HETEROCYCLES, Vol. 53, No. 6, 2000, pp. 1329 - 1336, Received, 2nd March, 2000

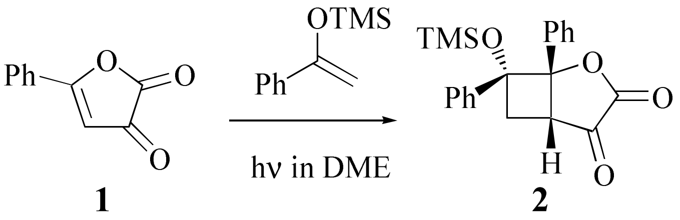
[2+2] PHOTOCYCLOADDITION REACTION OF 5-PHENYL-1*H*-FURAN- 2,3-DIONE TO PHENYLETHYLENE

Yoshie Horiguchi, Toshiaki Saitoh, Nobuyuki Koseki, Hideki Suzuki,
Jun Toda, and Takehiro Sano*

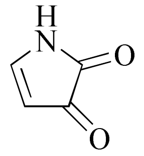
Showa Pharmaceutical University, 3-3165 Higashi-tamagawagakuen, Machida,
Tokyo 194-8543, Japan

Abstract - The photocycloaddition reaction of 5-phenylfuran-2,3-dione (**1**) to phenylethylene proceeded in a [2+2] manner with regio- and stereo-selectivities to give 2-oxabicyclo[3.2.0]heptane-3,4-diones with 7-*endo*-phenyl as a major adduct (**3**) and 7-*exo*-phenyl stereochemistries as a minor one (**4**). The reaction demonstrated that dioxofuran is a useful synthon for synthesis of substituted cyclobutane derivatives.

Recently we have demonstrated that [2+2] photocycloaddition reaction of 5-phenyl-1*H*-furan-2,3-dione (**1**) (5-Ph-dioxofuran) with 1-phenyl-1-trimethylsilyloxyethylene proceeded in a regio- and stereoselective manner to give the 7-*endo*-OTMS-7-*exo*-Ph-2-oxabicyclo[3.2.0]heptane-3,4-dione (**2**) as sole adduct in a high yield.[1] We also have disclosed by many examples[2] that 1-*H*-pyrrole-2,3-dione (dioxopyrroline), nitrogen analog of the dioxofuran, is an excellent olefin-acceptor on [2+2] photocycloaddition reaction. In this paper we describe photocycloaddition reaction of 5-Ph-dioxofuran with phenylethylene (styrene), demonstrating that the dioxofuran acts as an olefin-acceptor on photocycloaddition reaction.



