Exo-Selective formation of bicyclic oxetanes in the photocycloaddition reaction of carbonyl compounds with vinylene carbonate: the important role of intermediary triplet diradicals in the stereoselectivity

Manabu Abe,* Kana Taniguchi, and Takashi Hayashi

Department of Applied Chemistry, Graduate School of Engineering, Osaka University
(HANDAI), 2-1 Yamadaoka, Suita, Osaka 565-0871, Japan
E-mail: abe@chem.eng.osaka-u.ac.jp

Dedicated to Professor Waldemar Adam on the occasion of his 70th birthday

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Abstract

The photochemical [2+2] cycloaddition reaction, the Paternò-Büchi (PB) reaction, of carbonyl compounds **1a-d** with vinylene carbonate (**2**) was used to synthesize oxetanodioxolanones **3**. The reaction involves the exo-selective (exo/endo > 83/17) formation of the bicyclic oxetanes **3b-d**. Computational studies were performed to reveal the equilibrium structures of the intermediary triplet diradicals and their conformational distribution, which play an important role in determining the stereoselectivity of such PB reactions.

Keywords: Oxetanes, the Paternò-Büchi reaction, triplet diradicals, stereoelectronic effect

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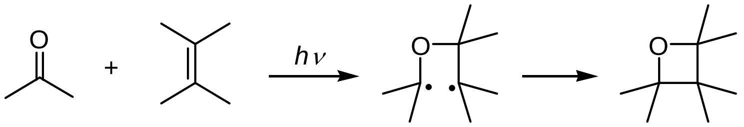
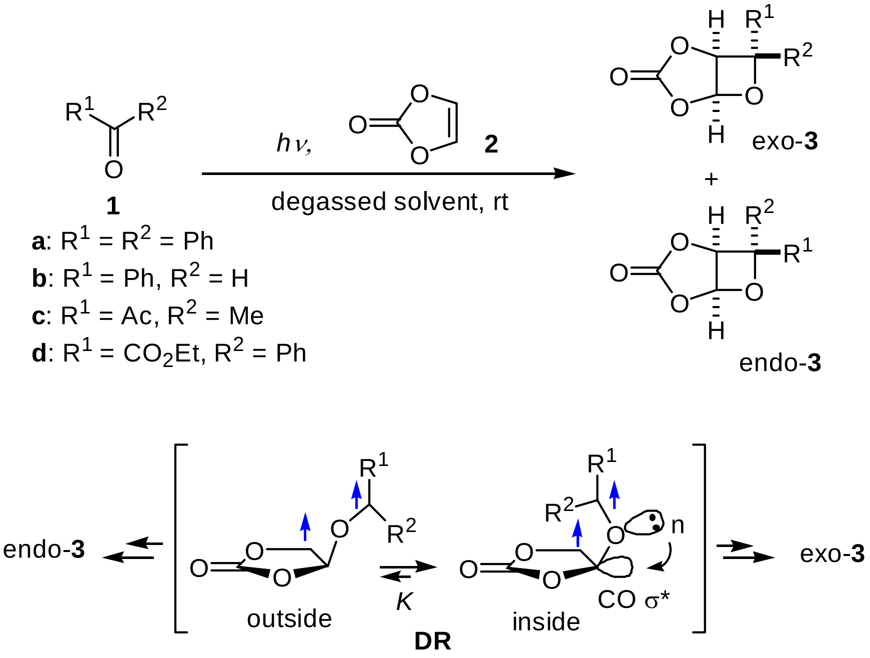
Introduction

Oxetanes, strained four-membered ethers, have attracted considerable attention, not only because of their biological activity, but also as synthetic intermediate.[1] Photochemical [2+2] cycloaddition reactions of carbonyl compounds with alkenes, the Paternò-Büchi (PB) reaction,[2] is a most promising method for preparing a wide variety of the synthetically useful strained compounds (eq. 1).

