Studies on the Oxidative Addition Reaction of 1,1-Dibromo-1-alkenes, α-Dehalopalladation, and the Intramolecular Bis(carbopalladation) Reaction of Alkenes. An Efficient Entry to Fused Bicycles

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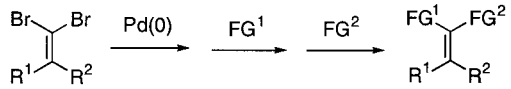
Twenty-three examples of 1,1-dihalo-1-alkenes were synthesized by the conventional alkylation methods. The oxidative addition reactions of 1,1-dibromo-2,2-diphenylethene or 1,1-dibromo-2-phenylpropene with a stoichiometric amount of $Pd(PPh_3)_4$ afforded 1,2-diphenylacetylene and 1-phenylpropyne, respectively, indicating that α-dehalopalladation reaction occurred to afford vinylic carbene intermediates. However, α-dehalopalladation reaction was not observed in all 1,1-dihalo-1-alkenes containing an extra C═C bond suitable for cyclic carbopalladation under the current reaction conditions probably due to the fast cyclic carbopalladation reaction of **40A**-type of palladium intermediates; A series of bicycles, i.e., fused 5,6-, 6,6-, 6,7-, and 7,7-bicyclic compounds, were prepared efficiently via this bicyclic carbopalladation protocol. Under condition A, within 0.5 h, **10** afforded the monocyclic product **37** in 79%. With prolonged reaction time, **37** was converted to bicycle **36**. Even with isolated **37**, the corresponding reaction under condition A afforded **36** in 92% NMR yield, indicating a stepwise oxidative addition−cyclic carbopalladation−β-elimination mechanism for this bicyclization reaction.

Introduction

Over the past several decades, dramatic advances in organic synthesis have been witnessed due to developments in organotransition metal chemistry. Among so many transition metals, which have provided fertile ground for the development of chemo-, regio-, and stereoselective organic transformations, palladium has been regarded as one of the most valuable entries. Indeed, palladium complexes can catalyze a large number of selective transformations, such as the Heck reaction,[1] the Pd(0)-catalyzed coupling reaction of organometallic reagents with organic halides (or equivalents),[2] and Tsuji−Trost-type π-allylpalladium chemistry,[3] etc., which would be either difficult or impossible by conventional methodologies.

Carbopalladation of alkenes, alkynes, and allenes provides efficient entries to stereodefined substituted alkenes and cyclic compounds via intermolecular and intramolecular reactions, respectively.[4] In most cases, only one carbon−halogen (or an appropriate leaving group) bond was involved. Among our effort devoted to reactions with more than one reactive centers, we became interested in the oxidative addition reaction of 2,2-bis-(ω-alkenyl)-1,1-dibromoethenes (Scheme 1). One formidable challenge in this bicyclization paradigm is α-dehalopalladation, from which the formation of an alkylidene carbene intermediate would be expected.

Scheme 1



Normally, 1,1-dihalo-1-alkenes (X = Cl, Br, I) are important starting materials in organic synthesis. There are a few reports on the Pd-catalyzed reaction of 1,1-dihalo-1-alkenes: (1) palladium-catalyzed hydrogenolysis of 1,1-dibromo-1-alkenes with tributyltin hydride to give (*Z*)-1-bromoalkenes;[5] (2) palladium-catalyzed cross coupling reaction of 1,1-dihalo-1-alkenes with vinylboronic acids,[6a−e] organostannanes,[6f−k] organoalanes,[6l] and organozinc or Grignard reagents;[6m,n] (3) palladium-catalyzed reductive reaction of 1,1-dibromo-1-alkenes with hydride

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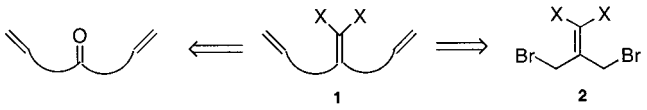
Scheme 2



X = Br, **2a**; X= Cl, **2b**.

anion;[7] (4) palladium-catalyzed carbonylation reaction of 1,1-dibromo-1-alkenes under phase-transfer catalysis (PTC) conditions.[8] In all of these cases, only one of the two carbon−halogen bonds is involved.[9] So far, no examples of a bicyclic carbopalladation reaction of 1,1-dihalo-1-alkenes to furnish bicyclic products have been reported.

In a preliminary communication,[10] we described a catalytic bicyclic carbopalladation reaction of 1,1-dibromo-1-alkenes for the efficient synthesis of fused bicyclic compounds. By this protocol, bicyclic compounds with different ring sizes as well as attached functional groups can be simultaneously constructed from the corresponding acyclic precursors in just "one shot", which is distinctive from the traditional "ring by ring" approach.[10]

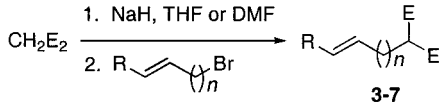
In this paper, we report the possibility of α-dehalopalladation, the scope of this bicyclization reaction, and a proposal for its mechanism.

Results and Discussion

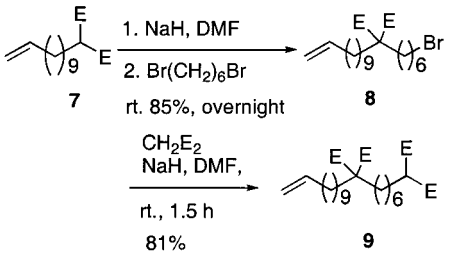
Synthesis of Starting Materials. Generally, 1,1-dibromo-1-alkenes can be prepared either via the dibromomethylenation reaction of the corresponding ketones using CBr_4/PPh_3[11] or by the reaction of an appropriate carbonyl compound with diethyl dibromomethylphosphonate.[12] However, these two methods are reported to be sensitive to the steric hindrance of the starting ketones. Thus, an efficient and convenient synthetic pathway to 1,1-dibromo-1-alkenes would be beneficial.

From the viewpoint of retrosynthetic analysis, we reasoned that 1,1-dihalo-3-bromo-2-(bromomethyl)propene **2** could be a key building block for the synthesis of the starting materials **1** (Scheme 2). Tetrahalide **2** could be synthesized in large quantity from acetone with a two-step procedure that we recently developed,[13] namely, a dihalomethylenation reaction followed by radical allylic α-bromination reaction of the resultant alkene.

