JOC Article

(2,5)-Ene Cyclization Catalyzed by Mesoporous Solid Acids: Isotope Labeling Study and ab Initio Calculation for Continuum from Concerted to Stepwise Ene Mechanism

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(2,5)-Ene reactions catalyzed by mesoporous solid acids are reported from the mechanistic point of view. The continuum (2,5)-ene mechanism from the concerted to the cationic cyclization followed by 1,2-hydride shift is evaluated. The solid-acid-catalyzed cyclization of the oxonium ion intermediate **4** derived from cyclic allylic lactol ether **3** bearing allylic hydroxy group affords the (2,5)-ene product as the enol form, eventually tautomerizing to the corresponding aldehyde **6**. The continuum from the concerted to stepwise mechanism is experimentally and theoretically verified in the present ene cyclization of the oxonium ion intermediate such as **4**. The stepwise cyclization leading to aldehyde **6** is thus shown to associate with the concerted version as a result of the stabilization of the β-hydroxycarbenium ion intermediate.

Introduction

Intramolecular ene reactions are a powerful tool for carbocyclization and hence receive much attention from synthetic and mechanistic viewpoints.[1,2] Conceptually, ene cyclizations are classified into six different types of cyclization, since ene and enophile moieties can be connected at three and two different positions, respectively (Figure 1). The positions, where the shortest tether connecting the 1,5-hydrogen shift system is attached, are expressed in (*m*,*n*) fashion.[3−5] The ring size may be shown in numerical prefix l-.[6] Among these types, the (2,5)-ene cyclization had never been reported.

Recently, we reported the first example of (2,5)-ene cyclization[7] involving the oxonium ion as an enophile[8] in the presence of mesoporous solid acids such as montmorillonite K10 and Amberlyst 15E[9−11] (Scheme 1). However, (2,5)-ene product **2** isomerized under the reaction conditions. Therefore, it was planned to trap the (2,5)-ene product as an enol form, so that the (2,5)-ene product

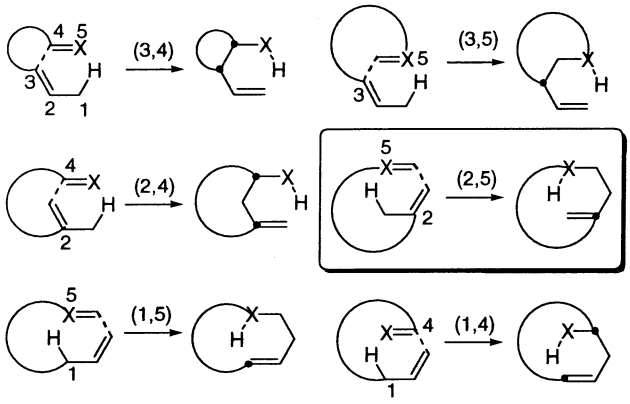

FIGURE 1. Classification of the intramolecular ene cyclization

(1) Comprehensive reviews on ene reactions: (a) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556. (b) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426. (c) Snider, B. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, p 1 and Vol. 2, p 527. (d) Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021.

(2) Comprehensive reviews on intramolecular ene reactions (ene cyclizations): (a) Conia, J. M.; Le Perchec, P. *Synthesis* **1975**, 1. (b) Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476. (c) Taber, D. F. *Intramolecular Diels−Alder and Alder Ene Reactions*; Springer-Verlag: Berlin, 1984.

(3) For l-(*m*,*n*) terminology of ene cyclization, see the review Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021.

(4) Account on l-(*m*,*n*) ene cyclization: Sarkar, T. K. *J. Indian Inst. Sci.* **1994**, *74*, 329.

(5) l-(*m*,*n*) Ene cyclization: (a) Mikami, K.; Sawa, E.; Terada, M. *Tetrahedron: Asymmetry* **1991**, *2*, 1403. (b) Mikami, K.; Osawa, A.; Isaka, A.; Sawa, E.; Shimizu, M.; Terada, M.; Kubodera, N.; Nakagawa, K.; Tsugawa, N.; Okano, T. *Tetrahedron Lett.* **1998**, *39*, 3359. (c) Okano, T.; Nakagawa, K.; Kubodera, N.; Ozono, K.; Isaka, A.; Osawa, A.; Terada, M.; Mikami, K. *Chem. Biol.* **2000**, *7*, 173. (e) Sarkar, T. K.; Ghorai, B. K.; Nandy, S. K.; Mukherjee, B.; Banerji, A. *J. Org. Chem.* **1997**, *62*, 6006. (f) Noguchi, M.; Mizukoshi, T.; Nishimura, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2201. (g) Loh, T.-P.; Hu, Q.-Y.; Tan, K.-T.; Cheng, H.-S. *Org. Lett.* **2001**, *3*, 2669.

(6) Also see the numerical prefix in Baldwin's rule: Baldwin, J. E. *Chem. Commun.* **1976**, 734.

(7) Ohmura, H.; Smyth, G. D.; Mikami, K. *J. Org. Chem.* **1999**, *64*, 6056.

(8) Ene reaction using oxonium ion as an enophile: (a) Overman, L. E.; Thompson, A. S. *J. Am. Chem. Soc.* **1988**, *110*, 2248. (b) Blumenkopf, T. A.; Bratz, M.; Castaneda, A.; Look, G. C.; Overman, L. E.; Rodriguez, D.; Thompson, A. S. *J. Am. Chem. Soc.* **1990**, *112*, 4386. (c) Blumenkopf, T. A.; Look, G. C.; Overman, L. E. *J. Am. Chem. Soc.* **1990**, *112*, 4399. (d) Mikami, K.; Kishino, H. *J. Chem. Soc., Chem. Commun.* **1993**, 1843. (e) Sonawane, H. R.; Maji, D. K.; Jana, G. H.; Pandey, G. *Chem. Commun.* **1998**, 1773.

(9) (a) In porphyrin synthesis, the cyclization is efficiently catalyzed in the mesopore of clay: Onaka, M.; Shinoda, T.; Izumi, Y.; Nolen, E. *Chem. Lett.* **1993**, 117. (b) Shinoda, T.; Onaka, M.; Izumi, Y. *Chem. Lett.* **1995**, 493; 495. (c) Izumi, Y.; Urabe, K.; Onaka, M. *Microporous Mesoporous Mater.* **1998**, *21*, 227.

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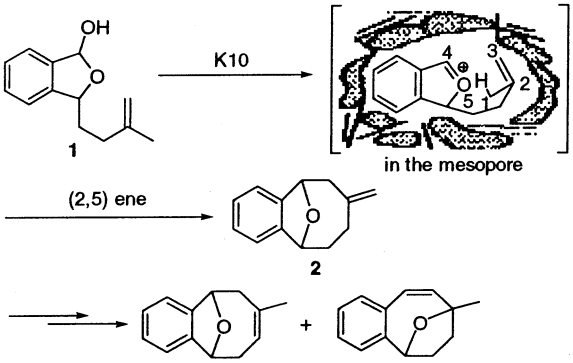
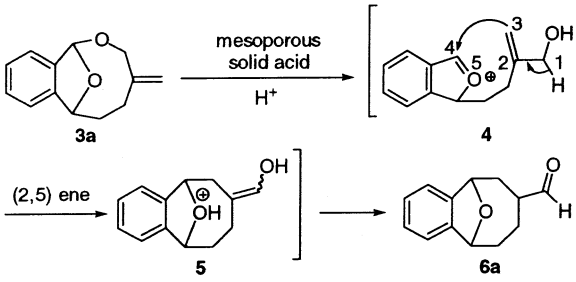
SCHEME 1



SCHEME 2



would be transformed to the corresponding aldehyde and, consequently, regioisomerization would be terminated. Therefore, cyclic allylic lactol ether **3** was selected as a substrate (Scheme 2).[12]

Results and Discussion

Preparation of Cyclic Allylic Lactol Ether 3. The preparation of cyclic ether **3a** is shown in Scheme 3. Homoallylic bromide **9** was prepared via regiospecific formaldehyde-ene reaction of methallyl ether **7**[13] followed by bromination. Bromide **9** was converted to the Grignard reagent, which was treated with the lithium salt of *o*-phthalaldehydic acid to give lactone **10**. Lactone **10** was reduced to lactol **11a** and then desilylated to give diol **12**. Finally, diol **12** was treated with TsOH to give the cyclic allylic lactol ether **3a** without any O → C rearranged product **6a**.