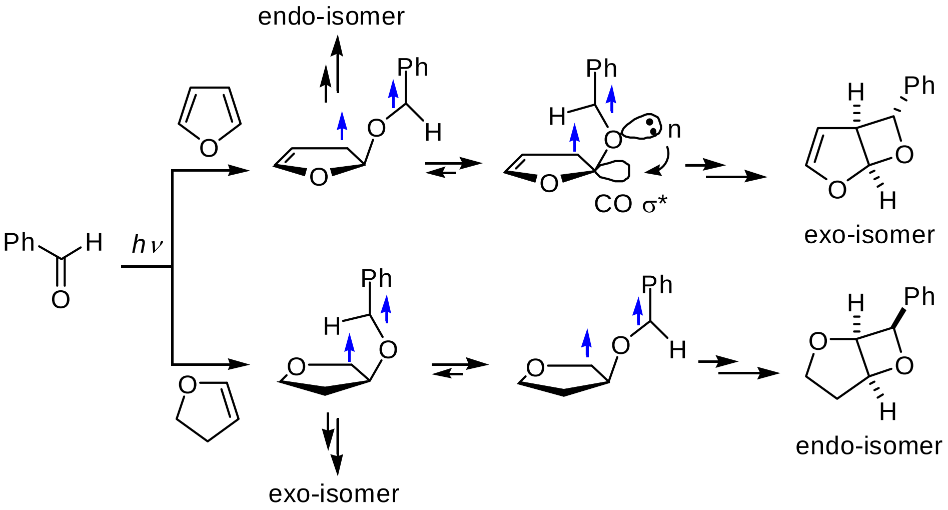


(1)

Over the past decade, mechanistic studies have provided reasonable models that permit to understand and predict the regio- and stereoselectivity of photochemical reactions. For example, we proposed recently a reasonable mechanism for the exo-selective formation of bicyclic oxetanes in PB reactions of benzaldehyde with furan derivatives (Scheme 1).[3] Thus, the stereoelectronic effect, i.e., the interaction of a lone-pair of electrons on the oxygen atom with the C-O σ* orbital, confers significant stability on the conformer that is the precursor of the exo-oxetane. The exo-selectivity is totally switched to endo-selectivity[4] in PB reactions with monocyclic alkenes such as dihydrofuran (Scheme 1). In the present study, we report on the PB reaction of carbonyl compounds **1** with vinylene carbonate (**2**) (Scheme 2)[5]. The conformational distributions of the intermediary triplet diradicals **DR**, K = [inside]/[outside], would be expected to be controlled by the stereoelectronic effect of the acetal moiety, which would lead to the selective formation of bicyclic oxetanes exo-**3**, $K > 1$. Informatively, Araki and coworkers reported that the exo-oxetane **3b** (R^1 = Ph, R^2 = H) was selectively formed as a by-product in the photoreaction of 1,3-bis(benzyloxy)-propan-2-one with vinylene carbonate (**2**).[6]



Scheme 1. Change in stereoselectivity, exo versus endo, in the Paternò-Büchi (PB) reaction of benzaldehyde with furan and dihydrofuran: notable stereoelectronic effect on the conformational distributions of the intermediary triplet 1,4-diradicals.



Scheme 2. Present study: the Paternò-Büchi reaction of vinylene carbonate (**2**)

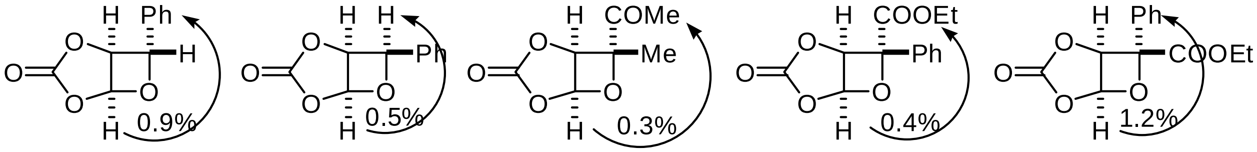
Results and Discussion

In an initial investigation, the reaction of benzophenone (**1a**) with vinylene carbonate (**2**) was performed in a degassed solvent under irradiation with a high-pressure Hg lamp (300 W) through a Pyrex filter (> 290 nm), to determine the optimal conditions for the synthesis of the bicyclic oxetane **3**. The results and the conditions used are summarized in Table 1. As shown in entries 1-3, the bicyclic oxetane **3a**[7] was obtained in good yields. To avoid the use of toxic benzene, we evaluated acetonitrile as a solvent for other photochemical reactions. Since the excess vinylene carbonate can be recovered by distillation under vacuum conditions (15 mmHg, 70 ^{o}C), 3 equivalents of vinylene carbonate was used in these reactions (entries 4-6). For the photochemical reaction of **1c**, a filter (hν > 320 nm) was used to avoid the photochemical decomposition of the bicyclic oxetane **3c**, which contains an acetyl moiety (entry 5). After careful spectroscopic analysis, including 600 MHz ^{1}H-NMR-NOE measurements, the highly exo-selective formation of the bicyclic oxetanes **3b-d** was confirmed in these relatively straightforward photochemical reactions (entries 4-6). The stereoselectivity, exo *versus* endo, was determined from the ^{1}H NMR peak areas, error ± 3%. The results of the NOE enhancement (%) measured for **3b-d** are summarized in Scheme 3, which allowed us to unequivocally determine the configuration of the oxetanes. To obtain information on the mechanism for the selective formation of exo-oxetanes, the potential energy surface (PES) around the dihedral angle θ (^{o}) was calculated for the triplet diradical **DRb** at the UB3LYP/6-31G(d)[8] level of theory with the GAUSSIAN 03 suite of programs[9] (Scheme 4). Among the possible conformers in **DRb**, only two conformers, inside (= *ca.* 60^{o}) and anti (= *ca.* 180^{o}), were calculated to be energy minimum structures. The outside conformer (θ = *ca.* 300^{o}) did not exist as an equilibrium structure.

