Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 47 (2006) 2527–2530
Tetrahedron Letters

Notable temperature effect on the stereoselectivity in the photochemical [2+2] cycloaddition reaction (Paternò–Büchi reaction) of 2,3-dihydrofuran-3-ol derivatives with benzophenone

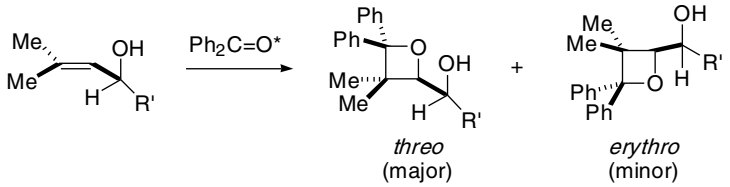
Manabu Abe,[a,*] Midori Terazawa,[a] Koichi Nozaki,[b] Araki Masuyama[a] and Takashi Hayashi[a]

[a]*Department of Applied Chemistry, Graduate School of Engineering, Osaka University (HANDAI), Suita 565-0871, Japan*
[b]*Department of Chemistry, Graduate School of Science, Osaka University, Toyonaka 560-0043, Osaka, Japan*

Received 12 January 2006; revised 6 February 2006; accepted 9 February 2006
Available online 28 February 2006

Abstract—A notable temperature effect (nonlinear Eyring plot) on stereoselectivity, trans-configured oxetane **2** versus cis-configured oxetane **2**, is reported in the photochemical [2+2] cycloaddition reaction (Paternò–Büchi reaction) of 2,3-dihydrofuran-3-ol derivatives **1** with benzophenone.

Like epoxides, oxetane derivatives are synthetically[1] and biologically[2] important because they possess a high strain-energy of 26 kcal/mol.[3] The photochemical [2+2] cycloaddition reaction of alkenes with carbonyl compounds, the so-called Paternò–Büchi reaction,[4] is a useful method for constructing the strained structures. However, the elucidation of the factors that control the regio- and stereoselectivity in oxetane formation remains a challenging subject.[5] Adam and co-workers recently reported on the hydroxy-directed diastereoselective formation of *threo*-oxetanes in the Paternò–Büchi reaction of acyclic allylic alcohols with benzophenone (Scheme 1).[6,7] They proposed that a hydrogen-bonded interaction[8] in exciplex is an important factor in controlling the stereoselectivity. They also found that the *threo* selectivity increases with increasing steric bulk of the substituent R′; *threo*/*erythro* = 90/10 (R′ = Me), 93/7 (R′ = Et), >95/5 (R′ = ^{t}Bu). The substituent effect clearly indicates that the steric bulk of the R′ substituent also plays an important role in controlling the diastereoselectivity of the reaction. In the present study, we selected cyclic allylic-alcohol derivatives (2,3-dihydrofuran-3-ols) **1** for the cycloaddition reaction and examined the effect of temperature on the stereoselectivity in the Paternò–Büchi reaction with benzophenone (Table 1 and Fig. 1). If hydroxy-directed diastereoselectivity applies to the cyclic system, the cis-selective formation of oxetanes **2** would be expected.

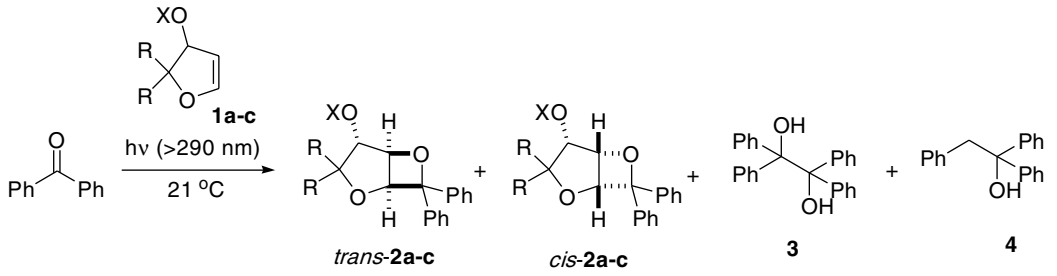


Scheme 1. The Paternò–Büchi reaction of acyclic allylic alcohols with benzophenone.

