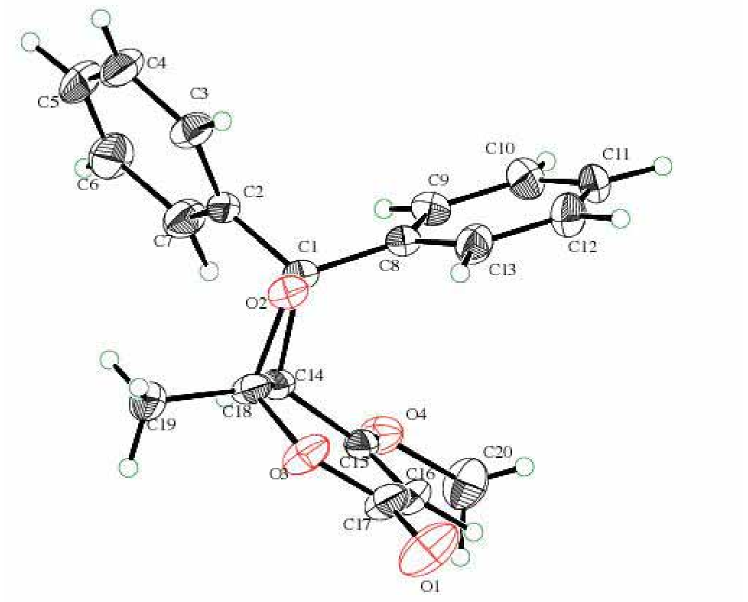
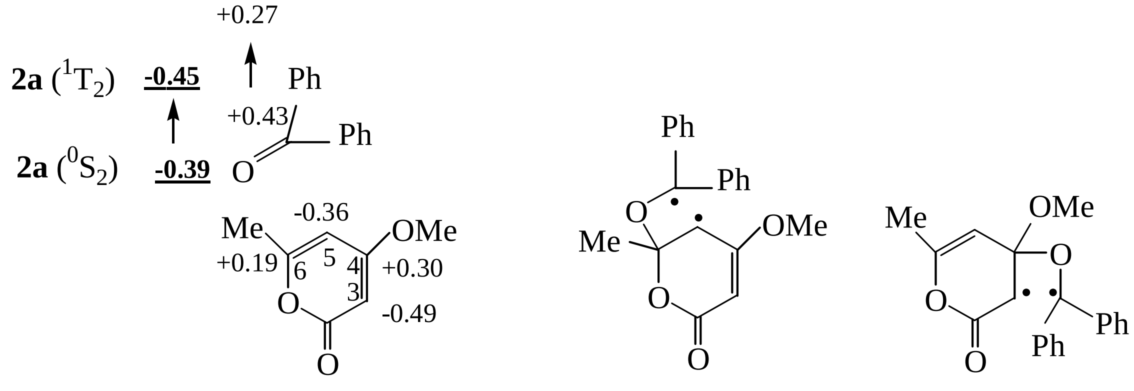


Figure 1 ORTEP drawing of **3a**

analyses. The photoreactions of **2d** and **2e**, whose compounds showed UV absorptions at 350 nm (ε 500) in acetonirtile, with 2-pyrones did not afford oxetanes but resulted in quantitative recovery of **2d** and **2e** in the solid state. The reaction is inferred to be caused by the short life times of **2d** and **2e** at the triplet exited states. Since it was hard to obtain a crystal structure for any of the mixed substrates between 2-pyrones (**1, 4**) and **2**, structure-reactivity correlation studies which had been shown in the 1:1 complex crystals of several 2-pyrones and maleimide[5-7] could not be performed in this system. But weak hydrogen bondings were estimated from the lower wavelength shifts of the carbonyl groups in the IR spectra: lactone and benzophenone carbonyls showed 5-10 and 3-8 cm^{-1} shifts, respectively, from each original absorption band.

Oxetane formation was found to proceed more effectively in the solid state than in solution (Table 1), because of occurring the preferential photo [2+2] dimerization reaction of **1** or **4**[11] in solution from the NMR spectral analysis. Unknown compounds were found from NMR spectral analysis as complex mixture in the solid state which were presumed to be formed *via* valence isomerization or ketene formation of 2-pyrones.[13] The photoreaction of **1** with **2a** was effectively quenched by adding equimolar naphthalene (E_T = 61 kcal/mol) in the solid state using a UV cut filter under 350 nm (the ε values of **1**, **2a** and naphthalene at 350 nm in acetonitrile are 10, 170 and 0, respectively). Thus, the yield of **3a** decreased from 86% (in the absence of naphthalene) to 5% (in the presence of naphthalene) from the NMR analysis using pyrazine as an internal standard. Similar result was also obtained in the solution photoreaction. The oxetane formation was suggested to proceed *via* triplet excited state of **2a** from the above results.