Scheme 3

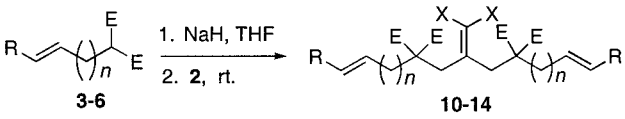


conditions			product	yield (%)
THF	2 h	*n* = 1, R = H	**3**	86
DMF	3 h	*n* = 2, R = H	**4**	64
THF	1 h	*n* = 1, R = Ph	**5**	61
THF	1 h	*n* = 1, R = E	**6**	61
DMF	2 h	*n* = 9, R = H	**7**	83



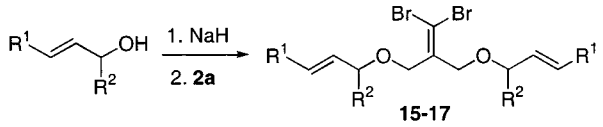
E = COOMe

Scheme 4



time			product	yield (%)
2 h	X = Br	*n* = 1, R = H,	**10**	86
overnight	X = Br	*n* = 2, R = H,	**11**	71
2h	X = Br	*n* = 1, R = Ph,	**12**	63
2h	X = Br	*n* = 1, R = E,	**13**	81
overnight	X = Cl	*n* = 1, R = H,	**14**	75

E = COOMe



conditions		product	yield (%)
THF, rt., 5 h	R^1 = H, R^2 = H	**15**	65
THF-HMPA, -78 °C to rt, 5h	R^1 = H, R^2 = CH_3	**16**	63
THF, rt., 2.5 h	R^1 = Ph, R^2 = H	**17**	62

The fragments containing one or two malonate unit(s) **3**−**7** and **9** were prepared by a simple alkylation reaction of dimethyl malonate with the corresponding bromides using NaH as the base (Scheme 3).

Those 1,1-dibromo-1-alkenes having two equal C=C bond fragments, i.e., **10**−**13**, were prepared by the treatment of **2a** with the appropriate alkyl-substituted malonates **3**−**6** (Scheme 4). Similarly, 1,1-dichloro-1-alkene **14** can be prepared from 1,1-dichloro-3-bromo-2-

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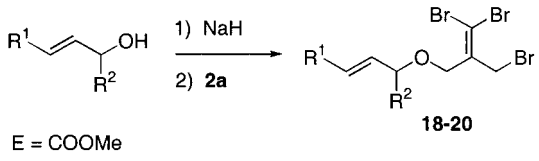
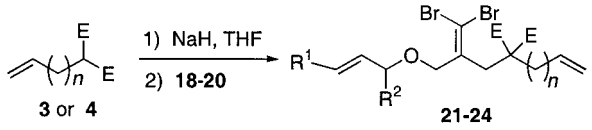
Scheme 5

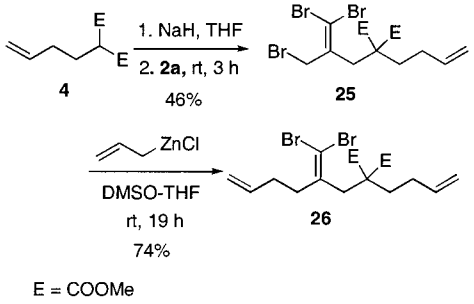


conditions		product	yield (%)
THF, rt, 0.5 h	R^1 = H, R^2 = H,	**18**	49
THF-HMPA, -78 °C to rt, 0.5h	R^1 = H, R^2 = Me,	**19**	40
THF, rt, 0.5h	R^1 = Ph, R^2 = H,	**20**	36



time		product	yield (%)
2.5 h	n = 1, R^1 = H, R^2 = H,	**21**	79
2 h	n = 2, R^1 = H, R^2 = H,	**22**	77
1.5 h	n = 1, R^1 = H, R^2 = Me,	**23**	90
1 h	n = 1, R^1 = Ph, R^2 =H,	**24**	81

Scheme 6



(bromomethyl)propene **2b**[13] and **3** in 75% yield. Diethers **15**−**17** were prepared by the reaction of **2a** with the sodium 2-alkenoxides (Scheme 4).

1,1-Dibromo-1-alkenes **21**−**24** with two different C=C bond-containing fragments were prepared by the alkylation of **3** or **4** with **18**−**20**, which, in turn, were prepared from the etherification of **2a** with the corresponding allylic alcohols (Scheme 5).

Compound **26** was prepared by the treatment of **25** with allyl zinc chloride in DMSO/THF, which was prepared from allyl chloride and zinc−copper couple (Scheme 6).[14]

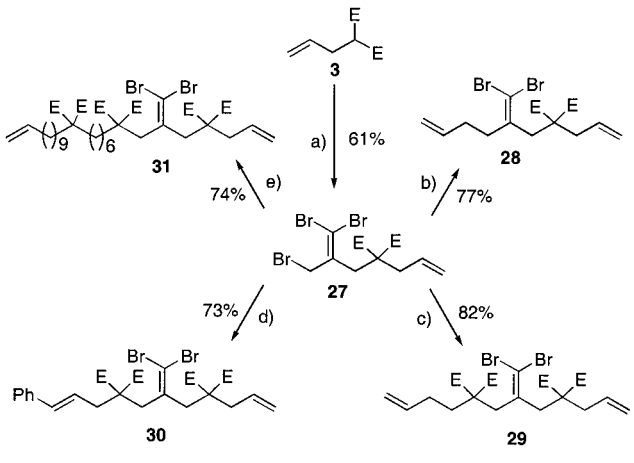
Compounds **28**−**31** were easily synthesized by either alkylation or etherification with the common starting precursor **27** as depicted in Scheme 7. Compound **33** was prepared by the sequential alkylation of **7** with **2a** and **3** (Scheme 7).

For use in a mechanistic study, compound **35** was prepared from **34** and **3** (Scheme 8).[13]

Optically pure compound (*S*,*S*)-**16** was prepared by etherification of the corresponding optically pure (*S*)-3-buten-2-ol with **2a**.[15] (*S*)-**23** was synthesized by alkylation

(14) LeGoff, E. *J. Org. Chem.* **1964**, *29*, 2048−2050.

Scheme 7

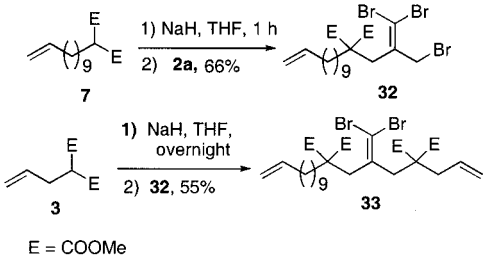


Conditions:

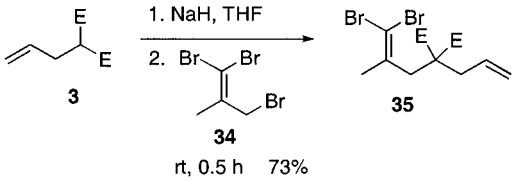
a) i) NaH, ii) **2a**, THF, 2 h b) Zn-Cu, allyl chloride, DMSO-THF, rt, 19 h

c) i) **4**, NaH, THF; ii) **27**, THF, 3 h d) i) **5**, NaH, THF, ii) **27**, THF, overnight

e) i) **9**, NaH, THF, ii) **27**, THF, overnight



Scheme 8



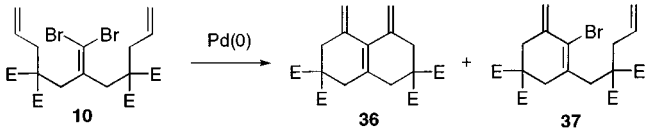
of **3** with (*S*)-**19**, which was also derived from (*S*)-3-buten-2-ol (Scheme 9).