Keywords: The Paternò–Büchi reaction; Photochemical [2+2] cycloaddition; Stereoselectivity; Oxetane; Triplet diradical.
* Corresponding author. Tel./fax: +81 6 6879 7930; e-mail: abe@chem.eng.osaka-u.ac.jp

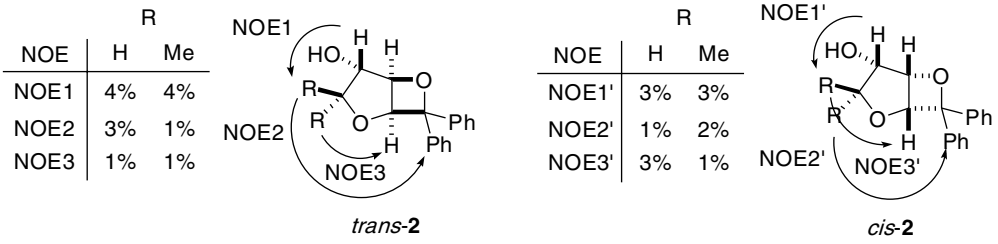
0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.02.046

Table 1. The Paternò–Büchi reaction of allylic-alcohol derivatives **1a–c** with benzophenone[a]



Entry	Substrate	X	R	Solvent	Yield of **2**[b] (%)	*trans*-**2**/*cis*-**2**[c]	Yield of **3**[b] (%)	Yield of **4**[b] (%)
1	**1a**	H	H	Toluene	78	53/47	12	6
2	**1a**	H	H	Methanol	40	96/4	30	—
3	**1b**	H	Me	Benzene	70	24/76	18	—
4	**1b**	H	Me	Toluene	57	24/76	28	14
5	**1b**	H	Me	Methanol	55	87/13	25	—
6	**1c**	TBDMS[d]	Me	Toluene	45	>97/3	36	Trace

[a] The photoreaction was conducted as follows: a degassed solution of **1** (0.11 M) and benzophenone (0.075 M) was irradiated for 3–4 h with a high-pressure Hg lamp (300 W) through a Pyrex filter. After removing the solvent, the product ratio, *trans*-**2**/*cis*-**2**, was directly determined by ^{1}H NMR (400 MHz) spectroscopic analysis.
[b] Isolated yield after column chromatography on silica gel.
[c] Determined by ^{1}H NMR (400 MHz) spectroscopic analysis, error ± 3%.
[d] TBDMS = *tert*-butyldimethylsilyl group.



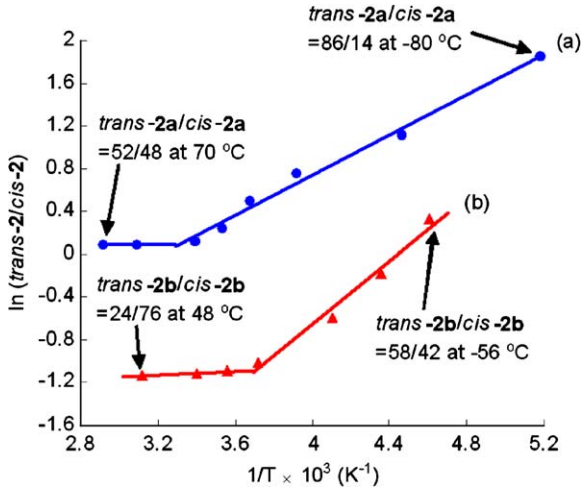


Figure 1. Eyring plots of the diastereoselectivity in the Paternò–Büchi reaction of benzophenone with (a) **1a** and (b) **1b** in toluene.