(2,5) Ene Cyclization. The key reaction of the cyclic ether **3a** was then examined in the presence of an acid (Table 1). In a manner similar to that employed in our early report on the intermolecular oxonium-ene reaction of allylic lactol ether,[14] a homogeneous Lewis acid, TMSOTf, was first used. However the substrate **3a**

SCHEME 3

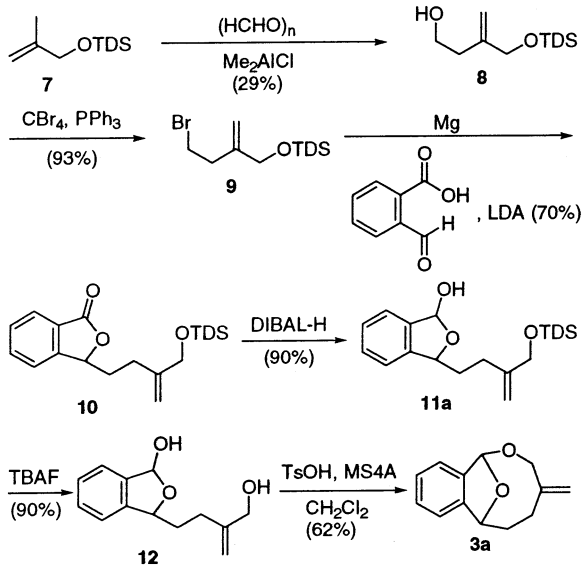
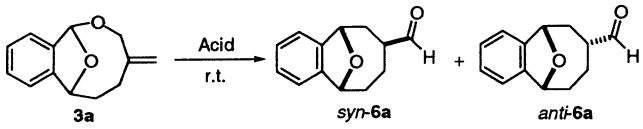


TABLE 1. Solid-Acid-Catalyzed Cyclization



entry	acid (g/mmol)	solvent (M)	time (h)	yield[a] (%)	*syn*:*anti*[b]
1[c]	TMSOTf (0.1 equiv)	CH_2Cl_2 (0.1)	3	tr	
2	K10 (0.8)	CH_2Cl_2 (0.1)	96	21	58:42
3	Amberlyst[d] (0.5)	CH_2Cl_2 (0.1)	9	46	54:46
4	Amberlyst[d] (0.5)	THF	78	43	55:45
5	Amberlyst[d] (0.5)	toluene	11	39	56:44
6	Amberlyst[d] (0.5)	CH_2Cl_2 (0.3)	4	32	54:46
7	Amberlyst[d] (0.5)	(0.01)	16	65	55:45
8	Amberlyst[d] (0.1)	(0.1)	84	41	55:45
9	Amberlyst[d] (1)	(0.1)	1.5	44	54:46
10	Amberlyst[d] (1)	(0.01)	5	72	54:46

[a] Combined yield of *syn*- and *anti*-**6a**. [b] Determined by capillary GC. [c] −78 °C → rt. [d] Amberlyst 15E.

decomposed in the presence of TMSOTf (entry 1). On the other hand, mesoporous solid acids were found to be effective for this reaction. Montmorillonite K10 gave the desired aldehyde **6a** though in low yield even after long reaction times (entry 2). Amberlyst 15E gave aldehyde **6a** in better yield within shorter reaction time; the yield was increased when the reaction was performed in CH_2Cl_2 rather than in THF or toluene (entries 3−5). Dilution of the substrate concentration also improved the yield (entries 3, 6, and 7). The time required for the reaction greatly depends on the amount of Amberlyst 15E (entries 8 and 9). Finally, the yield of **6a** was increased up to 72% in dilute (0.01 M) CH_2Cl_2 solution with 1 g of Amberlyst 15E (entry 10). In all cases, the isomer ratio of the aldehyde **6** was 1:1. As shown in Table 2, the ratio of syn and anti isomers of the aldehyde **6** was not changed throughout the reaction (5 min to 6 h). In contrast, the aldehyde **6** slowly isomerized to the other isomer after several hours as shown in the isomerization experiments of the separated syn and anti diastereomeric products **6a** (Table 3). These results indicate that the

(10) Ballantine, J. A. In *Solid Supports and Catalysts in Organic Synthesis*; Smith, K., Ed.; Ellis Horwood: London, 1992; Part 2, Chapter 4, pp 101−102. Kellendonk, F. J. A.; Heinerman, J. J. L.; van Santen, R. A. In *Preparative Chemistry Using Supported Reagents*; Laszlo, P., Ed.; Academic Press: New York, 1987; Part 8, Chapter 23, pp 456−457. Adams, J. M. In *Preparative Chemistry Using Supported Reagents*; Laszlo, P., Ed.; Academic Press: New York, 1987; Part 8, Chapter 27, pp 509−511.

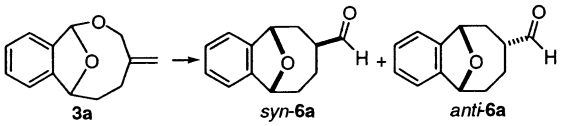
(11) (a) Tateiwa, J.; Hashimoto, K.; Yamauchi, T.; Uemura, S. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2361. (b) Tateiwa, J.; Kimura, A.; Takasuka, M.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2169.

(12) Recent communication: Ohmura, H.; Mikami, K. *Tetrahedron Lett.* **2001**, *42*, 6859.

(13) Mikami, K.; Shimizu, M.; Nakai, T. *J. Org. Chem.* **1991**, *56*, 2952.

(14) Intermolecular ene reaction of allylic lactol ethers: Mikami, K.; Kishino, H. *Tetrahedron Lett.* **1996**, *37*, 3705.

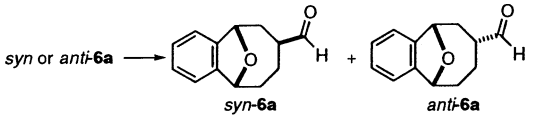
TABLE 2. Steady Isomer Ratio through the Reaction[a]



time	*syn*:*anti*[b]
5 min	54:46
15 min	53:47
6 h	54:46

[a] Amberlyst 15E (0.5 g/mmol), CH_2Cl_2, 0.1 M. [b] Determined by capillary GC.

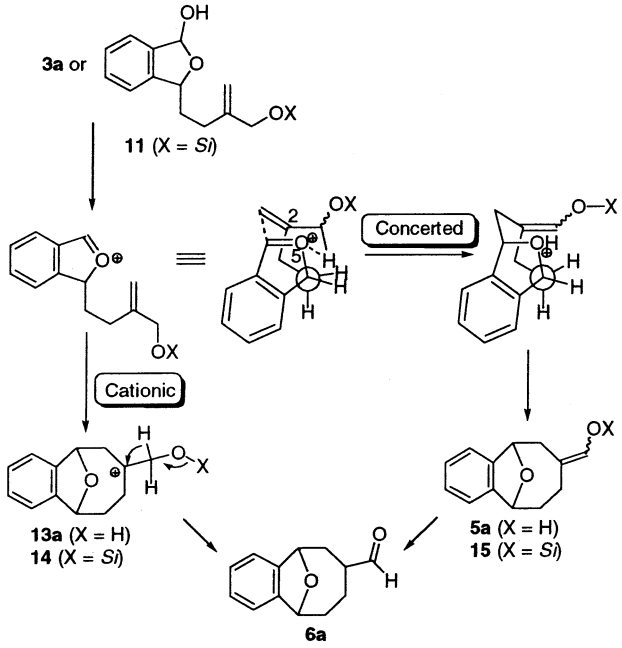
TABLE 3. Slow Isomerization between syn and anti Isomer[a]



time	*syn*:*anti*[b]	*syn*:*anti*[b]
start	89:11	14:86
5 min	90:10	16:84
15 min	85:15	22:78
5 h	53:47	53:47

[a] Amberlyst 15E (1 g/mmol), CH_2Cl_2, 0.01 M. [b] Determined by capillary GC.