Study of the Possibility of α-Dehalopalladation and Optimization of the Reaction Conditions. 1,1-Dibromo-1-alkene **10** was used as the first substrate to test the bicyclic carbopalladation protocol under different reaction conditions, and the results are summarized in Table 1.

As shown in Table 1, when the reaction was catalyzed by palladium in refluxing CH_3CN, the desired bicyclic product **36** was not formed in detectable yield (entries 1−3). Using Et_3N or K_2CO_3 as the base and $Pd(PPh_3)_4$ as the catalyst, the reactions were low yielding and not clean (entries 4−11). Under the catalysis of $Pd(PPh_3)_4$ using CH_3CN as the solvent and Et_3N as the base, **10** was cyclized to afford monocyclic product **37** cleanly; even with prolonged reaction time, the second cyclization was not observed (entry 12). When 10 mol % $Pd_2(dba)_3$−$CHCl_3$ was used, only monocyclic product **37** was formed in

(15) Balmer, E.; Germain, A.; Jackson, W. P.; Lygo, B. *J. Chem. Soc., Perkin Trans. 1* **1993**, 399−400.

Table 1. Bicyclic Carbopalladation Reaction of 10 under Catalysis of Palladium(0) Complex

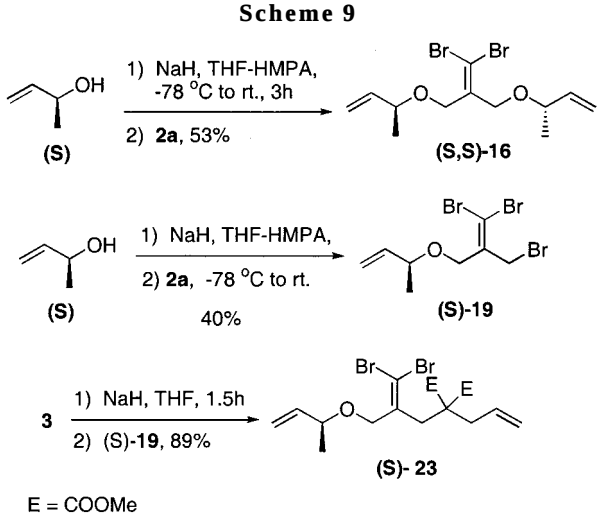


E = COOMe

entry	catalysis[a]	solvent[b]	base	time (h)	*T* (°C)	yield (%) **36**	yield (%) **37**
1	4% A	CH_3CN (0.011)	Et_3N [d]	6	reflux	0	0
2	20% A	CH_3CN (0.045)	K_2CO_3[c,d]	72	reflux	0	0
3	13% B	CH_3CN (0.045)	Ag_2CO_3	14	reflux	0	0
4	10% B	toluene (0.045)	Et_3N	7.5	reflux	34	0
5	11% B	toluene (0.03)	K_2CO_3[d]	25	reflux	20	0
6	10% B	xylene (0.051)	Et_3N	52	reflux	15	0
7	10% C	DMF (0.045)	K_2CO_3	13.5	100	43	0
8	11% B	xylene (0.03)	K_2CO_3[d]	38	reflux[f]	40	0
9	10% B	xylene (0.03)	K_2CO_3[d]	34	reflux	43	0
10	10% B	xylene (0.045)	K_2CO_3	24	80−85	22	21
11	15% B	DMF[e] (0.045)	K_2CO_3	12	90	0	47
12	10% B	CH_3CN (0.15)	Et_3N	23	56	0	75
13	10% C	xylene (0.045)	K_2CO_3	6.5	80	0	73
14	6% D	DMF (0.045)	K_2CO_3	23.5	95	62	16
15	10% B	xylene (0.047)	K_2CO_3[d]	24	80−85	68	0

[a] A = $Pd(OAc)_2$, PPh_3; B = $Pd(PPh_3)_4$; C = $Pd_2(dba)_3$−$CHCl_3$, dppe; D = $Pd_2(dba)_3$−$CHCl_3$, PPh_3. [b] The numbers in parentheses are the molar concentration of **10** in the solvent. [c] Ag_2CO_3 (1 equiv) was added. [d] *n*-Bu_4NCl was added. [e] EtOH (10 equiv) was added. [f] Before refluxing, the reaction was reacted at 70−80 °C for 45 min.

Scheme 9



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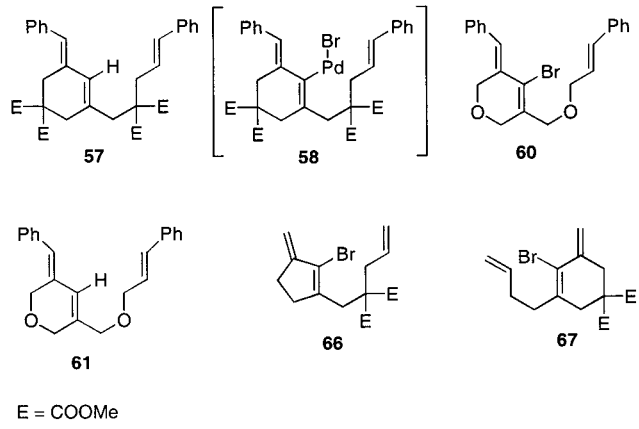


E = COOMe

Figure 1.

xylene after 6.5 h at 80 °C (entry 13). However, bicyclic product **36** was formed in 62% yield together with a 16% yield of monocycle **37** after heating in DMF for 23.5 h (entry 14). The ^1H NMR data of the obtained product **36** are as follows: 5.23 (s, 2 H), 5.04 (s, 2 H), 3.70 (s, 12 H), 2.82 (s, 4 H), 2.63 (s, 4 H) ppm. The simplicity of the ^1H NMR data led us to doubt the structure of this cyclized product, since steric interactions are likely to distort the six sp^2-carbon atoms out-of-plane. This would, in principle, make the cyclic protons chemical environmentally unequal, thus complicating the splitting patterns. Ultimately, we determined the structure of the cyclization product as **36** unambiguously by X-ray analysis, and the six sp^2-carbon atoms are truly not coplanar as judged from the ORTEP presentation (Figure 1 in the Supporting Information). The best results were obtained with 10 mol % $Pd(PPh_3)_4$, K_2CO_3 (10 equiv), and *n*-Bu_4NCl (2 equiv)[16] in xylene at 80−85 °C for 24 h (condition A) affording fused 6,6-bicyclic product **36** in 68% yield (entry 15).