The allylic-alcohol derivatives **1a**,[9] **1b**,[10] and **1c**[10] were prepared according to reported methods. The Paternò–Büchi reaction of **1a** (0.11 M) with benzophenone (0.075 M) was first carried out using a high-pressure mercury lamp (300 W) through a Pyrex filter in degassed toluene or methanol at 21 °C (entries 1–2). After irradiation for 3–4 h at 21 °C, the stereoselectivity of the oxetanes **2a**,[11] *trans*-**2a**/*cis*-**2a**, was directly determined by ^{1}H NMR (400 MHz) spectroscopic analyses, error ± 3%. The configuration of the oxetanes **2** formed in the reaction was unequivocally determined by ^{1}H NMR (600 MHz) NOE measurements. The photoreaction in toluene gave approximately 1:1 mixture of the bicyclic oxetanes *trans*-**2a** and *cis*-**2a** together with ca. a 20% yield of side reaction products **3** and **4** (entry 1). In methanol, the trans-configured oxetane **2a** was selectively produced (entry 2). The photoreaction of **1b** with benzophenone was next performed under conditions similar to those described for the reaction of **1a** (entries 3–5). In aprotic solvents, the cis-configured oxetane **2b**[12] was obtained as the major product, *trans*-**2b**/*cis*-**2b** = 24/76 (entries 3–4). In contrast, the trans-isomer **2b** was selectively produced when the reaction was conducted in methanol (entry 5). When the silyl ether **1c** (TBDMS = *tert*-butyldimethylsilyl) was used in the photochemical reaction, the highly stereoselective formation of the trans-configured oxetane **2c**[13] was observed together with the formation of products **3** and **4** (entry 6). All the product ratios did not change after prolonged irradiation.

To obtain information concerning the mechanism for the stereoselectivity observed in oxetane formation, the

effect of temperature on the stereoselectivity was examined. As shown in Figure 1, the Eyring plots, ln(*trans*-**2**/*cis*-**2**) against $1/T$, were not linear for the formation of both **2a** and **2b**, in which the trans-selectivity, *trans*-**2**/*cis*-**2**, increased nonlinearly with decreasing reaction temperature. Thus, the trans-configured oxetanes **2a** and **2b** were the major isomers at low temperatures, for example, *trans*-**2a**/*cis*-**2a** = 86/14 at −80 °C and *trans*-**2b**/*cis*-**2b** = 58/42 at −56 °C were produced. The trans-selectivity observed in the formation of oxetanes **2a** and **2b** cannot be explained based on hydrogen-bonded interaction.[6] As judged by the high trans-selectivity found for the reaction in methanol and of silyl ether **1c** (entries 2 and 6), steric factors appear to play an important role in controlling the faceselectivity, at least at low temperatures. Thus, the hydroxyl group is sterically more bulky in protic solvents than that in aprotic solvents. The silyloxyl group is sterically more hindered than the hydroxyl group.

The nonlinear Eyring plots clearly suggest that oxetanes **2a** and **2b** are formed in a reaction that involves two or more steps.[14] To obtain information on the nature of the intermediates in the photochemical reactions, transient absorption spectra were obtained for the reaction with **1a** on a picosecond time scale (λ_{exc} = 355 nm, 20 ps pulse width, Fig. 2). In the absence of **1a**, the triplet state of benzophenone ($\tau > 1$ μs,[15] λ_{max} = 523 nm[16]) was observed within 20 ps after laser excitation in degassed acetonitrile. Upon the addition of a 4.4 M acetonitrile solution of **1a**, the triplet state of benzophenone (Fig. 2a) was quenched within 1 ns, generating a new species (Fig. 2b) with an absorption maximum at 535 nm. The transient species decayed with almost first-order kinetics (τ = ca. 1.8 ns, k_d = ca. 5.6×10^8 s^{-1}) at 25 °C. The absorption spectrum of the new species is similar to that of the triplet diradical (λ_{max} = 535 nm, τ = 1.5 ns in acetonitrile)[17] reported for the photoreaction of 1,4-dioxene with benzophenone. Thus, it is reasonable to conclude that the new species are the triplet diradicals *trans*- and *cis*-^{3}**DR** as shown in Scheme 2.