SCHEME 4



ratio of syn and anti isomers of the aldehyde **6a** was kinetically determined (vide infra).

Continuum from Concerted to Stepwise Mechanism. Two possible mechanisms are conceivable for the ene reaction of **3a** to **6a** (X = H; Scheme 4). One is the concerted cyclization followed by tautomerization of enol **5a** to aldehyde **6a**. The other is stepwise cyclization to give β-hydroxy carbenium ion intermediate **13a** followed by 1,2-hydride shift.[15,16] To examine the continuum from the concerted to cationic mechanism in the (2,5)-ene reaction of **3a** to **6a**, the reaction using lactol **11** bearing a siloxy group at the allylic position was investigated (X = Si; Scheme 4). The concerted product would be obtained as the silyl enol ether **15** to give eventually the aldehyde **6a**. Thus, the reaction of the siloxy lactol **11a** (Si = TDS) with K10 and Amberlyst 15E was investigated (Table 4). First, the reaction of the lactol **11a** possessing thexyldimethylsilyl ether was studied with Amberlyst 15E to give aldehyde **6a** exclusively (entry 1). On the other hand, the reaction with K10 gave the silyl enol ether **15a** (entry 2). Then, lactol **11b** (Si = TBDPS) possessing the acid-stable *tert*-butyldiphenylsilyl ether group was investigated. The silyl enol ether **15b** was obtained in 8% yield in the presence of Amberlyst 15E (entry 3) and, eventually, in 16% yield using K10 (entry 4).

The isolated silyl enol ether **15a** was then protonated with Amberlyst 15E to the aldehyde **6a** (Table 5). Interestingly, aldehyde **6a** obtained by protonation of silyl enol ether **15a** was anti major at the early stage of the reaction. By contrast, in the reaction of siloxy lactol **11**, the isomer ratio of aldehyde **6a** inclined to syn as the yield of silyl enol ether **15a** increased (Table 4, entry 4). These results imply the involvement of the other cyclization pathway leading to *syn*-aldehyde **6a**; the syn-selective stepwise cyclization associates with anti-selective concerted cyclization.

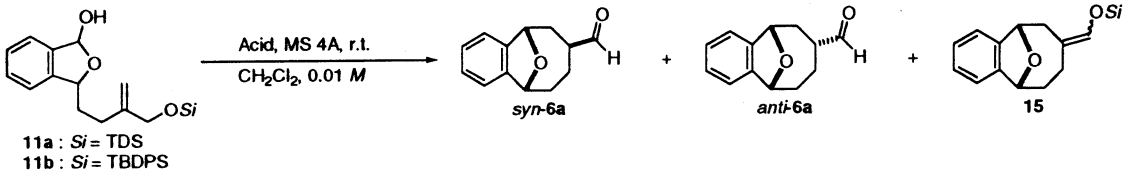
Ab Initio Calculations on Concerted and Stepwise Transition States. To evaluate the continuum mechanism of the (2,5)-ene reaction, from the cationic to the concerted cyclization, we carried out ab initio molecular orbital calculation[17] by the use of allyl alcohols **16** as a chemical model (Scheme 5). Two comparable transition states of **17** in the concerted cyclization and **18** in the stepwise cyclization were optimized at the HF/6-31G* level. In the case of $n = 1$ (e.g., the chemical model of **6a**), the 21.2 kcal/mol activation energy of the concerted transition state **17a** is larger than the 5.9 kcal/mol activation energy of the cationic transition state **18a**. This indicates that the cationic cyclization is favored over the concerted cyclization in the reaction of **6a**. As shown in Figure 2, the concerted (2,5)-ene transition state of **17a** has a significant amount of zwitterionic character (C^1-C^2 1.37 Å; C^2-C^3 1.53 Å) in comparison with the

(15) For a concerted (pericyclic) mechanism of internal [1,2] hydride (pinacol) migration to carbenium ion, see: (a) Mislow, K.; Siegel, M. *J. Am. Chem. Soc.* **1952**, *74*, 1060. (b) Ley, J. B.; Vernon, C. A. *J. Chem. Soc.* **1957**, 2987. (c) Collins, C. J.; Rainey, W. T.; Smith, W. B.; Kaye, I. A. *J. Am. Chem. Soc.* **1959**, *81*, 460. (d) Smith, W. B.; Bowman, R. E.; Kmet, T. *J. Am. Chem. Soc.* **1959**, *81*, 997. (e) Nakamura, K.; Osamura, Y. *J. Am. Chem. Soc.* **1993**, *115*, 9112. (f) Wennerberg, J.; Frejd, T. *Acta Chem. Scand.* **1998**, *52*, 95.

(16) For Overman's elegant and important works on Prins/pinacol reactions, see: (a) Overman, L. E. *Acc. Chem. Res.* **1992**, *25*, 352. For leading recent references: (b) MacMillan, D. W. C.; Overman, L. E. *J. Am. Chem. Soc.* **1995**, *117*, 10391. (c) Cloninger, M. J.; Overman, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 1092.

(17) All calculations were performed with a Gaussian 98 pakage. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr. J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.11; Gaussian, Inc.: Pittsburgh, PA, 2001.

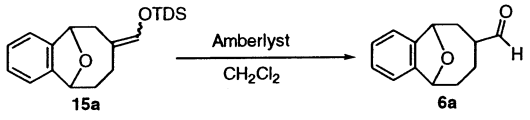
TABLE 4. Solid-Acid-Catalyzed Cyclization of Lactol 11[a]



entry	substrate	acid (g/mmol)	time	yield[b] of **6a** (%)	*syn*:*anti*[c]	yield[d] of **15** (%)
1	**11a**	Amberlyst[e] (1)	1.5 h	64	52:48	0[f]
2		K10 (0.8)	10 min	65	58:42	9
3	**11b**	Amberlyst[e] (1)	3 h	73	53:47	8
4		K10 (0.8)	10 min	60	67:33	16

[a] The reactions was carried out in the presence of MS 4Å in CH_2Cl_2 (0.01 M) at rt. [b] Combined yield of syn and anti isomers of **6a**. [c] dSetermined by capillary GC. [d] Combined yield of *Z*/*E* mixture of **15**. [e] Amberlyst 15E. [f] Trace amount of **15a** was detected by quenching the reaction in 20 min.

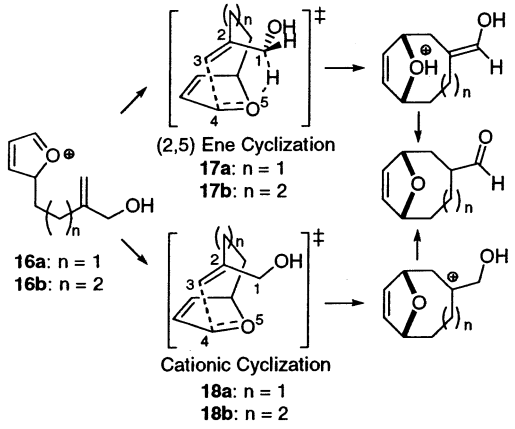
TABLE 5. Conversion of Silyl Enol Ether 15a to Aldehyde 6a[a]



time	*syn*:*anti*[b]
1 min	22:78
5 min	24:76
10 min	27:73

[a] Reaction was carried out in the presence of Amberlyst 15E (1 g/mmol) in 0.01 M at rt. **15a** was consumed in 30 min. [b] Determined by capillary GC.