Among the many methods for generating alkylidene carbenes,[17] sα-elimination is one of the most representtive approaches. Intramolecular reactions of methylenecarbenes derived by the reaction of 1,1-dibromoalkenes with organolithium[11,18,19] or magnesium[20] have been well

(16) For the efficiency of tetraalkylammonium salts in Heck type reactions, see: (a) Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287−1289. (b) Jeffery, T. *Tetrahedron Lett.* **1985**, *26*, 2667−2670. (c) Jeffery, T. *Synthesis* **1987**, 70−71. (d) Jeffery, T. *Tetrahedron* **1996**, *52*, 10113−10130.

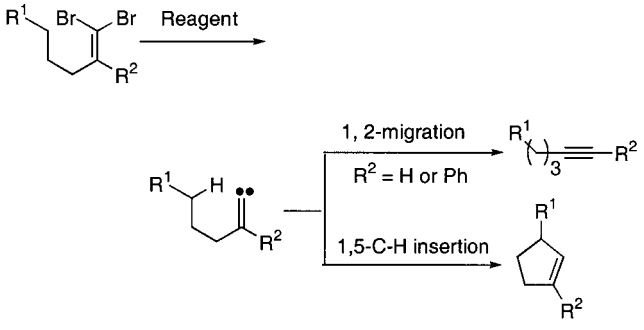
(17) For the formation of alkylidenecarbenes, see: (a) Stang, P. J. *Chem. Rev.* **1978**, *78*, 383−405. (b) Stang, P. J. *Acc. Chem. Res.* **1982**, *15*, 348−354.

(18) (a) Beny, J.-P.; Dhawan, S. N.; Kagan, J.; Sundlass, S. *J. Org. Chem.* **1982**, *47*, 2201−2204. (b) Padwa, A.; Wong, G. S. K. *J. Org. Chem.* **1986**, *51*, 3125−3133. (c) Kozikowski, A. P.; Okita, M.; Kobayashi, M.; Floss, H. G. *J. Org. Chem.* **1988**, *53*, 863−869. (d) Harada, T.; Hara, D.; Hattori, K.; Oku, A. *Tetrahedron Lett.* **1988**, *29*, 3821−3824. (e) Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron* **1989**, *45*, 363−380. (f) Nicolauo, K. C.; Marron, B. E.; Veale, C. A.; Webber, S. E.; Serhan, C. N. *J. Org. Chem.* **1989**, *54*, 5527−5535. (g) McIntosh, M. C.; Weinreb, S. M. *J. Org. Chem.* **1993**, *58*, 4823−4832. (h) Braun, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 430−451.

(19) (a) Baird, M. S.; Baxter, A. G. W.; Hoorfar, A.; Jefferies, I. *J. Chem. Soc., Perkin Trans I* **1991**, 2575−2581. (b) Hartzler, H. D. *J. Am. Chem. Soc.* **1964**, *86*, 526−527.

(20) Wakabayashi, N. *J. Org. Chem.* **1967**, *32*, 489−490.

Scheme 10



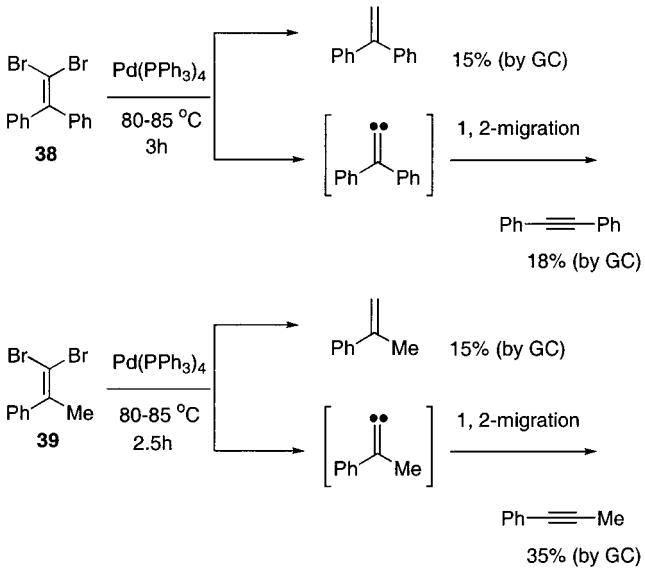
documented. Recently, an elegant generation of alkylidene carbenes from 1,1-dibromo-1-alkenes by the reaction with SmI_2 was reported by Tani et al.[21] Mori and co-workers found alkylidene carbenes could be produced by α-elimination wthin a 1,1-dibromoalkene precursors using stannyl anion generated from $Me_3SiSnBu_3$ and TASF.[22] The generated alkylidene carbene can undergo either an intramolecular 1,2-shift reaction or 1,5-C-H insertion reaction depending on the substituent at the α-position (Scheme 10).

Thus, the following experiments under these standard reaction conditions were designed to further study the possibility of alkylidene carbene gereration through an α-dehalopalladation reaction:

(1) We studied the oxidative addition reaction of 2,2-diphenyl-1,1-dibromoethene[23,24] with a stoichiometric amount of $Pd(PPh_3)_4$. In the event, the α-elimination reaction will presumably afford 1,2-diphenylacetylene[25] via the phenyl-migration reaction of the putative (diphenylmethylidene)carbene intermediate. We did observe the formation of the rearrangement product via Raman and GC−MS spectra by comparison with the authentic sample,[26] indicating that α-debromopalladation is feasible in this case. At the same time, 1,1-diphenylethene was also formed (Scheme 11). 1,1-Dibromo-2-phenylpropene reacted with a stoichiometric amount of $Pd(PPh_3)_4$ to afford α-methylstyrene and 1-phenylpropyne similarly. To the best of our knowledge, these results are the first entries of α-dehalopalladation reactions.[5−9]

(2) However, for the bicyclization reaction of **10** under condition A, after careful examination of the crude reaction mixture, 1,2-alkyl migration product **43**,[27] the intramolecular 1,5-C-H insertion[28] product **44**, the corresponding intermolecular C-H insertion products of carbene intermediate **41** with xylene,[29] i.e., **45** and **46**, and possible cyclopropanation products were not formed (Scheme 12).

Scheme 11



(3) As it was reported that carbene intermediates could react with diphenylmethane,[29] we studied the cyclization of **10** in the presence of diphenylmethane under condition A. In this case, the bicyclization products **36** and **40** (decarboxylation product of **36**) were isolated in 62% and 9% yields, respectively (Scheme 13). The formation of C−H bond insertion product **42** of the possible carbene intermediate **41** with diphenylmethane was not detected.