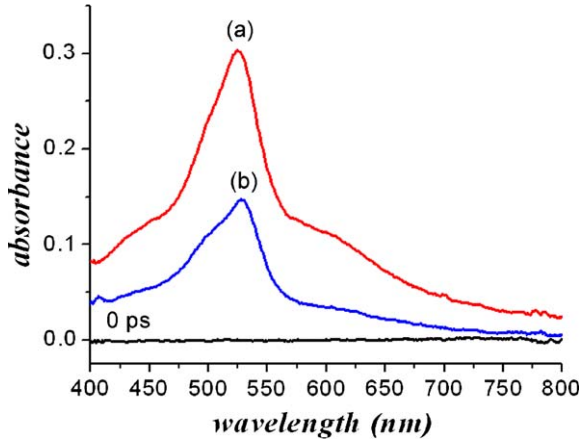
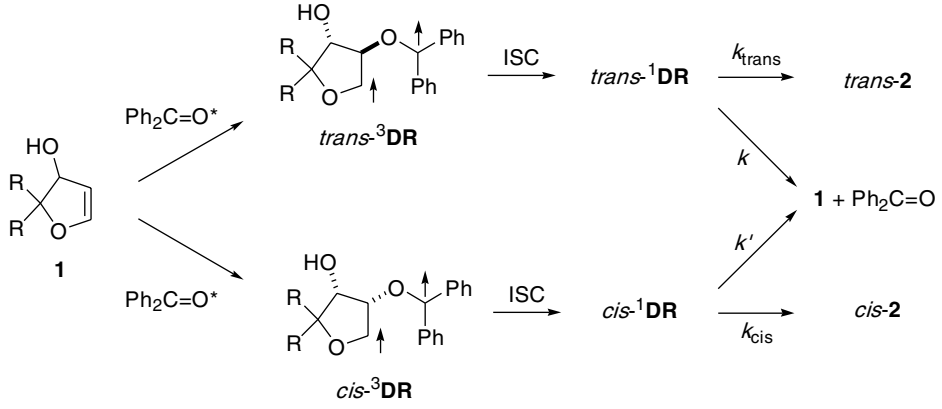


Figure 2. Transient absorption spectra of (a) triplet benzophenone and (b) triplet 1,4-diradicals formed during the irradiation of 4.4 M 2,3-dihydrofuran-3-ol (**1a**) with 0.02 M benzophenone in acetonitrile at 1 ns.

A plausible mechanism for the photochemical reaction is shown in Scheme 2. There are two steps that determine the stereoselectivity of the reaction: (1) the initial faceselectivity by triplet benzophenone, that is, [*trans*-^{3}**DR**] versus [*cis*-^{3}**DR**], and (2) the ratio of the relative rate constant of the bond-forming and bond-breaking step from the singlet 1,4-diradicals *trans*-^{1}**DR** and *cis*-^{1}**DR**, that is, k_{trans}/k versus k_{cis}/k'.[5b] Although the conclusive elucidation of the nonlinearity of the Eyring plots is currently under investigation, hydrogen-bonded interactions between the allylic alcohol and the triplet-excited carbonyl compound seems to be not the major factor in controlling the stereoselectivity in the formation of the oxetanes **2a**,**b**. Thus, the 'hydroxy-directed diastereoselectivity'[6] cannot simply apply to the case of the Paternò–Büchi reaction of cyclic allylic alcohols.

In summary, a notable temperature effect on the stereoselectivity in the Paternò–Büchi reaction of 2,3-dihydrofuran-3-ol derivatives **1** with benzophenone is found in this study. The remarkable finding should stimulate future studies on the mechanistically and synthetically fascinating stereoselectivity in Paternò–Büchi reactions of allylic alcohols.