SCHEME 5



transition structure of the normal ene reaction reported by Houk[18] and an almost dissociated C−H bond (C^1−H 2.04 Å) because the hydroxy group on C^1 facilitates stabilization of the cationic charge on C^1. The concerted transition state **17a** is destabilized by the electrostatic factors as well as the geometrical requirement by forming a highly distorted tricyclo structure in the concerted mechanism. On the other hand, in the case of $n = 2$, the transition state of **17b** also shows zwitterionic character (C^1−C^2 1.53 Å; C^2−C^3 1.37 Å) but smaller dissociation of the C^1−H bond (C^1−H = 1.93 Å). The activation energy of **17b** (16.9 kcal/mol) is only 1.0 kcal/mol larger than that of **18b** (15.9 kcal/mol). At this stage, these two concerted and cationic pathways become comparable. The concerted and cationic mechanisms can be regarded to

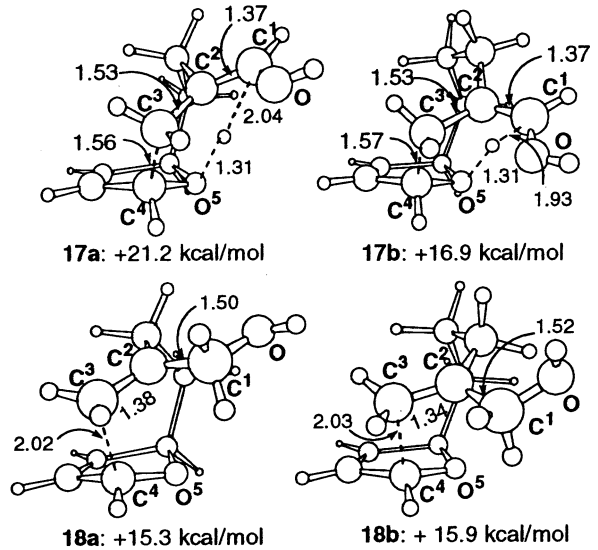


FIGURE 2. 3D structures of the transition states for the concerted (**17a** and **18a**) and cationic (**17b** and **18b**) cyclization (HF/6-31G*). Bond lengths are shown in Å.

be continuum, depending on the structures of substrates and acids.

Isotope Labeling Study.[1919] To confirm the continuum mechanism, the deuterated cyclic allylic lactol ether **3b** was considered as a substrate (Scheme 6). The intermediate **5b** could be obtained via concerted mechanism,[20] followed by protonation with Amberlyst 15E leading to α-protonated *anti*-aldehyde **6b**. Through cationic mechanism, α-deuterated *syn*-aldehyde **6c** would be obtained through [1,2] deuteride shift.[21] Therefore, by measuring the α-D ratio of **6**, the continuum could be evaluated.

The deuterated cyclic allylic lactol ether **3b** was treated with Amberlyst 15E and quenched within 5 min to

(18) Loncharich, R. J.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 6947.

(19) General reviews on isotope effects: (a) Carpenter, B. K. *Determination of Organic Reaction Mechanisms*; Wiley: New York, 1984. (b) Kwart, H. *Acc. Chem. Res.* **1982**, *15*, 401.

(20) H/D Isotope effect is observed in ene reactions, see: (a) Stephenson, L. M.; Mattern, D. L. *Acc. Chem. Res.* **1980**, *13*, 419. (b) Snider, B. B.; Eyal, R. *J. Am. Chem. Soc.* **1985**, *107*, 8160. (b) Song, Z.; Chrisope, D. R.; Beak, P. *J. Org. Chem.* **1987**, *52*, 3938. (c) Singleton, D. A.; Hang, C. *J. Org. Chem.* **2000**, *65*, 895.

(21) It is known that H/D isotope effect in 1,2-migrations is quite small: Westheimer, F. H. *Chem. Rev.* **1961**, *61*, 265.

SCHEME 6

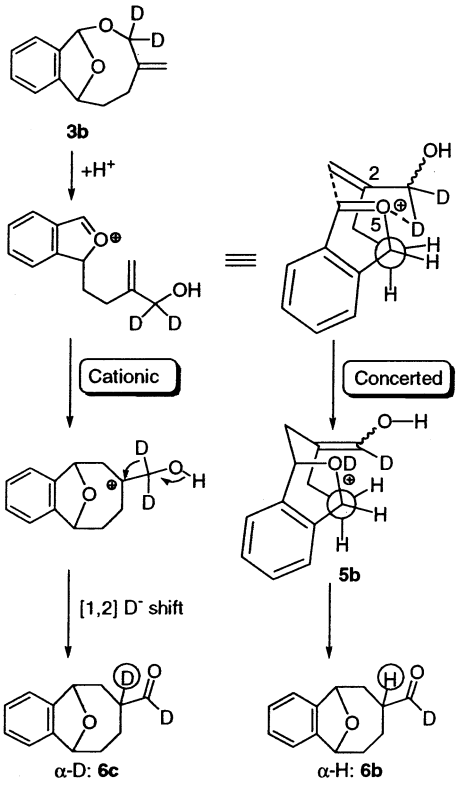
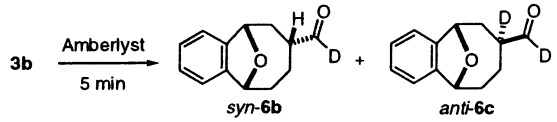


TABLE 6. Syn:Anti Ratio in 6b:6c



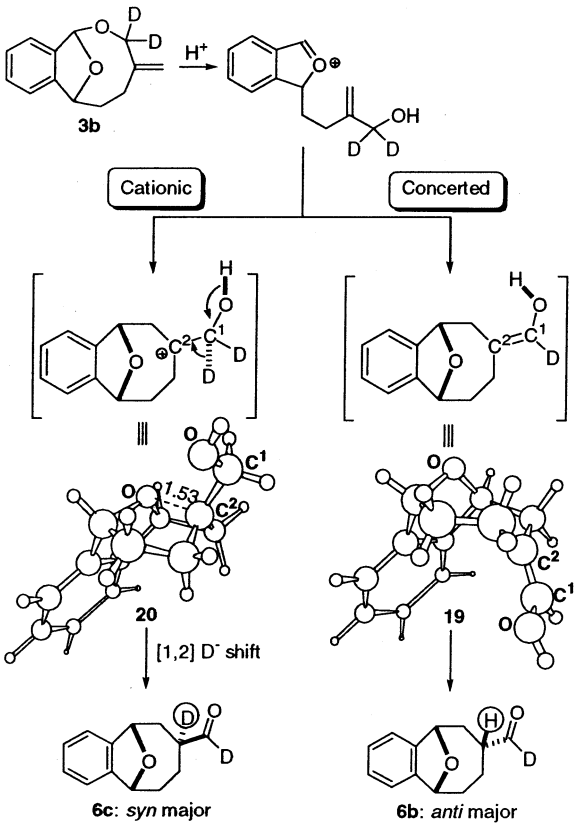
6b : 6c

	6b (*syn*/*anti*)	**6c** (*syn*/*anti*)
$(M + Na)^+$	49:51	
$(M + K)^+$	(34/66)	(74/26)
$(M + Na)^+$	42:58	
$(M + K)^+$	(31/69)	(71/29)

prevent isomerization (replacement of α-D with H) of the resultant aldehyde **6**. The syn and anti isomers **6** were separated, and their molecular weight was measured by LCMS to show that the **6b** (H):**6c** (D) ratio was ca. 1:1 and that **6b** was anti major along with syn major **6c** (Table 6).

The continuum mechanism is thus exemplified in Scheme 7. The concerted cyclization preferentially afforded the anti product via protonation of the resultant enol from the convex face. Indeed, the 3D structure of the enol **19** optimized at the HF/6-31G* level clearly shows that protonation readily occurs from the less hindered convex face. The cationic cyclization preferentially provided the syn-deuterated product by 1,2-deuteride shift from the concave face. The resultant cationic intermediate in the cationic pathway has a different structure from the resultant enol in the concerted pathway. The 3D structure of the cationic intermediate **20**

SCHEME 7



optimized at the HF/6-31G* level illustrates the presence of stereoelectronic interaction between oxygen lone pair orbital and vacant p-orbital on C^2 ($O-C^2 = 1.53$ Å)[22] and the suitable position of duteride in the concave face for the 1,2-shift. Therefore, 1,2-deuteride shift readily proceeds from the convex face. Overall, the ca. 1:1 ratio of syn and anti isomers of the aldehydes as the mixture of **6b** and **6c** were kinetically determined as the result of the continuum mechanism (vide supra).