Scheme 1

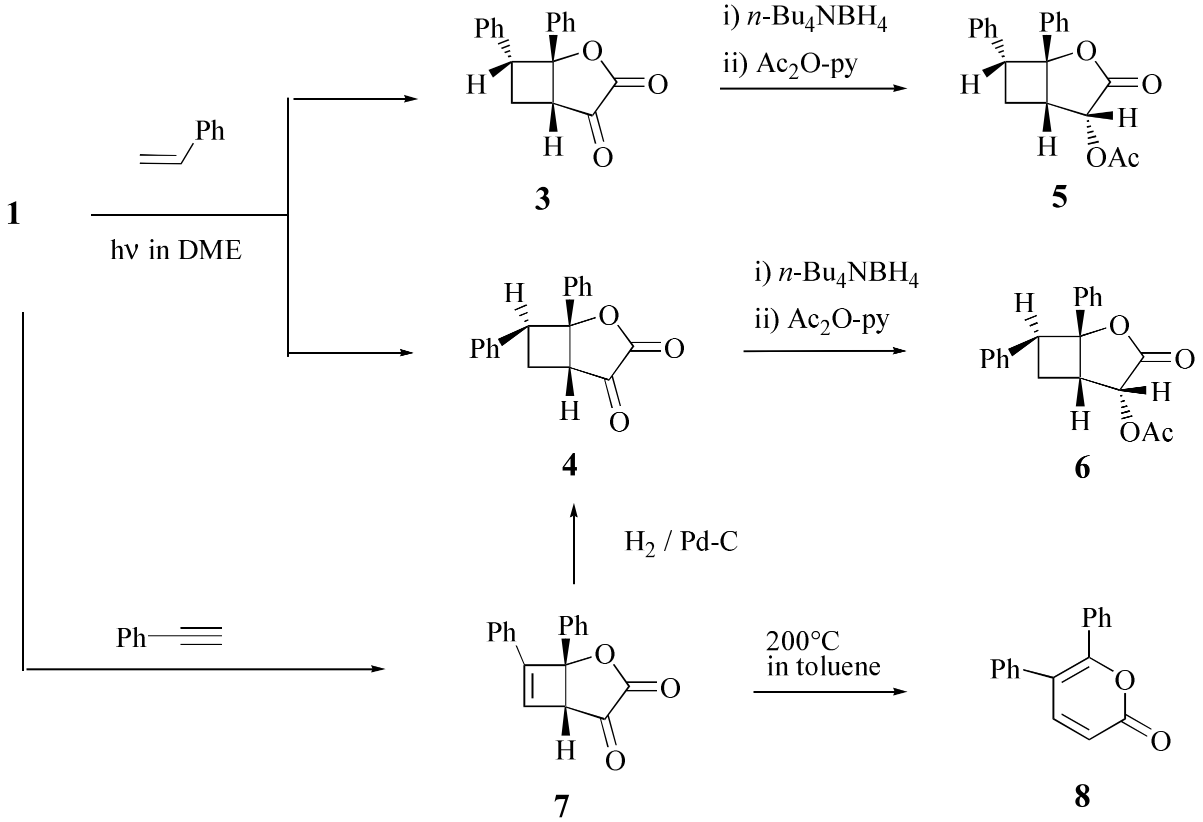


dioxopyrroline

Irradiation of a solution of **1** with styrene in dimethoxyethane (DME) with a high pressure Hg lamp (λ>300 nm light) for 25 min. at 0 °C caused [2+2] cycloaddition reaction to give two adducts (**3** and **4**) in 30% and 5% yields, respectively. Their analytical and spectral data indicated that they are cyclobutane derivatives with 2-oxabicyclo[3.2.0]heptane-3,4-dione ring system. The ^{1}H- and ^{13}C-NMR spectra revealed the presence of two methine and one methylene groups and the signals due to the methylene protons appeared as two sets of a clean triple doublet either in **3** or **4**, indicating that they have a same partial structure of -CH-CH$_2$-CH-. Thus, each adduct is concluded to be an isomer on the stereochemistry of the newly introduced chiral centers.

Some chemical evidences also supported the assigned structures as follows. Reduction of **3** and **4** with tetra-*n*-butylammonium borohydride followed by acetylation gave a monoacetate (**5** and **6**) as sole product, respectively. The high stereoselectivity in this reduction implied that the stereochemistry of the ring junction is *cis*, since the bulky reducing agent should exclusively approach from sterically less hindered convex face of the 2-oxabicyclo[3.2.0]heptane ring.[3]

Photocycloaddition of **1** to phenylacetylene under similar conditions gave a cyclobutene derivative (**7**), though in only 18 % yield. The cyclobutene (**7**) was hydrogenated on 5% Pd-C to give a dihydro derivative (20% yield) which was identical with the minor photoadduct (**4**).[4] Furthermore, heating of **7** in toluene at 200 °C caused a ring expansion reaction with a cheletropic loss of CO to give a pyrone derivative (**8**). The ^{1}H-NMR spectra of **8** were found to be identical with those of 5,6-diphenyl- 2*H*-pyran-2-one.[5]