(4) It is also noteworthy that the reaction of the 1,1-dibromo-1-alkene with one methyl and one terminal C=C bond connected, i.e., **35**, under condition A afforded two monocyclic products **48** and **49** (the decarboxylation product of **48**) containing the original C−Br bond cis to the methyl group in 32% and 32% yields, respectively.

(21) (a) Kunishima, M.; Hioki, K.; Ohara, T.; Tani, S. *J. Chem. Soc., Chem. Commun.* **1992**, 219−220. (b) Kunishima, M.; Hioki, K.; Tani, S.; Kato, A. *Tetrahedron Lett.* **1994**, *35*, 7253−7254.

(22) Sato, H.; Isono, N.; Miyoshi, I.; Mori, M. *Tetrahedron* **1996**, *52*, 8143−8158.

(23) Köbrich, G. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 49−68.

(24) (a) Posner, G. H.; Loomis, G. L.; Sawaya, H. S. *Tetrahedron Lett.* **1975**, 1373−1376. (b) Speziale, A. J.; Ratts, K. W. *J. Am. Chem. Soc.* **1962**, *84*, 854−859.

(25) For 1,2-migration of α-aryl groups of alkylidene carbenes, see: (a) Stang, P. J.; Mangum, M. G.; Fox, D. P.; Haak, P. *J. Am. Chem. Soc.* **1974**, *96*, 4562−4569. (b) Stang, P. J.; Fox, D. P.; Collins, C. J.; Watson, C. R., Jr. *J. Org. Chem.* **1978**, *43*, 364−365. (c) Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1982**, *47*, 1837−1845.

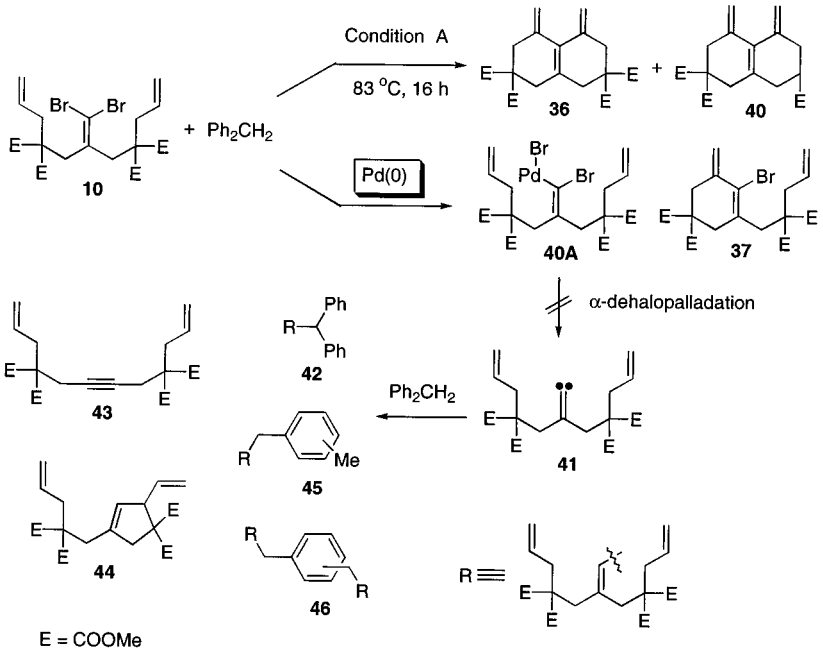
(26) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467−4470.

(27) For 1,2-shift reaction of alkylidenecarbenes, see: (a) Bothnerby, A. A. *J. Am. Chem. Soc.* **1955**, *77*, 3293−3296. (b) Wolinsky, J. *J. Org. Chem.* **1961**, *26*, 704−711. (c) Erickson, K. L.; Wolinsky, J. *J. Am. Chem. Soc.* **1965**, *87*, 1142−1143. (d) Newman, M. S.; Gromelski, S. J. *J. Org. Chem.* **1972**, *37*, 3220−3224. (e) Kobrich, G.; Merkel, D.; Thiem, K.-W. *Chem. Ber.* **1972**, *105*, 1683−1693. (f) Wolinsky, J.; Clark, G. W.; Thorstenson, P. C. *J. Org. Chem.* **1976**, *41*, 745−750. (g) Kowalski, C. J.; Fields, K. W. *J. Am. Chem. Soc.* **1982**, *104*, 321−323. (h) Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1982**, *47*, 1837−1845. (i) McDouall, J. J. W.; Schlegel, H. B.; Francisco, J. S. *J. Am. Chem. Soc.* **1989**, *111*, 4622−4627. (j) Walsh, R.; Untiedt, S.; Stohlmeier, M.; Meijere, A. *Chem. Ber.* **1989**, *122*, 637−642. (k) Ochiai, M.; Ito, T.; Takaoka, Y.; Masaki, Y.; Kunishma, M.; Tani, S.; Nagao, Y. *J. Chem. Soc., Chem. Commun.* **1990**, 118−119. (l) Fischer, D. R.; Williamson, B. L.; Stang, P. J. *Synlett* **1992**, 535−536. (m) Ohira, S.; Moritani, M.; Ida, T.; Yamato, M. *J. Chem. Soc., Chem. Commun.* **1993**, 1299−1300. (n) Likhotvorik, I. R.; Brown, D. W.; Jones, Jr., M. *J. Am. Chem. Soc.* **1994**, *116*, 6175−6178.