Scheme 2. A plausible mechanism for the formation of oxetane **2** in the Paternò–Büchi reaction of **1** with benzophenone.

Acknowledgements

This work was partially supported by the Ministry of Education, Science, Sports, and Culture, Japan, Grant-in-Aid for Scientific Research (B), No. 17350019, and Mitsubishi Chemical Corporation Fund.

References and notes

1. (a) Schreiber, S. L.; Hoveyda, A. H.; Wu, H. *J. Am. Chem. Soc.* **1983**, *105*, 660; (b) Carless, H. A. J. In *Synthetic Organic Photochemistry*; Horspool, W. M., Ed.; Plenum Press: New York, 1984; p 425; (c) Porca, J. A.; Schreiber, S. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 5, p 168; (d) Griesbeck, A. G. In *Organic Photochemistry and Photobiology*; Horspool, W. M., Song, P., Eds.; CRC Press: New York, 1995; p 522, and 550; (e) Bach, T. *Liebigs Ann./Recueil* **1997**, 1627; (f) Bach, T. *Synthesis* **1998**, 683.
2. (a) Norbeck, D. W.; Kramer, J. B. *J. Am. Chem. Soc.* **1988**, *110*, 7217; (b) Huang, J.-M.; Yokokawa, R.; Yang, C.-S.; Fukuyama, Y. *Tetrahedron Lett.* **2000**, *41*, 6111.
3. Libmann, J. F.; Greenberg, A. *Chem. Rev.* **1976**, *76*, 311.
4. (a) Paternó, E.; Chieffi, G. *Gazz. Chim. Ital.* **1909**, *39*, 341; (b) Büchi, G.; Inman, C. G.; Lipinsky, E. S. *J. Am. Chem. Soc.* **1954**, *76*, 4327; (c) Arnold, D. R.; Hinman, R. L.; Glick, A. H. *Tetrahedron Lett.* **1964**, *5*, 1425; (d) Yang, N. C.; Nussim, M.; Jorgenson, M. J.; Murov, S. *Tetrahedron Lett.* **1964**, *5*, 3657.
5. (a) Griesbeck, A. G.; Mauder, H.; Stadtmüller, S. *Acc. Chem. Res.* **1994**, *27*, 70; (b) Abe, M.; Kawankami, T.; Ohata, S.; Nozaki, K.; Nojima, M. *J. Am. Chem. Soc.* **2004**, *126*, 2838; (c) Griesbeck, A. G.; Abe, M.; Bondock, S. *Acc. Chem. Res.* **2004**, *37*, 919; (d) Hei, X. M.; Song, Q. H.; Li, X. B. *J. Org. Chem.* **2004**, *70*, 2522.
6. (a) Adam, W.; Peters, K.; Peters, E. M.; Stegmann, V. R. *J. Am. Chem. Soc.* **2000**, *122*, 2958; (b) Adam, W.; Stegmann, V. R. *Synthesis* **2001**, 1203.
7. Griesbeck, A. G.; Bondock, S. *J. Am. Chem. Soc.* **2001**, *123*, 6191.
8. For the concept of hydrogen-bonding as a tool for directing photochemical reactions, see: (a) Yokoyama, A.; Mizuno, K. *Org. Lett.* **2000**, *2*, 3457; (b) Bach, T.; Bergmann, H.; Harms, K. *J. Am. Chem. Soc.* **1999**, *121*, 10650; (c) Sieburth, S. McN; McGee, K. F., Jr. *Org. Lett.* **1999**, *1*, 1775; (d) Sydnes, L. K.; Hansen, K. I.; Oldroyd, D. L.; Weedon, A. C.; Jorgensen, E. *Acta Chem. Scan.* **1993**, *47*, 916; (e) D'Auria, M.; Racioppi, R.; Romaniello, G. *Eur. J. Org. Chem.* **2000**, 3265.