Scheme 2

The stereochemistries of three chiral carbons at 1, 5, and 7 positions in the photoadducts were unambiguously determined by NMR spectral evidences. All protons and carbons of **3** including two phenyl groups at C_1 and C_7 were assigned by H-H correlation spectroscopy (COSY), C-H COSY and the high-resolution heteronuclear multiple bond correlation (HR-HMBC) analyses (Table 1). The HR-HMBC of **3** clearly revealed that the major adduct (**3**) has the skeletal structure as shown by the bold line depicted in Figure1. In the ^{1}H-NMR spectrum of **3** the signal of C_7-H (δ 4.13) appeared as a triple doublet with J=1, 9, and 10 Hz. This small coupling (1 Hz) which was observed at the signal of C_5-H (δ 3.79) and therefore should be attributable to the long range coupling between the C_5 and C_7 protons. The fact strongly suggested that those hydrogens are in *syn*-stereochemistry with a W type arrangement. The stereochemistry was finally established by difference nuclear Overhauser effect (DEF-NOE) of **3** in which irradiation of C_5-H signal caused a 9% increase of C_6-βH signal (δ 2.69) together with a 50% increase of 1-phenyl proton (δ 7.14-7.16), and then irradiation of the C_6-βH signal caused a 15% increase of the C_7-H signal. Thus, C_1-Ph, C_5-H and C_7-H of **3** are *cis* as depicted in Figure 1. Therefore, the structure of the major adduct (**3**) is unambiguously determined as 7-*endo*-phenyl-1-phenyl-2- oxabicyclo[3.2.0]heptane- 3,4-dione.

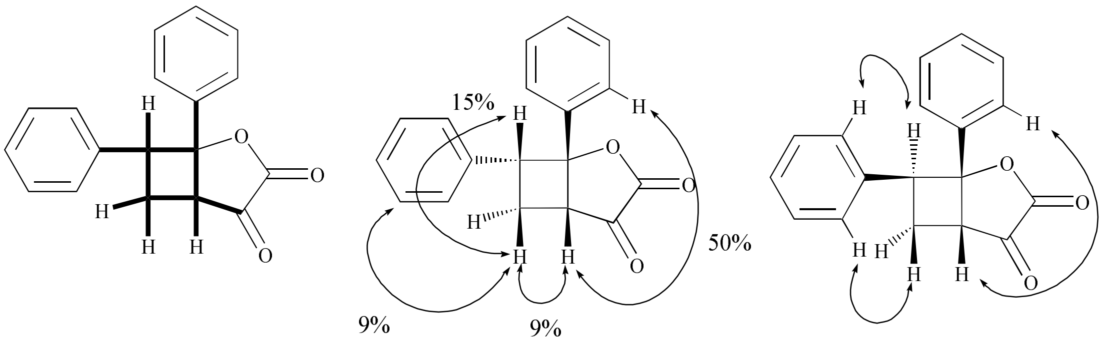
Table 1 ^{1}H- and ^{13}C-NMR Assignment of Photoadducts (**3** and **4**)

	7-*endo*-Ph (**3**)		7-*exo*-Ph (**4**)	
	^{1}H	^{13}C	^{1}H	^{13}C
position				
1		89.4		86.9
3		160.3		160.3
4		195.4		193.1
5	3.79 (ddd, *J*=1, 4, 11 Hz)	43.8	3.82 (dd, *J*=7, 10 Hz)	45.5
6		23.4		24.3
6a	2.96 (ddd, *J*=9, 11, 14 Hz)		3.05 (ddd, *J*=7, 10, 13 Hz)	
6b	2.66 (ddd, *J*=4, 10, 14 Hz)		2.63 (ddd, *J*=7, 10, 13 Hz)	
7	4.13 (ddd, *J*=1, 9, 10 Hz)	53.8	4.38 (dd, *J*=9.5, 10 Hz)	49.7
1-Ph				
1'		134.3		134.9
2', 6'	7.14-7.16 (m)	125.7	7.39-7.42 (m)	124.7
3', 5'	7.19-7.23* (m)	128.4	7.44-7.47 (m)	125.1
4'	7.19-7.23* (m)	128.8	7.39-7.42 (m)	128.4
7-Ph				
1"		136.5		138.6
2",6"	6.93-6.95 (m)	127.6	7.13-7.14 (m)	128.9
3", 5"	7.07-7.10 (m)	128.3	7.29-7.36* (m)	129.4
4"	7.11-7.14 (m)	127.3	7.29-7.36* (m)	127.9

*Overlapped signal

The structure of minor adduct (**4**) was determined by NMR spectra in which all protons and carbons were assigned by comparison with those of **3** as shown in Table 1. The 2D-nuclear Overhauser and exchange spectroscopy (NOESY) spectra indicated that C_1-Ph, C_5-H and C_5-Ph are in *cis*-arrangement, thus determining that the structure of **4** is 7-*exo*-phenyl-1-phenyl-2- oxabicyclo[3.2.0]heptane-3,4-dione, a stereoisomer of **3** concerning on the stereochemistry of C_7 phenyl group.