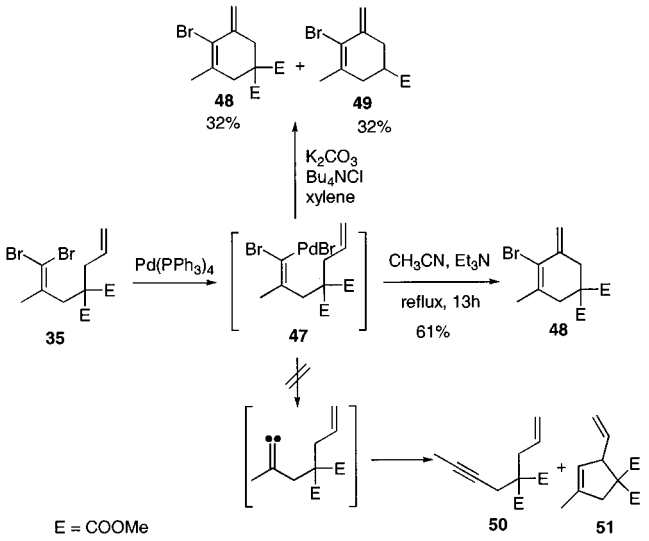
(28) For intramolecular 1,5-C−H insertion of alkylidenecarbene, see: (a) Walsh, R. A.; Bottini, A. T. *J. Org. Chem.* **1970**, *35*, 1086−1092. (b) Fischer, R. H.; Baumann, M.; Kobrich, G. *Tetrahedron Lett.* **1974**, 1207−1208. (c) Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1979**, *62*, 852−865. (d) Gilbert, J. C.; Giamalva, D. H.; Weerasoonriya, U. *J. Org. Chem.* **1983**, *48*, 5251−5256. (e) Gilbert, J. C.; Blackburn, B. K. *Tetrahedron Lett.* **1984**, 25, 4067−4070. (f) Gilbert, J. C.; Giamalva, D. H.; Baze, M. E. *J. Org. Chem.* **1985**, *50*, 2557−2563. (g) Gilbert, J. C.; Blackburn, B. K. *J. Org. Chem.* **1986**, *51*, 4087−4089. (h) Ohira, S.; Okai, K.; Moritani, T. *J. Chem. Soc., Chem. Commun.* **1992**, 721−722. (i) Kim, S.; Cho, C. M. *Tetrahedron Lett.* **1994**, 35, 8405−8408. (j) Williamson, B. L.; Tykwinski, R. R.; Stang, P. J. *J. Am. Chem. Soc.* **1994**, *116*, 93−98. (k) Tykwinski, R. R.; Stang, P. J.; Persky, N. E. *Tetrahedron Lett.* **1994**, 35, 23−26. (l) Schildknegt, K.; Bohnstedt, A. C.; Feldman, K. S.; Sambandam, A. *J. Am. Chem. Soc.* **1995**, *117*, 7544−7545. (m) Ohira, S.; Sawamoto, T.; Yamato, M. *Tetrahedron Lett.* **1995**, 36, 1537−1538. (n) Taber, D. F.; Meagley, R. P.; Doren, D. J. *J. Org. Chem.* **1996**, *61*, 5723−5728.

(29) Doyle, M. P.; Taunton, J.; Oon, S. M.; Liu, M. T. H.; Soundararajan, N.; Platz, M. S. Jackson, J. E. *Tetrahedron Lett.* **1988**, *29*, 5863−5866.

Scheme 12



Scheme 13



When the reaction was performed in refluxing CH_3CN for 13 h under the catalysis of $Pd(PPh_3)_4$ using Et_3N as the base, **48** could be isolated in 61% yield. It is obvious that the reaction proceeds via a simple cyclic carbopalladation process instead of an α-debromopalladation-1,2-alkyl shift to form alkyne **50**[27] or an 1,5-C−H bond insertion to produce **51** (Scheme 13).[28] Here, the carbon−bromine bond trans to the methyl group in **35** appears to be regiospecifically activated, perhaps as a consequence of coordination between the palladium atom and the C=C bond.

In summary, 1-bromo-1-alkenylpalladium bromides, formed by the oxidative addition reaction of **10** and **35**, underwent a faster cyclic carbopalladation reaction rather than an α-debromopalladation reaction.

The Scope of Bicyclic Carbopalladation Reactions. Having established the standard reaction conditions for bicyclic carbopalladation reaction of **10**, we tried to investigate the scope and cyclization patterns of this bicyclization reaction. Some typical examples are summarized in Table 2. From Table 2, it is obvious that a series of bicycles, i.e., fused 5,6- (entry 12, Table 2), 6,6- (entries1−6 and 8−11, Table 2), 6,7- (entries 14 and 15, Table 2), and 7,7-bicyclic compounds (entry 16, Table 2), can be efficiently prepared.

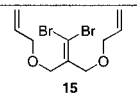
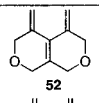
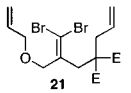
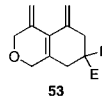
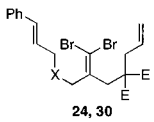
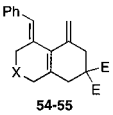
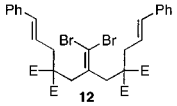
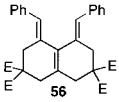
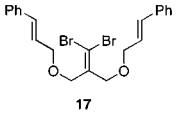
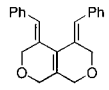
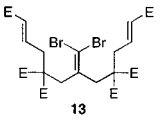
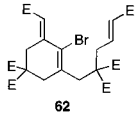
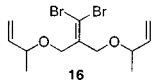
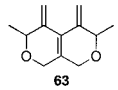
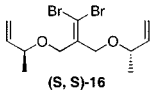
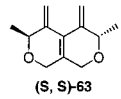
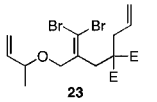
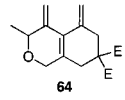
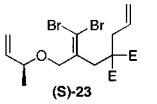
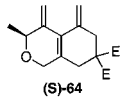
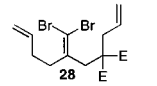
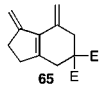
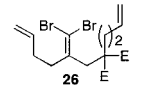
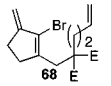
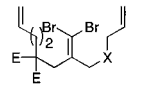
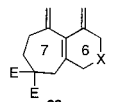
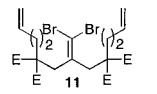
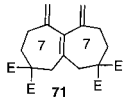
To explore the influence of steric effects on the reactivity of C=C double bonds, the bicyclic carbopalladation reactions of four additional precursors in which the double bonds were substituted with one or two phenyl groups were studied. Products **54** and **55** could be synthesized in xylene under condition B in 37% and 46% yields, respectively (entries 3 and 4, Table 2). From precursor **12**, in which the two C=C bonds were both substituted with phenyl groups, the bicyclic product **56** can also be prepared in reasonable yield accompanied by the formation of the monocyclic reduction product **57** (entry 5, Table 2). The formation of **57** may be due to the high steric hindrance of the phenyl group. Thus, the phenyl-substituted C=C bond was apparently did not insert into the C−Pd bond of intermediate **58**. Instead, the second C−Pd bond was reduced to afford **57** (Figure 1).[30]

For precursor **17**, the bicyclic product **59** can be prepared only in 19% yield under condition C at 85 °C for 23.5 h, together with the monocyclic product **60** (20% yield) and the corresponding monocyclic reduction product **61** (12% yield) (entry 6, Table 2). For **13**, in which the two C=C bonds were substituted with methoxycarbonyl groups, only monocyclic product **62** was isolated in 94% yield under catalysis by $Pd_2(dba)_3$-$CHCl_3$. No bicyclic product was formed in any detectable yield (entry 7, Table 2).