Figure 2 shows the electron densities of the ground states of **1** ($^0S_1$) and **2a** ($^0S_2$), together with the triplet excited state of **2a** ($^1T_2$) by using MOPAC PM5 calculation. The formation of two types of biradicals (**A** and **B**) is estimated from the ground state and excited state interactions between **1** and **2a** concerning their electron densities (Figure 2). The biradical (**A**) is inferred to be more stable than the biradical (**B**) from the consideration about the resonance structures of the dihydro-2-pyrone ring. The regioselectivity of the oxetane formation is explained reasonably by considering the electrostatic interaction owing to the higher electron density at the carbonyl oxygen of **2a** ($^1T_2$) with the C6 of **1** ($^0S_1$) to give the biradical (**A**) and product (**3** or **5**), successively. These reactions are similar to the case of 2-pyrones with maleimide in the solid-state photoreaction concerning the electrostatic interaction.[7]



1 ($^0S_1$)　　**A**　　**B**

Figure 2 Electron density change of **2a** from the ground state ($^0S_2$) to the triplet state ($^1T_2$) and ground state electron density ($^0S_1$) of **1**

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10. X-Ray crystal data for **3a** ($C_{20}H_{18}O_4$): T = 296 K, Mo-Kα (Rigaku RAXIS-RAPID imaging plate diffractometer, λ = 0.71069 Å), crystal dimensions 0.18 x 0.82 x 0.12 mm^3 (a colorless needle), a = 10.508 (1), b = 15.146 (1), c = 10.871 (1) Å, β = 97.941(2) °, monoclinic, space group Cc (#9), Z = 4, $\mu_{MoK\alpha}$ = 0.87 cm^{-1}, Mr = 322.36, V = 1713.5 (3) Å^3, anode power 50KV x 32 mA, ρ_{calc} = 1.250 g/cm^3, $2\theta_{max}$ = 54.9°, F (000) = 680.00, 6582 reflections measured, 1885 observed (I > 0.00 σ (I), $2\theta < 54.95°$), number of parameters 217. The structure was solved by direct method and was refined on SIR 92.[14] The data/parameter ratio 8.69. R = 0.135, Rw = 0.113, GOF = 1.06, max/min residual density +0.43/- 0.42 eÅ^{-3}. All calculations were performed using the teXan crystallographic software package of Molecular Structure Corporation.
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12. All the new compounds gave the correct analytical and MS data. Selected spectral data are given below. **3b**: mp 45-46 ℃; ^{1}H NMR ($CDCl_3$) δ 1.64, 2.26, 2.36, 3.36 (each 3H, s), 4.08 (1H, s), 4.99 (1H, s), 7.21-7.31 (8H, m). IR (KBr) 1718 cm^{-1}. **3c** (1:1 mixture): ^{1}H NMR ($CDCl_3$) δ 1.63, 1.65 (each 3H, s), 3.32, 3.37 (each 3H, s), 3.75, 3.82 (each 3H, s), 4.09 (2H, s), 4.97, 5.02 (each 1H, s), 6.76, 6.97 (each 2H, d, J = 9.2 Hz), 7.2-7.4 (7H, m). IR (KBr) 1718 cm^{-1}. **3f** (1:1 mixture): ^{1}H NMR ($CDCl_3$) δ 1.65, 1.66 (each 3H, s), 3.37, 3.42 (each 3H, s), 4.04, 4.13 (each 1H, s), 5.01, 5.02 (each 1H, s), 7.26-7.46 (14H, m), 8.50, 8.68 (each 2H, d, J = 6.0 Hz). IR (KBr) 1720 cm^{-1}. **5a**: mp 75-78 ℃, ^{1}H NMR ($CDCl_3$) δ 1.64, 2.39 (each 3H, s), 4.19 (1H, s), 4.57, 4.59 (each 1H, d, J = 11.2 Hz), 5.13 (1H, s), 7.1-7.4 (14H, m). IR (KBr) 1720 cm^{-1}. **5b**: mp 34-36 ℃; ^{1}H NMR ($CDCl_3$) δ 1.63, 2.29, 2.34, 2.39 (each 3H, s), 4.11 (1H, s), 4.18, 4.58 (each 1H, d, J = 11.2 Hz), 5.12 (1H, s), 7.0-7.3 (12H, m). IR (KBr) 1710 cm^{-1}. **5c** (1:1 mixture): ^{1}H NMR ($CDCl_3$) δ 1.62, 1.64 (each 3H, s), 2.38 (6H, s), 3.76, 3.79 (each 3H, s), 4.12 (2H, s), 4.12 (2H, d, J = 11.2 Hz), 4.21 (2H, d, J = 11.2 Hz), 4.55, 4.60 (each 1H, s), 5.11, 5.15 (each 1H, s), 6.76 (2H, d, J = 8.8 Hz), 6.89 (2H, d, J = 8.8 Hz), 7.07-7.42 (11H, m). IR (KBr) 1710 cm^{-1}. **5f** (1:1 mixture): ^{1}H NMR ($CDCl_3$) δ 1.64, 1.65 (each 3H, s), 2.40, 2.42 (each 3H, s), 4.06, 4.15 (each 1H, s), 4.16, 4.62 (each 1H, d, J = 11.2 Hz), 5.15, 5.18 (each 1H, s), 7.09-7.42 (11H, m), 8.64, 8.66 (each 2H, d, J = 6.0 Hz). IR (KBr) 1718 cm^{-1}.
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