Figure 1 HR-HMBC and DFE-NOE of **3**, and NOESY of **4**



HR-HMBC of **3** DFE-NOE of **3** NOESY of **4**

In conclusion the photocycloaddition reaction of 5-phenylfuran-2,3-dione (**1**) to phenylethylene proceeded in a [2+2] manner with regio- and stereo-selectivities to give 7-*endo*-phenyl-1-phenyl-2-oxabicyclo[3.2.0]heptane-3,4-dione (**3**) as a major adduct and 7-*exo*-phenyl-stereoisomer (**4**) as a minor one. This result demonstrates that the dioxofuran takes play a role as an olefin-acceptor on photocycloaddition reaction just like the dixopyrroline does,[2] and as well the reaction provides a simple method for synthesis of functionalized cyclobutane derivatives.

EXPERIMENTAL

Unless otherwise stated, the following procedures were adopted. All melting points were measured on a Yanagimoto micro hot-stage melting point apparatus (Yanagimoto MP type) and are uncorrected. IR spectra were taken in Nujol mulls or KBr disks for solids and CH_2Cl_2 solution for gums with a Hitachi 260-10 spectrophotometer and values are given in cm^{-1}. UV spectra were measured with a Hitachi U-3200 spectrophotometer in dioxane and values are given in λ_{max} nm (ν). NMR spectra were recorded on a JEOL JNM-α500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) or a JNM-AL300 (^{1}H, 300 MHz; ^{13}C, 75 MHz) NMR spectrometer in $CDCl_3$ solution using tetramethylsilane (TMS) as an internal standard. The chemical shifts are given in δ values. HR-HMBC spectra were recorded on a JEOL JNM-α500 [Δ_2(delay time of pulse)=300 ms, J=1.7 Hz]. Low-resolution MS spectra (LRMS) and high-resolution MS spectra (HRMS) were determined on a JEOL JMS-HX110A or JMS-D300 spectrometer at 30 eV with a direct inlet system. Elemental analyses were recorded on a Yanaco CHN-corder MT-3. For column chromatography, silica gel (Mallinckrodt type 150A or Wako-Gel C-200) was used. Thin layer chromatography (TLC) was performed on Merck precoated Silica-Gel 60 F254 plates. The photolysis was done by internal irradiation using a 300

W high-pressure mercury lamp (Eikosha Halos PIH 300) with a Pyrex filter. 5-Ph-dioxofuran (**1**) was prepared according to the known procedure.[6]

Photocycloaddition of 1 with Styrene A solution of **1** (2.0 g, 11.5 mmol) and styrene (6.0 g 58 mmol) in DME (300 mL) was irradiated at 0 °C for 25 min. After removal of the solvent *in vacuo*, the residue in benzene was chromatographed over SiO_2. Elution with CH_2Cl_2-benzene (1:1) gave **3** (950 mg) and **4** (169 mg) in yield of 30% and 5%, respectively.

dl-(1*R**,5*S**,7*S**)-1,7-Diphenyl-2-oxabicyclo[3.2.0]heptane-3,4-dione (**3**): Colorless prisms crystallized from ethyl acetate-hexane, mp 153-154 °C. IR: 1790. HRMS *m/z* (M^+): Calcd for $C_{18}H_{14}O_3$: 278.0943. Found: 278.0948. *Anal.* Calcd for $C_{18}H_{14}O_3$ C; 77.68, H; 5.07. Found C; 77.45, H; 5.19.

dl-(1*R**,5*S**,7*R**)-1,7-Diphenyl-2-oxabicyclo[3.2.0]heptane-3,4-dione (**4**): Colorless needles crystallized from ethyl acetate-hexane, mp 147-149 °C. IR: 1790, 1775. HRMS *m/z* (M^+): Calcd for $C_{18}H_{14}O_3$: 278.0943. Found: 278.0941.