Conclusion

The (2,5)-ene cyclizations of cyclic allylic lactol ethers **3** have thus been reported from the mechanistic point of view. Since the oxonium ion intermediate **4** derived from **3** bears an allylic hydroxy group, the concerted product is obtained as the enol form so that this can tautomerize to the corresponding aldehyde **6**. In this ene cyclization, the continuum from the concerted to cationic mechanism is evaluated by ab initio molecular orbital calculation. The choice of the concerted versus cationic mechanism of the ene cyclization depends on the structural features of the substrate and additional acids. Indeed, the involvement of the cationic cyclization followed by 1,2-hydride shift leading to the *syn*-aldehyde α-D-**6c** (CD═O) is experimentally verified in the labeling study, while the involvement of the concerted cyclization in the reaction of cyclic allylic lactol ether **3** is also confirmed by the formation of *anti*-aldehyde **6c** (CD═O) in the labeling study and silyl enol ether **15** leading eventually to *anti*-aldehyde **6a** (CH═O).

(22) Paquett, L. A.; Scott, M. K. *J. Am. Chem. Soc.* **1972**, *94*, 6760 and references therein.

Experimental Section

General. Chemical shifts (δ) of ^{1}H NMR are expressed in parts per million downfield from tetramethylsilane as an internal standard ($\delta = 0$) or $CHCl_3$ within a solvent ($\delta = 7.26$). Multiplicity is indicated as bs (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet), sept (septet), and m (multiplet), and coupling constants (J) are reported in Hz. Chemical shifts (δ) of ^{13}C NMR are expressed in parts per million in $CDCl_3$ as an internal standard ($\delta = 77$).

Capillary gas chromatographic (GC) analyses were carried out on a capillary column coated with OV-1701 by using N_2 as a carrier gas. High-performance liquid chromatographic (HPLC) analyses were carried out on an ultraviolet (UV) spectrophotometric detector (254 nm). Analytical thin-layer chromatography (TLC) was performed on glass plates precoated with silica gel (layer thickness 0.25 and 0.2 mm). Visualization was accomplished by UV light (254 nm), anisaldehyde, potassium permanganate, and 2,4-dinitrophenylhydrazine. Column chromatography was performed on silica gel 60N (spherical, neutral, 100−210 μm) employing hexane−diethyl ether mixture as an eluent, unless otherwise noted. All experiments were carried out under argon atmosphere unless otherwise noted. Tetrahydrofuran, diethyl ether, and toluene were distilled from sodium/benzophenone ketyl immediately prior to use.

Preparation of (1*R,7*R**)-4-Methylene-2,12-dioxabenzobicyclo[5.2.1]decane (3a). 3-Dimethylthexylsilyloxy-2-methylpropene (7).** To a stirred solution of thexyldimethylsilyl chloride (27.4 g, 153.1 mmol) and dry DMF (70 mL) was added a solution of β-methallyl alcohol (9.2 g, 127.6 mmol) in DMF (50 mL) and imidazole (22 g, 323 mmol) at room temperature. The reaction mixture was stirred for 1.5 h and then poured into 1 N hydrochloric acid. The aqueous phase was extracted with ether several times, and then the combined organic phase was washed with a saturated aqueous solution of sodium bicarbonate, water, and brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was distilled (85 °C, 7 mmHg) to afford 26.9 g (98%) of 3-dimethylthexylsilyloxy-2-methylpropene **7**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.87 (s, 6H), 0.90 (d, $J = 7.2$ Hz, 6H), 1.59−1.67 (m, 1H), 1.70 (s, 3H), 4.02 (s, 2H), 4.80 (s, 1H), 4.98 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ −3.5, 18.5, 19.0, 20.3, 25.3, 34.2, 66.6, 109.1, 144.7. IR (neat) 2962, 2870, 1464, 1253, 1116, 1087, 847, 832, 777 cm^{-1}.

3-(Dimethylthexylsilyloxymethyl)-3-butene-1-ol (8). To a stirred solution of 3-dimethylthexylsilyloxy-2-methylpropene **7** (32.3 g, 150.6 mmol), paraformaldehyde (4.5 g, 150.6 mmol) and dry dichloromethane (350 mL) in the presence of MS 4Å, was added dimethylaluminum chloride (145 mL of 1.04 M solution in hexane, 151 mmol) at −78 °C. The reaction temperature was gradually raised to room temperature, and the mixture was stirred for 10 h. To the reaction mixture was then added a saturated aqueous solution of sodium sulfate and ether. After 12 h, to the mixture was added anhydrous sodium sulfate. The mixture was filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ether = 2:1) to afford 10.7 g (29%) of 3-(dimethylthexylsilyloxymethyl)-3-butene-1-ol **8**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.85 (s, 6H), 0.88 (d, $J = 6.9$ Hz, 6H), 1.63 (set, $J = 6.9$ Hz, 1H), 2.31 (t, $J = 6.3$ Hz, 2H), 3.70 (t, $J = 6.3$ Hz, 2H), 4.07 (s, 2H), 4.91 (s, 1H), 5.10 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ −3.5, 18.4, 20.2, 25.2, 34.1, 36.8, 61.3, 66.2, 112.6, 145.5. IR (neat) 3338, 2962, 2870, 1657, 1466, 1255, 1083, 1050, 832, 777 cm^{-1}.

Bromo-3-(dimethylthexylsilyloxymethyl)-3-butene (9). To a stirred solution of 3-(dimethylthexylsilyloxymethyl)-3-butene-1-ol **8** (6.9 g, 28.3 mmol) in dry dichloromethane (190 mL) was added triphenylphosphine (8.9 g, 33.9 mmol) and carbontetrabromide (14.1 g, 42.45 mmol). The reaction mixture was stirred for 5 min and then poured into saturated aqueous sodium bicarbonate. The aqueous phase was extracted with CH_2Cl_2 several times, and then the combined organic phase was washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ether = 10:1) to afford 8.1 g (93%) of 1-bromo-3-(dimethylthexylsilyloxymethyl)-3-butene (**9**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.86 (s, 6H), 0.89 (d, $J = 6.9$ Hz, 6H), 1.64 (set, $J = 6.9$ Hz, 1H), 2.61 (t, $J = 7.8$ Hz, 2H), 3.49 (t, $J = 7.8$ Hz, 2H), 4.08 (s, 2H), 4.90 (s, 1H), 5.12 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ −3.5, 18.5, 20.3, 25.2, 31.0, 34.1, 36.3, 65.5, 111.5, 145.7. IR (neat) 2962, 2868, 1466, 1255, 1089, 832, 777 cm^{-1}.

3-(Dimethylthexylsilyloxymethyl)-3-butenylmagnesium bromide. A round-bottom, two-necked, 100-mL flask equipped with reflux condenser was charged with magnesium (1.8. g, 74 mmol) and iodide, which was stirred for 12 h. To this reaction vessel was added THF (2 mL) and a solution of 1-bromo-3-(dimethylthexylsilyloxymethyl)-3-butene **9** (7.3 g, 23.6 mmol) 1,2-dibromoethane in THF (22 mL) dropwise, and the mixture was stirred for several hours.