When **16** was submitted to condition B, the ^1H NMR signals for the vinyl protons of the bicyclic product **63** were observed as follows: 5.36 (s, 1H), 5.31 (s, 1H), 5.20 (s, 1H), 5.15 (s, 1H) ppm. It is obvious that a 1:1 ratio of

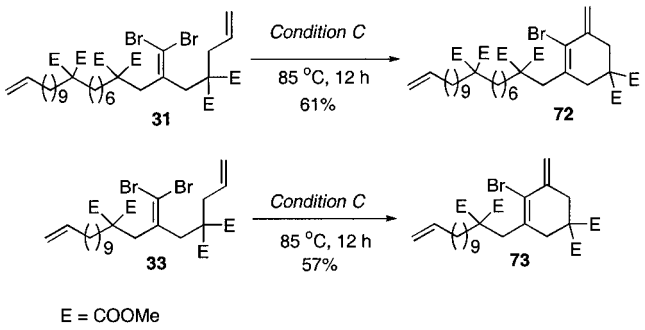
(30) (a) Abelman, M. M.; Oh, T.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 4130−4133. (b) Zask, A.; Helquist, P. *J. Org. Chem.* **1978**, *43*, 1619−1620. (c) Ma, S.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 6345−6357.

Table 2. Synthesis of Bicycles via Bicarbopalladation

entry	substract	condition[a]	time (h)	product	yield (%)
1	 **15**	A, 85 °C	15.5	 **52**	83
2	 **21**	$Pd_2(dba)_3$-$CHCl_3$ (5 mol%) K_2CO_3 (5 equiv), dppe (20 mol%) DMF	11	 **53**	63
	 **24, 30**			 **54-55**	
3	X = O **(24)**	B, 85 °C	24	**54**	37
4	X = CE_2 **(30)**	B, 90 °C	22	**55**	46
5[b]	 **12**	B, 85 °C	22.5	 **56**	39
6[c]	 **17**	C, 85 °C	23.5	 **59**	19
7	 **13**	$Pd_2(dba)_3$-$CHCl_3$ (5 mol%) PPh_3 (20 mol%) Ag_2CO_3 (3 equiv) xylene, 90 °C	14	 **62**	94
8	 **16**	C, 85 °C	20	 **63** **1:1 diastereomers**	55
9	 **(S, S)-16**	C, 85 °C	21	 **(S, S)-63**	55
10	 **23**	B[d] 85 °C	26	 **64**	67
11	 **(S)-23**	B[d] 85 °C	14.5	 **(S)-64**	67
12[e]	 **28**	C, 85 °C	13.5	 **65**	33
13	 **26**	A, 85 °C	23	 **68**	60
					
14	X = O **(22)**	A, 83 °C	15	**69**	57
15	X = CE_2 **(29)**	A, 85 °C	11	**70**	56
16	 **11**	A,[f] 80 °C	5	 **71**	38

the diastereomers of **63** were formed (entry 8, Table 2). (*S*,*S*)-**16** was synthesized and afforded the optically pure product (*S*,*S*)-**63**, with the retention of the absolute configuration of the chiral center,[31] in 55% yield under the same condition. Its ^{1}H NMR spectrum showed the signal of the vinylic protons at 5.36 (s, 1H) and 5.20 (s, 1H) ppm, respectively, which led us to assign the other set of signal in the ^{1}H NMR spectrum of **63** to the meso diastereomer (entry 9, Table 2). Similarly, from **23** and the corresponding optically pure precursor (*S*)-**23**, bicyclic product **64** and (*S*)-**64**, respectively, could be prepared successfully. Thus, bicyclic products with different stereochemistry in different rings can also be synthesized in one step (entries 10 and 11, Table 2).

Scheme 14



Under condition C, **28** could give 5,6-bicyclic product **65** in 33% yield together with monocyclic products **66** and **67** in 8% and 3% yields, respectively (entry 12, Table 1 and Figure 1). In this reaction, the ratio of **65**/**66**/**67** did not change with prolonged reaction time. The attempt to prepare fused 5, 7-bicycles failed. From **26**, the reaction only gave monocyclic product **68** under condition A (entry 13, Table 2).

Apart from the results given above, we tried and failed to construct fused 6, 14- and 6, 21-bicyclic products from 31 and 33. Under the usual reaction conditions, **31** and **33** gave monocyclic products **72** and **73**, respectively (Scheme 14).

Oxidative Addition Reaction of 1,1-Dichloro-1-alkene. To test the possibility of bicyclic carbopalladation of 1,1-dichloro-1-alkenes, **14** was submitted to condition A. After reacting for 13 h at 80 °C, the starting material was almost quantitatively recovered. On the other hand, when a 1:1 mixture of **10** and **14** was reacted under the same conditions, the bicyclic product **36** could be isolated in 64% yield together with quantitative recovery of starting material **14**. Obviously, the bicyclic carbopalladation of 1,1-dichloro-1-alkenes did not proceed due to the low reactivity of carbon−chlorine bonds toward palladium in the oxidative addition reaction (Scheme 15).[32]

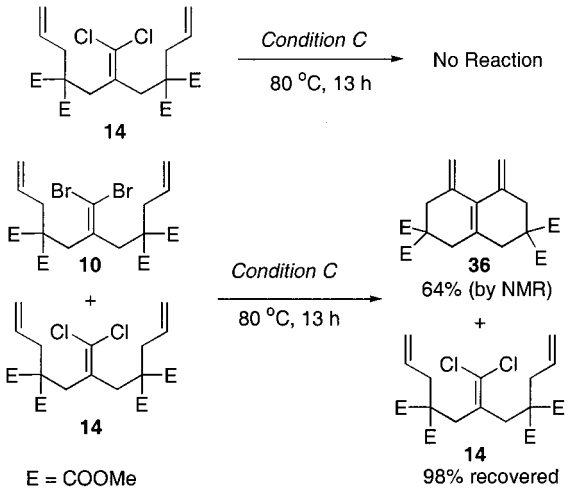
Mechanism. For the propose of mechanistic study, the cyclization of the monocyclic product **37**, which was prepared from monocyclization of **10** under the catalysis of $Pd(PPh_3)_4$ (75% yield, entry 12, Table 1), was attempted under condition A for 16 h and the bicyclic product **36** was formed in 92% ^{1}H NMR yield (Scheme 16).

Furthermore, when compound **10** was submitted to condition A for 0.5 h, the monocyclic product **37** could be isolated in 79% yield. At this point, the bicyclic product **36** was not formed. Thus, a stepwise cyclization catalytic

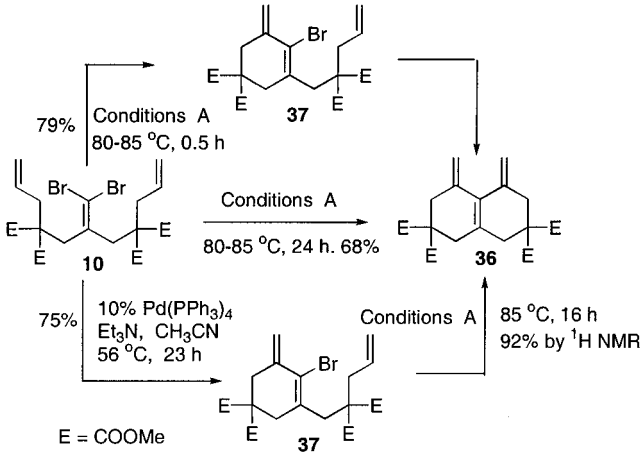
(31) HPLC (Column: Chiralcel OD (Daicel); Eluent: *n*-hexane/2-propanol = 100:4) showed a simple peak for these optically active compounds.