***n*-Bu$_4$NBH$_4$ Reduction of 3 and 4** *n*-Bu_4NBH_4 (50 mg, 0.195 mmol) was added to a solution of **3** or **4** (each 100 mg, 0.36 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The mixture was allowed to react at rt for 1 h under stirring and extracted with CH_2Cl_2. The extract was washed with H_2O, dried over $MgSO_4$, and evaporated *in vacuo*. The residue in pyridine (2 mL) was treated with acetic anhydride (1 mL) at room temperature for 12 h. The reaction mixture was extracted with CH_2Cl_2. The extract was washed with 5% HCl, 10% $NaHCO_3$, and H_2O, dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by column chromatography (benzene) to give **5** (87 mg, 75%) or **6** (82 mg, 70%).

dl-(1*R**,4*R**,5*S**,7*S**)-3-Acetoxy-1,7-diphenyl-2-oxabicyclo[3.2.0]heptan-3-one (**5**): Pale yellow gum. IR: 1785, 1750. ^{1}H-NMR: 2.25 (3H, s, $COCH_3$), 2.46 (1H, ddd, *J*=6, 10, 14 Hz, H-6), 2.65 (1H, ddd, *J*=7, 10, 14 Hz, H-6), 3.96-4.06 (2H, m, H-5 and 7), 5.62 (1H, d, *J*=8 Hz, H-4), 6.97-7.17 (10H, m, Ph). ^{13}C-NMR: 20.0 (C6), 20.5 ($OCO\underline{C}H_3$), 38.9 (C5), 51.4 (C7), 70.9 (C4), 91.2 (C1), 125.9-128.2 (10C, Ph), 135.5 (1C, Ph), 137.7 (Ph), 169.7 (C-3), 171.8 ($O\underline{C}OCH_3$). LRMS *m/z* : 322(M^+), 280 (M^+-42), 178 (base peak). *Anal.* Calcd for $C_{20}H_{18}O_4$ C; 74.52, H; 5.63. Found C; 74.34, H; 5.75.

dl-(1*R**,4*S**,5*S**,7*R**)-3-Acetoxy-1,7-diphenyl-2-oxabicyclo[3.2.0]heptan-3-one (**6**): Colorless prisms crystallized from ethyl acetate-hexane, mp 127-129 °C. IR: 1795, 1745. ^{1}H-NMR: 2.23 (3H, s, $COCH_3$), 2.52 (2H, dd, *J*=8, 10Hz, H-6), 3.73 (1H, q, *J*=8 Hz, H-5), 3.73 (1H, *J*=8 Hz, H-5), 4.12 (1H, t, *J*= 10 Hz, H-7), 5.57 (1H, d, *J*=8 Hz, H-4), 7.10-7.46 (10H, m, Ph). ^{13}C-NMR: 20.5 ($OCO\underline{C}H_3$), 21.3 (C6), 40.0 (C5), 48.9 (C7), 70.3 (C4), 89.5 (C1), 124.9-128.8 (10C, Ph), 135.7 (Ph), 139.0 (Ph), 169.7 (C3), 171.9 ($O\underline{C}OCH_3$). LRMS *m/z*: 322(M$^+$), 280 (M$^+$-42), 149 (base peak). *Anal*. Calcd for $C_{20}H_{18}O_4$ C; 74.52, H; 5.63. Found C; 74.38, H; 5.78.

Photocycloaddition of 1 with Phenylacetylene A mixture of **1** (3.0 g, 17.24 mmol) and phenylacetylene (5.1 g, 86 mmol) was irradiated at 0 °C for 25 min. After removal of the solvent *in vacuo*, the residue was purified by column chromatography (benzene) to give 1,7-diphenyl-2-oxabicyclo [3.2.0]heptan-6-ene-3,4-dione (**7**) (750 mg, 16%) as pale yellow needles crystallized from CH_2Cl_2-Et_2O, mp 164-166 °C. IR: 1800, 1775. ^{1}H-NMR: 3.78 (1H, d, *J*=1 Hz, H-5), 6.57 (1H, d, *J*=1 Hz, H-6), 7.35-7.48 (10 H, m, Ph). ^{13}C-NMR: 54.4 (C5), 85.2 (C1), 122.3 (C6), 125.1 (2C, Ph), 126.3 (2C, Ph), 128.8 (3C, Ph), 128.9 (Ph), 129.1 (2C, Ph), 130.2 (Ph), 134.5 (Ph), 154.5 (C7), 160.5 (C3), 189.9 (C4). HRMS *m/z* (M$^+$): Calcd for $C_{18}H_{12}O_3$: 276.0786. Found: 276.0811.