3-(3-Dimethylthexylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1(3*H*)-one (10). To a stirred solution of diisopropylamine (1.9 mL, 14.3 mmol) in dry THF (70 mL) at −78 °C was added *n*-BuLi (6.2 mL of 1.5 M solution in hexane, 9.3 mmol). The reaction mixture was kept at −78 °C for 20 min and at 0 °C for 30 min and then cooled to −78 °C again. To this mixture was added a solution of *o*-phthalaldehydic acid (1.4 g, 9.5 mmol) in dry THF (27 mL). The resulting solution was kept at −78 °C for 1 h, and 3-(dimethylthexylsilyloxymethyl) butenylmagnesium bromide (THF solution, 23.6 mmol) was added. The reaction mixture was allowed to warm to room temperature, stirred for 3 h, and then poured into 1 N HCl. The aqueous phase was extracted with ethyl acetate several times, and the combined organic phase was rinsed with brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ether = 3:1) to afford 2.4 g (70%) of 3-(3-dimethylthexylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1(3*H*)-one **10**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.09 (s, 9H), 0.85 (s, 6H), 0.87 (d, $J = 6.9$ Hz, 6H), 1.62 (sept, $J = 6.9$ Hz, 1H), 1.81−1.97 (m, 1H), 2.12−2.30 (m, 3H), 4.06 (s, 2H), 4.86 (s, 1H), 5.08 (s, 1H), 5.50 (dd, $J = 3.3$, 8.7 Hz, 1H), 7.44 (dd, $J = 1.2$, 7.5 Hz, 1H), 7.53 (t, $J = 7.5$ Hz, 1H), 7.67 (dt, $J = 1.2$, 7.5 1H), 7.89 (d, $J = 7.5$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ −3.5, 18.5, 20.3, 25.2, 27.9, 33.1, 34.1, 65.8, 80.8, 109.6, 121.68, 125.7, 126.2, 129.1, 134.0, 147.1, 149.8, 170.5. IR (neat) 2962, 1769, 1466, 1253, 1079, 833 cm^{-1}.

***cis*/*trans* Mixture of 3-(3-Dimethylthexylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1-ol (11a).** To a stirred solution of 3-(3-dimethylthexylsilyloxymethyl-3-butenyl)-2-benzofuran-1(3*H*)-one **10** (2.4 g, 6.6 mmol) in dry dichloromethane (36.5 mL) at −78 °C was added DIBAL-H (7.7 mL of 0.95 M solution in toluene, 7.3 mmol). The reaction was kept at −78 °C for 2.5 h and then quenched by addition of saturated aqueous solution of sodium sulfate and allowed to warm to room temperature. To the mixture was added anhydrous sodium sulfate and ether. The mixture was stirred for 1 h, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ether = 3:1) to afford 2.2 g (90%) of a *cis*/*trans* mixture of 3-(3-dimethylthexylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1-ol **11a**. ^{1}H NMR (300 MHz, C_6D_6, *cis*/*trans* mixture) δ 0.09 (s, 12H), 0.90 (s, 6H), 0.91 (s, 6H), 0.94 (d, $J = 6.9$ Hz, 6H), 0.95 (d, $J = 6.9$ Hz, 6H), 1.58−2.07 (m, 6H), 2.14−2.36 (m, 4H), 3.59 (t, $J = 7.2$ Hz, 2H), 4.01 (s, 2H), 4.03 (s, 2H), 4.89 (s, 1H), 4.92 (s, 1H), 5.03 (dd, $J = 3.9$, 7.5 Hz, *trans*-1H), 5.20 (s, 1H), 5.22 (s, 1H), 5.31−5.35 (m, *cis*-1H), 6.36 (d, $J = 7.2$ Hz, *trans*-1H), 6.43 (dd, $J = 1.8$, 7.2 Hz, *cis*-1H), 6.83−6.87 (m, 2H), 7.02−7.10 (m, 4H), 7.23−7.26 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, *cis*/*trans* mixture) δ−3.3, 18.8, 20.6, 25.5, 28.4, 28.7, 34.5, 34.6, 36.0, 66.1, 82.1, 82.8, 101.1, 108.9, 121.1, 121.3, 123.3, 123.4, 129.1, 129.2, 140.2, 140.5, 142.8, 142.9, 148.6, 148.7. IR (neat) 3364, 2960, 1464, 1253, 1112, 832 cm^{-1}.

***cis*/*trans* Mixture of 3-(4-Hydroxy-3-methylenebutyl)-1,3-dihydro-2-benzofuran-1-ol (12).** To a stirred solution of a *cis*/*trans* mixture of 3-(3-dimethyltexylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1-ol **11a** (2.2 g, 6.0 mmol) and dry THF (70 mL) at 0 °C was added tetrabutylammonium fluoride (6.6 mL of 1.0 M solution in THF, 6.6 mmol). The reaction was kept at room temperature for 2 h and then quenched by addition of water. The aqueous phase was extracted with ether, and the combined organic phase was rinsed with brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ether = 1:3) to afford 1.1 g (85%) of *cis*/*trans* mixture of 3-(4-hydroxy-3-methylenebutyl)-1,3-dihydro-2-benzofuran-1-ol **12**. ^{1}H NMR (300 MHz, $CDCl_3$, *cis*/*trans* mixture) δ 1.75−2.01 (m, 2H), 2.04−2.34 (m, 6H), 4.04 (s, 2H), 4.05 (s, 2H), 4.88 (bs, 2H), 5.01 (s, 1H), 5.04 (s, 1H), 5.21 (dd, J = 3.6, 7.5 Hz, 1H), 5.46 (dt, J = 2.1, 7.2 Hz, 1H), 6.42 (s, 1H), 6.48 (d, J = 2.1 Hz, 1H), 7.21−7.23 (m, 2H), 7.33−7.44 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, *cis*/*trans* mixture) δ 28.1, 28.3, 33.9, 35.2, 65.8, 82.0, 82.7, 100.6, 100.7, 109.8, 110.0, 121.0, 121.1, 123.0, 123.1, 128.0, 128.1, 129.2, 129.3, 139.2, 139.3, 142.0, 142.1, 148.3, 148.5. IR (neat) 3294, 2922, 1657, 1441, 1249, 1017, 903, 758 cm^{-1}.

(1R*,7R*)-4-Methylene-2,12-dioxabenzobicyclo[5.2.1]-decane (3a). To a stirring solution of a *cis*/*trans* mixture of 3-(4-hydroxy-3-methylenebutyl)-1,3-dihydro-2-benzofuran-1-ol **12** in dry dichloromethane (500 mL) (1.1 g, 5.1 mmol) at room temperature in the presence of MS 4Å (2.3 g) was added *p*-toluenesulfonic acid monohydrate (97 mg, 0.51 mmol). The reaction was kept at room temperature for 15 min and poured into a saturated aqueous solution of sodium bicarbonate. The aqueous phase was extracted with dichloromethane, and the combined organic phase was rinsed with brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography (hexane/ether = 6:1) to afford 637 mg (62%) of (1*R**,7*R**)-4-methylene-2,12-dioxabenzobicyclo[5.2.1]decane **3a**. ^{1}H NMR (300 MHz, C_6D_6) δ 1.48 (dt, J = 3.6, 12.6 Hz, 1H), 1.64−1.70 (m, 1H), 1.95 (dt, J = 4.5, 13.2 Hz, 1H), 2.24 (ddt, J = 4.2, 12.9, 14.4 Hz, 1H), 3.45 (d, J = 12.9 Hz, 1H), 4.10 (d, J = 12.9 Hz, 1H), 4.90 (s, 1H), 5.06 (s, 1H), 5.15 (t, J = 3.3, 1H), 6.55 (s, 1H), 6.76 (d, J = 6.9 Hz, 1H), 7.01−7.12 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.6, 38.0, 67.6, 82.6, 104.7, 117.2, 121.4, 123.4, 128.0, 129.5, 136.9, 143.1, 148.6. IR (neat) 2932, 1640, 1462, 1255, 1087, 915 cm^{-1}. EI-MS m/z = 202 ($M^{+\bullet}$). HRMS (EI) calcd for $C_{13}H_{14}O_2$ 202.0994, found 202.0997 ($M^{+\bullet}$).