Table 1. The Paterno-Buchi reaction of **1** with vinylene carbonate (**2**)[a]

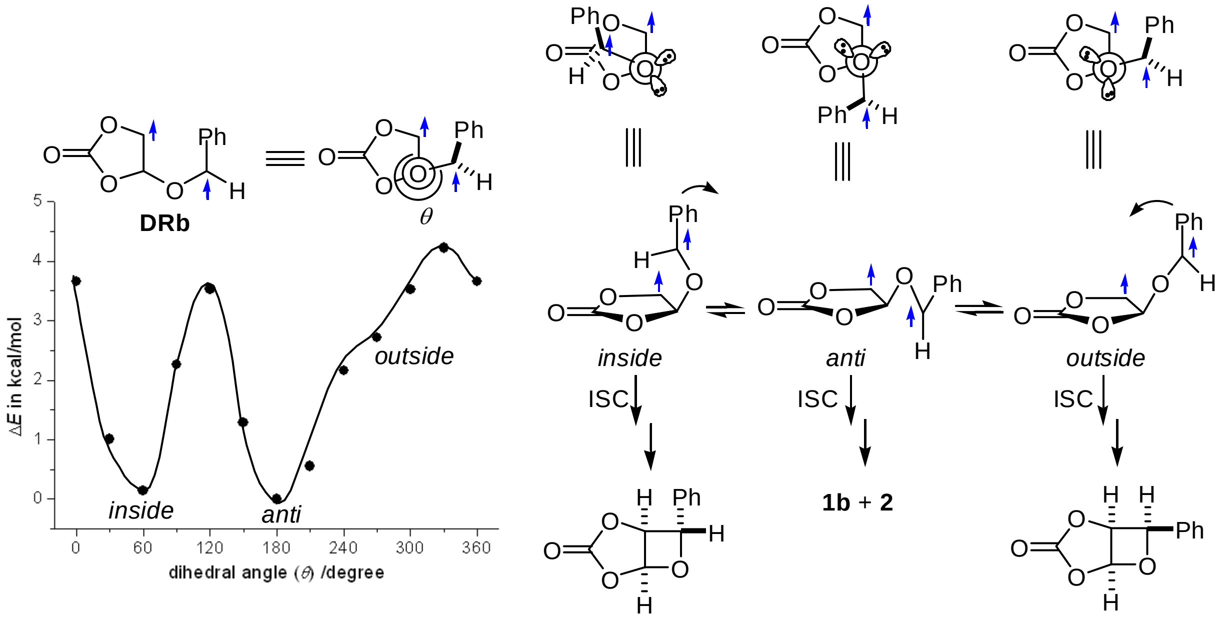
Entry	**1** (R^1, R^2)	Solvent	Equiv. of **2**	Time /h	Yield of **3**[b] (exo : endo)[c]
1	**1a** (Ph, Ph)	benzene	3 equiv.	32	**3a**: 85
2	**1a** (Ph, Ph)	benzene	1 equiv.	32	**3a**: 76
3	**1a** (Ph, Ph)	acetonitrile	3 equiv.	32	**3a**: 89
4	**1b** (Ph, H)	acetonitrile	3 equiv.	44	**3b**: 57 (91 : 9)
5[d]	**1c** (Ac, Me)	acetonitrile	3 equiv.	36	**3c**: 78 (> 97 : 3)
6	**1d** (COOEt, Ph)	acetonitrile	3 equiv.	18	**3d**: 23 (83 : 17)

[a] All photoreactions of **1** (0.3 M) were performed in a degassed solvent with a high pressure Hg lamp (300 W) through a Pyrex filter at ambient temperature (ca. 20 °C). [b] Isolated yields. [c] Determined by ^{1}H NMR peak areas. [d] The photoreaction was performed through a solution filter (> 320 nm).



exo-**3b** endo-**3b** exo-**3c** exo-**3d** endo-**3d**

Scheme 3. The configurational determination, NOE enhancements (%), of the bicyclic oxetanes prepared in this study.



exo-**3b** endo-**3b**

Scheme 4. Potential energy surface (PES) analysis around the dihedral angle (θ °) of the triplet diradical **DRb**. The energies, Δ*E* in kcal/mol, were relative to the most stable conformer.