9. (a) Cohen, N.; Banner, B. L.; Laurenzano, A. J.; Carozza, L. *Org. Synth. Collect.* **1990**, *Vol. 7*, 297; (b) Cohen, N.; Banner, B. L.; Lopresti, R. J.; Wong, F.; Rosenberger, M.; Liu, Y.; Thom, E.; Liebman, A. A. *J. Am. Chem. Soc.* **1983**, *105*, 3661; (c) Ireland, R. E.; Wilcox, C. S.; Thaisrivongs, S. *J. Org. Chem.* **1978**, *43*, 786.
10. Pirrung, M. C.; Lee, Y. R. *J. Am. Chem. Soc.* **1995**, *117*, 4814.
11. Spectroscopic data for new compound **2a**. *trans-4-Hydroxy-7,7-diphenyl-2,6-oxabicyclo[3.2.0]heptane* (*trans*-**2a**): ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.61 (br s, O*H*), 3.71 (dd, $J = 10.5$, 3.2 Hz, 1H), 3.88 (d, $J = 10.5$ Hz, 1H), 4.39 (m, 1H), 5.17 (d, $J = 3.5$ Hz, 1H), 5.22 (d, $J = 3.5$ Hz, 1H), 7.22–7.53 (m, 10H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 73.8 (d), 75.4 (t), 84.4 (d), 86.0 (d), 92.4 (s), 124.7 (d), 124.8 (d), 126.9 (d), 127.3 (d), 127.9 (d), 128.4 (d), 141.0 (s), 144.2 (s); IR (neat): $\nu = 3420$, 3058, 2949, 1494, 1447, 1096 cm^{-1}; HRMS (M^+) *m*/*z* calcd for $C_{17}H_{16}O_3$: 268.1099. Found: 268.1095. *cis-4-Hydroxy-7,7-diphenyl-2,6-oxabicyclo[3.2.0]heptane* (*cis*-**2a**): ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.24 (d, $J = 10.8$ Hz, O*H*), 3.02 (t, $J = 9.0$ Hz, 1H), 3.94 (dd, $J = 9.0$, 7.2 Hz, 1H), 4.24 (m, 1H), 4.99 (d, $J = 4.2$ Hz, 1H), 5.10 (t, $J = 4.2$ Hz, 1H), 7.18 (m, 3H), 7.28 (t, $J = 7.2$ Hz, 3H), 7.38 (m, 2H), 7.45 (m, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 71.1 (d), 71.8 (t), 80.5 (d), 84.1 (d), 92.4 (s), 124.6 (d × 2), 127.1 (d), 127.4 (d), 128.2 (d), 128.6 (d), 140.4 (s), 144.2 (s); IR (KBr): $\nu = 3518$, 2984, 2952, 1103, 1082 cm^{-1}; HRMS (M^+) *m*/*z* calcd for $C_{17}H_{16}O_3$: 268.1099. Found: 268.1101.
12. Spectroscopic data for new compound **2b**. *trans-4-Hydroxy-3,3-dimethyl-7,7-diphenyl-2,6-dioxabicyclo-[3.2.0]heptane* (*trans*-**2b**): ^{1}H NMR (270 MHz, C_6D_6): δ 0.89 (br s, 1H), 1.01 (s, 3H), 1.08 (s, 3H), 3.84 (br s, 1H), 4.82 (dd, $J = 4.3$, 1.4 Hz, 1H), 4.96 (d, $J = 4.3$ Hz, 1H), 6.97–7.02 (m, 2H), 7.09–7.15 (m, 4H), 7.53–7.56 (m, 4H); ^{13}C NMR (67.8 MHz, C_6D_6): δ 23.3 (q), 27.0 (q), 82.0 (d), 84.1 (d), 88.2 (s), 88.9 (d), 91.3 (s), 125.4 (d), 126.5 (d), 126.9 (d), 127.2 (d), 127.8 (d), 128.7 (d), 142.6 (s), 145.4 (s); IR (KBr): $\nu = 3424$, 2984, 2939, 1451, 1114 cm^{-1}; HRMS (M^+) *m*/*z* calcd for $C_{19}H_{20}O_3$: 296.1412. Found: 296.1417. Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.75; H, 6.77. *cis-4-Hydroxy-3,3-dimethyl-7,7-diphenyl-2,6-dioxabicyclo-[3.2.0]heptane* (*cis*-**2b**): ^{1}H NMR (270 MHz, C_6D_6): δ 0.82 (s, 3H), 1.09 (s, 3H), 3.06 (d, $J = 9.2$ Hz, 1H), 3.53 (dd, $J = 9.2$, 5.9 Hz, 1H), 4.64 (d, $J = 4.3$ Hz, 1H), 4.81 (dd, $J = 5.9$, 4.3 Hz, 1H), 6.94–7.02 (m, 2H), 7.08–7.13 (m, 4H), 7.39–7.51 (m, 4H); ^{13}C NMR (67.8 MHz, C_6D_6): δ 22.2 (q), 26.9 (q), 76.9 (d), 82.1 (d), 82.6 (d), 88.2 (s), 91.7 (s), 125.2 (d), 125.9 (d), 127.2 (d), 127.4 (d), 128.1 (d), 128.7 (d), 142.0 (s), 145.0 (s); IR (KBr): $\nu = 3487$, 3061, 2966, 1451, 1397, 1106, 1065 cm^{-1}; HRMS (M^+) *m*/*z* calcd for $C_{19}H_{20}O_3$: 296.1412. Found: 296.1419. Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.95; H, 6.73.
13. Spectroscopic data for new compound **2c**. *trans-4-(tert-Butyl)dimethysiloxy-3,3-dimethyl-7,7-diphenyl-2,6-dioxabicyclo[3.2.0]heptane* (*trans*-**2c**): ^{1}H NMR (600 MHz, C_6D_6): δ 0.01 (s, 3H), 0.09 (s, 3H), 0.90 (s, 9H), 1.09 (s, 3H), 1.13 (s, 3H), 4.22 (d, $J = 1.8$ Hz, 1H), 4.94 (dd, $J = 4.8$, 1.8 Hz, 1H), 5.04 (d, $J = 4.8$ Hz, 1H), 6.98–7.02 (m, 2H), 7.08–7.18 (m, 4H), 7.54–7.60 (m, 4H); ^{13}C NMR (67.8 MHz, C_6D_6): δ −5.2 (q), −4.7 (q), 18.1 (s), 23.3 (q), 25.9 (q × 3), 26.7 (q), 83.3 (d), 84.2 (d), 87.8 (d), 88.9 (s), 91.0 (s), 125.5 (d), 126.6 (d), 126.9 (d), 127.2 (d), 127.8 (d), 128.6 (d), 142.6 (s), 145.5 (s); IR (KBr): $\nu = 3430$, 2952, 2861, 1470, 1254, 1106 cm^{-1}; HRMS (M^+) *m*/*z* calcd for $C_{25}H_{34}O_3Si$: 410.2277. Found: 410.2266.
14. (a) Bushmann, H.; Scharf, D. N.; Hoffmann, N. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 47; (b) Göbel, T.; Scharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1329; (c) Hale, K. J.; Ridd, J. H. *J. Chem. Soc., Chem. Commun.* **1995**, 357; (d) Gypser, A.; Norrby, P.-O. *J. Chem. Soc., Perkin Trans. 2* **1997**, 939.
15. Poter, G.; Wilkinson, F. *Trans. Faraday Soc.* **1962**, *58*, 1686.
16. Green, B. I.; Hockstrasser, R. M.; Weisman, R. *J. Chem. Phys.* **1979**, *70*, 1247.
17. (a) Freilich, S. C.; Peters, K. S. *J. Am. Chem. Soc.* **1981**, *103*, 6255; (b) Freilich, S. C.; Peters, K. S. *J. Am. Chem. Soc.* **1985**, *107*, 3819.