***cis*/*trans*-3-(3-*tert*-Butyldiphenylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1-ol (11b).** The titled compound was prepared from 3-*tert*-butyldiphenylsilyloxy-2-methylpropene according to the procedure described for *cis*/*trans* mixture of 3-(3-dimethylthexylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1-ol **11a**. ^{1}H NMR (300 MHz, C_6D_6, *cis*/*trans* mixture) δ 1.16 (s, 18H), 1.57−1.95 (m, 4H), 2.09−2.30 (m, 4H), 3.58 (bs, 1H), 3.65 (bs, 1H), 4.16 (s, 2H), 4.18 (s, 2H), 4.93−4.99 (m, 3H), 5.24−5.28 (m, 1H), 5.35−5.37 (m, 2H), 6.33 (d, J = 4.5 Hz, 1H), 6.38 (s, 1H), 6.76−6.79 (m, 2H), 6.99−7.08 (m, 4H), 7.19−7.23 (m, 14 H), 7.75−7.80 (m, 5H). ^{13}C NMR (75 MHz, C_6D_6, *cis*/*trans* mixture) δ 19.5, 27.0, 28.5, 28.8, 34.5, 36.1, 66.8, 81.9, 82.6, 101.0, 109.1, 109.2, 121.1, 121.3, 123.3, 123.4, 127.7, 128.1, 128.3, 129.0, 129.1, 130.0, 140.1, 140.4, 142.8, 142.9, 148.1. IR (neat) 3364, 2934, 1657, 1464, 1112, 704 cm^{-1}.

General Procedure for Solid-Acid-Catalyzed Oxonium Ene Reaction of (1*R,7*R**)-4-methylene-2,12-dioxabenzobicyclo[5.2.1]decane (3a).** To a stirred solution of **3a** (49 mg, 0.24 mmol) in dichloromethane (24 mL) at room temperature was added solid acid. The reaction was kept at room temperature for reported time, filtered through Celite, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ether = 3:1) to afford the aldehyde **6**.

General Procedure for Solid-Acid-Catalyzed Oxonium Ene Reaction of cis/*trans*-Mixture of 3-(3-Dimethyltexylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1-ol (7a) and *cis*/*trans*-Mixture of 3-(3-*tert*-Butyldiphenylsilyloxymethyl-3-butenyl)-1,3-dihydro-2-benzofuran-1-ol (11b). To a stirring solution of **11** and dichloromethane at room temperature in the presence of MS 4Å was added solid acid. The reaction was kept at room temperature for the reported time, filtered through Celite, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ether = 3:1) to afford the aldehyde **6**.

(1*S,3*R**,6*R**)-3-Formyl-11-oxabenzobicyclo[4.2.1]-nonane (*anti*-6a).** ^{1}H NMR (300 MHz, C_6D_6) δ 0.51 (dddd, J = 3.0, 10.5, 12.3, 14.1 Hz, 1H), 1.35−1.44 (m, 2H), 1.49−1.56 (m, 1H), 1.68 (dddd, J = 3.3, 4.2, 11.7, 13.8 Hz, 1H), 2.27 (dddd, J = 1.2, 5.7, 8.4, 13.8 Hz, 1H), 2.35−2.45 (m, 1H), 5.22 (d, J = 8.4 Hz, 1H), 5.27 (d, J = 4.2 Hz, 1H), 6.68−6.78 (m, 2H), 6.96−7.02 (m, 2H), 9.10 (s, 1H). ^{13}C NMR (75 MHz, C_6D_6) δ 21.3, 35.5, 36.4, 50.6, 79.5, 83.4, 120.5, 120.7, 127.6, 127.8, 141.1, 146.1, 201.5. IR (neat) 2930, 1723, 1462, 1367, 1249, 1069, 1002, 756 cm^{-1}. EI-MS m/z = 202 ($M^{+\bullet}$). HRMS (EI) calcd for $C_{13}H_{14}O_2$ 202.0994, found 202.0998 ($M^{+\bullet}$). Capillary GC (OV-1701, 170 °C, inj/det 200 °C). t_R = 21.1 min.

(1*S,3*S**,6*R**)-3-Formyl-11-oxabenzobicyclo[4.2.1]-nonane (*syn*-6a).** ^{1}H NMR (300 MHz, C_6D_6) δ 1.20 (dddd, J = 0.9, 5.1, 9.6, 14.1 Hz, 2H), 1.38−1.51 (m, 2H), 1.59 (dt, J = 5.1, 9.9 Hz, 1H), 1.62−1.69 (m, 1H), 1.97 (ddd, J = 5.7, 9.6, 14.1 Hz, 1H), 2.10 (ddt, J = 5.1, 7.5, 14.1 Hz, 1H), 5.19 (d, J = 7.5 Hz, 1H), 5.29 (d, J = 4.5 Hz, 1H), 6.68−6.78 (m, 2H), 6.96−7.04 (m, 2H), 9.14 (s, 1H). ^{13}C NMR (75 MHz, C_6D_6) δ 24.2, 33.5, 37.5, 46.8, 81.1, 81.5, 120.5, 120.7, 127.5, 127.8, 142.2, 145.4, 202.2. IR (neat) 2966, 2910, 1725, 1412, 1263, 1062, 1013, 801 cm^{-1}. EI-MS m/z = 202 ($M^{+\bullet}$). HRMS (EI) calcd for $C_{13}H_{14}O_2$ 202.0994, found 202.0989 ($M^{+\bullet}$). Capillary GC (OV-1701, 170 °C, inj/det 200 °C). t_R = 21.8 min.

(*Z*/*E*)-(1*S,6*R**)-3-(Dimethylthexylsilyloxymethylene)-11-oxabenzobicyclo[4.2.1]nonane (15a).** The assignments of *E*/*Z* isomers were performed by ^{1}H NMR, ^{13}C NMR, ^{1}H−^{1}H COSY, and ^{13}C−^{1}H COSY. ^{1}H NMR (300 MHz, C_6D_6, *E*/*Z* mixture) δ −0.15 (s, *E*-3H), −0.07 (s, *Z*-3H), −0.06 (s, *E*-3H), −0.01 (s, *Z*-3H), 0.73 (s, *E*-3H), 0.75 (s, *E*-3H), 0.82 (s, *Z*-6H), 0.83 (d, J = 6.9 Hz, *E*-6H), 0.87 (d, J = 6.6 Hz, *Z*-6H), 1.39−1.67 (m, *E*/*Z*-5H), 1.95 (d, J = 13.8 Hz, *E*-1H), 1.96−2.18 (m, *E*/*Z*-3H), 2.28−2.43 (m, *E*-2H), 2.57 (dt, J = 1.2, 14.7 Hz, *Z*-1H), 2.63 (ddd, J = 1.5, 5.7, 13.8 Hz, *E*-1H), 3.07 (ddd, J = 1.2, 6.6, 14.7 Hz, *Z*-1H), 5.35 (appd, J = 6.3 Hz, *E*/*Z*-3H), 5.41 (d, J = 6.0 Hz, *Z*-1H), 5.61 (s, *E*-1H), 5.96 (s, *Z*-1H), 6.72−7.03 (m, *E*/*Z*-8H). ^{13}C NMR (75 MHz, C_6D_6, *E*/*Z* mixture) δ −3.5, −3.3, 18.8, 18.9, 20.2, 20.3, 23.6, 25.3, 25.4, 27.6, 33.9, 34.4, 36.5, 37.6, 42.2, 81.4, 81.9, 82.0, 82.3, 116.6, 117.6, 120.3, 120.4, 120.7, 120.9, 127.1, 127.2, 127.3, 127.4, 136.2, 136.3, 143.6, 144.1, 144.3, 145.1. IR (neat) 2960, 1667, 1462, 1255, 1143, 835 cm^{-1}.