The energetic preference for the inside and anti conformers can be reasonably explained by stereoelectronic effects, i.e. gauche effects,[10] on the conformational stability of the ketals. Thus, the orbital-overlap of the *n*-orbital of oxygen with the σ* orbital of the C-O bond in the ring are quite effective in the two conformers, inside and anti. However, the overlap is very poor in the conformer of the outside (Scheme 4). The phenyl-ring in the optimized structures of intermediary triplet diradical **DRb** is located perpendicular to the ring (Scheme 4). The energetic preference of the perpendicular orientation can be reasonably explained by orbital interactions between the 2p AO of oxygen and the radical p-orbital of the benzyl-radical moiety.[11] According to the memory effect[12], the inside conformer would be expected to give exo-**3b** by the *outward* rotation of the phenyl group; see the curved arrow in the inside conformer (Scheme 4).[13] The outside conformer may afford the endo-**3a** by the *inward* rotation of the phenyl group. The anti conformer would be reconverted to the starting compounds **1b** and **2** after the ISC process to the singlet states. The PES analyses (Scheme 4) clearly suggest that, among the productive conformers, only the inside conformer exists as an energy minimum structure. Thus, the selective formation of the exo-oxetane **3b** would be expected in the PB reactions. In fact, the highly exo-selective formation of the oxetanes **3** was observed (Table 1).

In summary, the exo-selective formation of bicyclic oxetane **3** occurs in the PB reaction of vinylene carbonate. The conformational distributions of the intermediary triplet 1,4-diradicals, which are controlled by stereoelectronic effects, play a crucial role in determining the stereoselectivity of the reaction. Thus, the energetic preference of the inside conformer in intermediary triplet diradicals is proposed to be responsible for the selective formation of exo-oxetanes **3b-d**.

Experimental Section

General Procedures. ^{1}H–NMR spectra (270 MHz) and ^{13}C–NMR spectra (67.8 MHz) were recorded on a JEOL EX 270 spectrometer. Chemical shifts (d) are given in ppm relative to the residual $CHCl_3$ (7.26 ppm) as the internal standard. Photolyses were performed by means of a high-pressure Hg lamp through a Pyrex filter (hν > 290 nm) or a cut-off filter (hν > 320 nm). Solvent, e.g. acetonitrile and benzene, was of spectroscopic grade.

Irradiation of carbonyl compounds 1 with vinylene carbonate (2). An argon-degassed solution of **1** (4 mmol) and **2** (12 mmol) in 12 ml of benzene or acetonitrile was irradiated through a Pyrex filter (hν > 290 nm), except for the reaction of **1c** (hν > 320 nm). After removing the solvent and excess vinylene carbonate, the products were separated by flash columm chromatography on silica gel (SiO_2, EtOAc/n-hexane).

7,7-Diphenyl-2,4,6-trioxabicyclo[3.2.0]heptan-3-one (3a). IR (KBr) : 1803, 1361, 1150, 1101, 926 cm^{-1}; ^{1}H-NMR (270 MH$_Z$, $CDCl_3$) δ 5.69 (d, 1 H, *J* = 3.8 Hz), 6.40 (d, 1 H, *J* = 3.8 Hz), 7.32-7.45 (m, 10 H); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 80.7 (d), 95.6 (s), 101.1 (d), 125.1 (2 x d), 125.9 (2 x d), 128.5 (4 x d), 128.8 (2 x d), 137.3 (s), 140.8 (s), 153.8 (s); HRMS (CI) Calcd for

$C_{16}H_{13}O_4$ 269.0814, found 269.0807; Anal.Calcd for $C_{16}H_{12}O_4$ C 71.64, H 4.51, found C 71.51, H 4.51.

***exo*-7-Phenyl-2,4,6-trioxabicyclo[3.2.0]heptan-3-one (exo-3b).** IR (KBr) :1813, 1361, 1160, 1092 cm^{-1}; ^{1}H-NMR (270 MH_Z, $CDCl_3$) δ 5.14 (dd, 1 H, *J* = 2.4 Hz 3.8 Hz), 5.84 (d, 1 H, *J* = 2.4 Hz), 6.47 (d, 1 H, *J* = 3.8 Hz), 7.39-7.51 (m, 5 H); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 80.1 (d), 90.6 (d), 102.7 (d), 125.4 (2 x d), 128.9 (2 x d), 129.4 (d), 135.5 (s), 154.3 (s); HRMS (EI) Calcd for $C_{10}H_8O_4$ 192.0423, found 192.0421; Anal.Calcd for $C_{10}H_8O_4$ C 62.50, H 4.20, found C 62.22, H 4.07.