Pyrolysis of 7 A solution of **7** (35 mg) in dry toluene (10 mL) was heated at 200°C for 15 h in a sealed tube under Ar atmosphere. After evaporation of the solvent *in vacuo*, the residue was purified by column chromatography (AcOEt: hexane=1:3) to give **8** (12 mg, 39%) and starting material (**7**) (13 mg, 37 %). 5,6-diphenyl-2*H*-pyran-2-one (**8**): Pale yellow prisms crystallized from Et_2O-hexane, mp104-107 °C (lit.,[5] 98-102 °C). IR: 1735, 1629. UV: 231 (13,000), 333 (6400). ^{1}H-NMR: 6.37 (1H, d, *J*= 10 Hz), 7.16-7.37 (10 H, m, Ph), 7.46 (1H, d, *J*= 10 Hz). ^{13}C-NMR: 114.0 (C3), 117.8 (C5), 127.9 (C4’), 128.1 (C3’, C5’), 128.9 (C3”, C5”), 129.1 (C2’, C6’), 129.2 (C2”, C6”), 130.0 (C4”), 132.0 (C1’), 136.2 (C1”), 147.9 (C4), 158.1 (C6), 161.8 (C2). LRMS *m/z*: 248 (M$^+$)(base peak). HRMS *m/z* (M$^+$): Calcd for $C_{17}H_{12}O_2$: 248.0836. Found: 248.0836.

REFERENCES AND NOTES

1. T. Sano, N. Koseki, T. Saitoh, Y. Horiguchi, J. Toda, F. Kiuchi, and Y. Tsuda, *Chem. Pharm. Bull.*, 1997, **45**, 608.
2. T. Sano, Y. Horiguchi, Y. Tsuda, K. Furuhata, H. Takayanagi, and H. Ogura, *Chem. Pharm. Bull.*, 1987, **35**, 9; T. Sano, M. Hirose, Y. Horiguchi, H. Takayanagi, H. Ogura, and Y. Tsuda, *ibid*., 1987, **35**, 4730; T.

Sano, Y. Horiguchi, K. Imafuku, and Y. Tsuda, *ibid.*, 1990, **38**, 366; T. Sano, Y. Horiguchi, K. Imafuku, M. Hirose, H. Takayanagi, H. Ogura, and Y. Tsuda, *ibid.*, 1990, **38**, 370; T. Sano, Y. Horiguchi, F. Kiuchi, and Y. Tsuda, *ibid.*, 1993, **41**, 64; T. Sano, H. Enomoto, Y. Kurebayashi, Y. Horiguchi, and Y. Tsuda, *ibid.*, 1993, **41**, 471; T. Sano, H. Enomoto, K. Yasui, Y. Horiguchi, F. Kiuchi, and Y. Tsuda, *ibid.*, 1993, **41**, 846.

3. The configuration of 4-OAc was determined as *endo* on the basis of the steric compression effect (γ-effect) observed in their ^{13}C-NMR spectra. [γ-effect: A. P. Marchand,"Stereochemical Applications of NMR Studies in Rigid Bicyclic System," Verglag Chemie International Inc., Florida, 1982, p. 59.]
4. This stereochemical result suggested that the *exo*-side is sterically hindered by C_1-*exo*-Ph. The similar stereochemistry has been observed by the catalytic reduction of the nitrogen analog. [T. Sano, Y. Horiguchi, and Y. Tsuda, *Chem. Pharm. Bull.*, 1990, **38**, 3283.]
5. T. Dubuffet, B. Cimetiere, and G. Lavielle, *Synth. Commun.*, 1997, **27**, 1123.
6. T. Saitoh, T. Oyama, K. Sakurai, Y. Niimura, M. Hinata, Y. Horiguchi, J. Toda, and T. Sano, *Chem. Pharm. Bull.*, 1996, **44**, 956.