(*Z*/*E*)-(1*S,6*R**)-3-(*tert*-Butyldiphenylsilyloxymethylene)-11-oxabenzobicyclo[4.2.1]nonane (15b).** The assignments of *E*/*Z* isomers were performed by ^{1}H NMR, ^{13}C NMR, ^{1}H−^{1}H COSY, and ^{13}C−^{1}H COSY. ^{1}H NMR (300 MHz, C_6D_6, *E*/*Z* mixture) δ 1.05 (s, *E*-9H), 1.11 (s, *Z*-9H), 1.27−1.37 (m, *Z*-1H), 1.49−1.57 (m, *Z*-1H), 1.73 (dddd, J = 1.2, 5.7, 9.3, 13.2 Hz, *E*-1H), 1.81 (d, J = 13.8 Hz, *E*-1H), 1.90−2.02 (m, *Z*-2H), 2.26 (ddt, J = 5.4, 7.2, 13.2 Hz, *E*-1H), 2.48−2.64 (m, *E*-3H), 2.89 (dt, J = 1.2, 14.4 Hz, *Z*-1H), 3.11 (ddd, J = 1.2, 5.7, 14.4 Hz, *Z*-1H), 5.30 (d, J = 5.4 Hz, *E*-1H), 5.37 (d, J = 5.7 Hz, *Z*-1H), 5.41 (d, J = 6.9 Hz, *E*-1H), 5.50 (d, J = 5.7 Hz, *Z*-1H), 5.78 (s, *E*-1H), 6.04 (s, *Z*-1H), 6.67−7.75 (m, *Z*/*E*-28H). ^{13}C NMR (75 MHz, C_6D_6, *E*/*Z* mixture) δ 19.3, 19.4, 23.9, 26.6, 26.7, 27.6, 33.7, 36.7, 37.2, 41.8, 81.7, 81.8, 81.9, 82.3, 116.8, 117.5, 120.4, 120.6, 120.9, 127.1, 127.2, 127.3, 127.4, 128.1, 130.0, 130.1, 133.2, 133.3, 133.4, 133.5, 135.6, 135.7, 135.9, 136.8, 136.9, 143.4, 143.9, 144.7, 145.2. IR (neat) 2932, 1667, 1429, 1141, 1114, 702 cm^{-1}.

(1*R,7*R**)-3-Dideuterated-4-methylene-2,12-dioxabenzobicyclo[5.2.1]decane (3b).** The titled compound was prepared from of 3-dideuterated-3-dimethylthexylsilyloxy-2-methylpropene according to the procedure described for (1*R**,7*R**)-4-methylene-2,12-dioxabenzobicyclo[5.2.1]decane **3a**. ^{1}H NMR (300 MHz, C_6D_6) δ 1.47 (dt, J = 3.0, 13.2 Hz, 1H), 1.65 (ddt, J = 3.0, 5.1, 14.4 Hz, 1H), 1.95 (dt, J = 4.2, 13.2 Hz, 1H), 2.24 (ddt, J = 4.2, 12.9, 14.4 Hz, 1 H), 4.91 (d, J = 0.9 Hz, 1H), 5.06 (s, 1H), 5.15 (t, J = 3.3 Hz, 1H), 6.57 (s, 1H), 6.74−6.77 (m, 1H), 6.99−7.12 (m, 3H).^{13}C NMR (75 MHz, C_6D_6) δ 30.5, 38.0, 82.5, 104.8, 116.1, 121.5, 123.4, 129.3, 138.2, 143.6, 149.3. IR (neat) 3074, 2930, 1634, 1371, 1255, 1094, 1009 cm^{-1}.

Preparation of 3-Dideuterated-3-dimethylthexylsilyloxy-2-methylpropene. To a stirred suspension of lithium aluminum deuteride (4.5 g, 107.2 mmol) and ether (450 mL) at −78 °C was added methyl methacrylate (10.5 g, 104.9 mmol) in ether (50 mL), and reaction temperature was gradually warmed to room temperature. To this reaction mixture was then added water (4.6 mL), 15% sodium hydroxide (4.6 mL), water (13.8 mL), and ethyl acetate. The mixture was stirred for 1 h, filtered, and concentrated. The crude product obtained (8.1 g) was subjected to the next treatment without purification. To a stirring solution of crude product (8.1 g) and dry DMF (40 mL) were added dimethylthexylsilyl chloride (20.6 g, 136.6 mmol) in DMF (15 mL) and imidazole (14.3 g, 210 mmol) at 0 °C. The temperature of the reaction mixture was warmed to room temperature and immersed for 3 h and then poured into 1 N hydrochloric acid. The aqueous phase was extracted with ether several times, and then the combined organic phase was washed with saturated aqueous sodium bicarbonate, water, and brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ether = 50:1) to afford 15.4 g (68%, 2 steps) of 3-dideuterated-3-dimethylthexylsilyloxy-2-methylpropene. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.87 (s, 6H), 0.90 (d, J = 6.9 Hz, 6H), 1.64 (sept, J = 6.9 Hz, 1H), 1.70 (s, 3H), 4.80 (s, 1H), 4.97 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ −3.4, 18.5, 19.0, 20.3, 25.3, 34.2, 109.2, 144.7. IR (neat) 2962, 1659, 1466, 1253, 1139, 1118, 830 cm^{-1}.

Mixture of (1*S,3*R**,6*R**)-12-Deuterated-3-formyl-11-oxabenzobicyclo[4.2.1]nonane (*anti*-6b) and (1*S**,3*R**,6*R**)-3,12-Dideuterated-3-formyl-11-oxabenzobicyclo[4.2.1]nonane (*anti*-6c).** The titled compound was synthesized according to the general procedure described for the solid-acid-catalyzed oxonium ene reaction of the (1*R**,7*R**)-4-methylene-2,12-dioxabenzobicyclo[5.2.1]decane **3a.** ^{1}H NMR (300 MHz, C_6D_6) δ 0.52 (dddd, J = 3.0, 10.5, 12.3, 14.4 Hz, 1H), 1.36−1.45 (m, 2H), 1.47−1.57 (m, 1H), 1.70 (ddd, J = 4.2, 12.3, 13.8 Hz, 1 H), 2.27 (dddd, J = 1.2, 6.0, 8.4, 13.8 Hz, 1H), 2.35−2.44 (m, 0.7H), 5.22 (d, J = 8.4 Hz, 1H), 5.27 (d, J = 4.2 Hz, 1H), 6.68−6.78 (m, 2H), 6.96−7.02 (m, 2H). ^{13}C NMR (75 MHz, C_6D_6) δ 21.2, 21.3, 35.4, 35.5, 36.4, 50.3, 50.4, 79.5, 83.4, 120.5, 120.7, 127.6, 127.8, 141.1, 146.1. IR (neat) 3030, 2928, 1711, 1462, 1064, 1006 cm^{-1}.

Mixture of (1*S,3*S**,6*R**)-12-Deuterated-3-formyl-11-oxabenzobicyclo[4.2.1]nonane (*syn*-6b) and (1*S**,3*S**,6*R**)-3,12-Dideuterated-3-formyl-11-oxabenzobicyclo[4.2.1]nonane (*syn*-6c).** The titled compound was synthesized according to the general procedure described for the solid-acid-catalyzed oxonium ene reaction of the (1*R**,7*R**)-4-methylene-2,12-dioxabenzobicyclo[5.2.1]decane **3a**. ^{1}H NMR (300 MHz, C_6D_6) δ 1.20 (dddd, J = 1.2, 5.1, 9.9, 14.4 Hz, 1H), 1.38−1.51 (m, 1.3H), 1.59 (dt, J = 5.4, 9.9 Hz, 1H), 1.62−1.68 (m, 1 H), 1.92−2.02 (m, 1H), 2.10 (ddt, J = 5.1, 7.5, 14.1 Hz, 1H), 5.19 (d, J = 7.5 Hz, 1H), 5.29 (dd, J = 0.9, 5.4 Hz, 1H), 6.67−6.79 (m, 2H), 6.96−7.04 (m, 2H). ^{13}C NMR (75 MHz, C_6D_6) δ 24.1, 24.2, 33.6, 37.3, 37.4, 46.6, 81.1, 81.5, 120.5, 120.7, 127.5, 127.8, 142.2, 145.4. IR (neat) 3030, 2928, 1711, 1462, 1071, 1007 cm^{-1}.

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Supporting Information Available: Geometries of the representative stationary points. This material is available free of charge via the Internet at http://pubs.acs.org.

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