***endo*-7-Phenyl-2,4,6-trioxabicyclo[3.2.0]heptan-3-one (endo-3b).** IR (KBr) :1809, 1160, 1106 cm^{-1}; ^{1}H-NMR (270 MH_Z, $CDCl_3$) δ 5.57 (dd, 1 H, *J* = 3.5 Hz, 4.3 Hz), 6.08 (d, 1 H, *J* = 4.3 Hz), 6.38 (d, 1 H, *J* = 3.5 Hz), 7.34-7.48 (m, 5 H); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 77.0 (d), 87.1 (d), 101.9 (d), 125.9 (2 x d), 128.9 (2 x d), 129.4 (d), 133.0 (s), 154.2 (s); HRMS (EI) Calcd for $C_{10}H_8O_4$ 192.0423, found 192.0426; Anal.Calcd for $C_{10}H_8O_4$ C 62.50, H 4.20, found C 62.50, H 4.33

***exo*-7-Acetyl-7-methyl-2,4,6-trioxa-bicyclo[3.2.0]heptan-3-one (exo-3c).** IR (KBr): 1851, 1715, 1368, 1152, 1094, 985, 769 cm^{-1}; ^{1}H-NMR (270 MH_Z, $CDCl_3$) δ 1.55 (s, 3 H), 2.32 (s, 3 H), 5.41 (d, 1 H, *J* = 3.8 Hz), 6.17 (d, 1 H, *J* = 3.5 Hz); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 17.9 (q), 23.8 (q), 77.8 (d), 94.0 (s), 100.7 (d), 154.1 (s), 206.1 (s); HRMS (CI) Calcd for $C_7H_9O_5$ 173.0450, found 173.0442; Anal.Calcd for $C_7H_8O_5$ C 48.84, H 4.68, found C 48.91, H 4.73.

Ethyl 3-oxo-7-phenyl-2,4,6-trioxabicyclo[3.2.0]heptane-7-carboxylate (exo-3d). IR (liquid film): 1829, 1737, 1273, 1141, 1061 cm^{-1}; ^{1}H-NMR (270 MH_Z, $CDCl_3$) δ 1.28 (t, 3 H, *J* = 7.0 Hz), 4.30 (q, 2 H, *J* = 7.0 Hz), 5.82 (d, 1 H, *J* = 3.8 Hz), 6.39 (d, 1 H, *J* = 3.5 Hz), 7.35-7.53 (m, 5 H); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 13.7 (q), 62.9 (t), 78.5 (d), 92.3 (s), 101.3 (d), 125.3 (2 x d), 128.7 (2 x d), 129.4 (d), 131.6 (s), 153.2 (s), 168.4 (s); HRMS (CI) Calcd for $C_{13}H_{13}O_6$ 265.0712, found 265.0706; Anal.Calcd for $C_{13}H_{12}O_6$ C 59.09, H 4.58, found C 59.08, H 4.65.

Ethyl 3-oxo-7-phenyl-2,4,6-trioxabicyclo[3.2.0]heptane-7-carboxylate (endo-3d). IR (KBr): 1819, 1740, 1142 cm^{-1}; ^{1}H-NMR (270 MH_Z,$CDCl_3$) δ 1.32 (t, 3 H, *J* = 7.2 Hz), 4.31 (q, 2 H, *J* = 7.2 Hz), 5.41 (d, 1 H, *J* = 3.8 Hz), 6.31 (d, 1 H, *J* = 3.2 Hz), 7.44-7.61 (m, 5 H); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 13.9 (q), 63.1 (t), 81.3 (d), 91.4 (s), 100.3 (d), 125.4 (2 x d), 128.8 (2 x d), 129.4 (d), 134.6 (s), 153.5 (s), 166.3 (s); HRMS (CI) Calcd for $C_{13}H_{13}O_6$ 265.0712, found 265.0713; Anal.Calcd for $C_{13}H_{12}O_6$ C 59.09, H 4.58, found C 59.18, H 4.74.

Computational method. Geometry optimizations were performed at the UB3LYP level of theory with the 6-31G(d) basis set. The geometries of stationary points were all located and vibrational analyses were performed with the Gaussian 03 suite of programs.

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