(32) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. In *Purification of Laboratory Chemicals*, 2nd ed.; Pergamon: Oxford, 1980.

Scheme 15



Scheme 16



cycle is proposed for this reaction as summarized in Scheme 17.

Conclusion

(1) The oxidative addition reaction of 1,1-dihalo-1-alkenes is a coordination-directed highly regioselective reaction;

(2) An α-dehalopalladation reaction was observed for the first time in the reaction of 1,1-dibromo-2,2-diphenylethene or 1,1-dibromo-2-phenylpropene with a stoichiometric amount of $Pd(PPh_3)_4$. However, the α-dehalopalladation reaction was not observed in any precursors for bicyclization under the reaction conditions tested, probably due to the fast intramolecular carbopalladation reaction of the C=C bonds;

(3) A new and highly convenient bicyclic carbopalladation reaction was developed. By this protocol, a serial of bicycles, i.e., fused 5,6-, 6,6-, 6,7-, and 7,7-bicyclic compounds, can be efficiently prepared. This reaction should open up new and efficient opportunities for the construction of bicyclic products.

(4) Under different reaction conditions, the monocyclization and bicyclization can be controlled;

(5) The bicyclic carbopalladation reaction proceeded in a stepwise manner.

Experimental Section

General Techniques. The ^1H NMR spectra were recorded using $CDCl_3$ as the solvent and internal standard. NMR yields were determined by using methylene bromide as the internal reference. GC yields were determined on Perkin-Elmer autosystem XL using EC-5 (Column: Alltech, 30 m × 0.32 mm, film thickness: 0.25 μm). Unless otherwise stated, all reactions were run under a nitrogen atmosphere. All commercially available reagents were used without further purification unless otherwise stated. All solvents used were of reagent grade and were further dried.[33] Reactions were monitored by TLC. $Pd(PPh_3)_4$,[34] $Pd(OAc)_2$,[35] and $Pd_2(dba)_3-CHCl_3$[36] were prepared as reported.

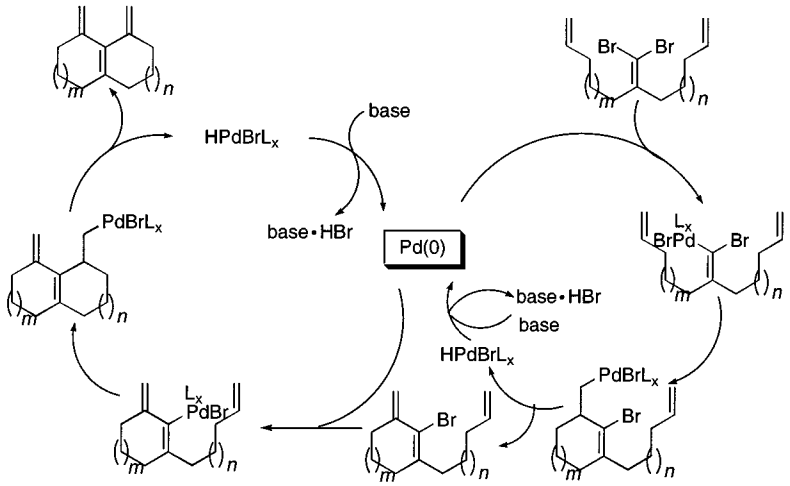
Starting Materials. (1) Preparation of Dimethyl 2-(2′-Propenyl)malonate (3).[37] **Representative Procedure (Procedure A).** To a suspension of NaH (11.00 g, 60% in paraffin oil, 0.28 mol) in THF (200 mL) was added dimethyl malonate (33.00 g, 0.25 mol) slowly through a dropping funnel. After the addition, the mixture was stirred for additional 15 min at room temperature. Then, allyl bromide (30.25 g, 0.25 mol) was added dropwise at room temperature. After 2 h, the reaction mixture was quenched with water, extracted with ether, and washed with brine. The combined organic extracts were dried over $MgSO_4$ and evaporated. The crude product was further purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1) to give **3** (37.10 g, 86%) as a colorless liquid: ^1H NMR δ 5.9−5.6 (m, 1H), 5.25−4.95 (m, 2H), 3.75 (s, 6H), 3.48 (t, J = 7.6 Hz, 1H), 2.66 (t, J = 6.79 Hz, 2H); IR (neat) 2954, 1734, 1638, 1438 cm^{-1}.

(2) 6-(1′,1′-Dibromomethylene)-4,8-dioxa-1,10-undecadiene (15) (Procedure B). To a suspension of NaH (200 mg, 60% in paraffin oil, 5.00 mmol, 20 min) in THF (5 mL) was added allyl alcohol (300 mg, 5.17 mmol) slowly through a dropping funnel. After the addition, the mixture was stirred for an additional 20 min at room temperature. Then **2a** (700 mg, 1.88 mmol) in THF (5 mL) was added dropwise at room temperature. After the mixture was stirred at room temperature for 5 h, the reaction was quenched with water, extracted with ether, and washed with brine. The combined organic extracts were dried over $MgSO_4$ and evaporated. The crude product was further purified by flash column chromatography (petroleum ether/ethyl acetate = 100:1) to give **15** (400 mg, 65%) as a colorless liquid: ^1H NMR δ 5.95−5.70(m, 2H), 5.35−5.0 (m, 4H), 4.15 (s, 4H), 3.93 (m, 4H); MS (70 eV, EI) m/z 327 (3.29) [M^+(2 × ^{81}Br)-H], 325 (3.23) [M^+(^{81}Br, ^{79}Br)-H], 323 (1.05) [M^+(2 × ^{79}Br)-H], 149 (100.00) [M^+ − 2 × Br(1 × ^{81}Br, 1 × ^{79}Br)-CH_2]; IR (neat) 2924, 1448, 1422, 1162 cm^{-1}. Anal. Calcd for $C_{10}H_{14}Br_2O_2$: C, 36.84; H, 4.33. Found: C, 37.05; H, 4.31.

(3) Synthesis of 6-(1′,1′-Dibromomethylene)-3,9-dimethyl-4,8-dioxa-1,10-undecadiene (16). Representative Procedure (Procedure C). To the suspension of NaH (0.93 g, 55% in paraffin oil, 21.31 mmol) in THF (15 mL) was added 3-buten-2-ol (1.40 g, 19.44 mmol) dropwise. After the addition, the mixture was stirred at room temperature for 1.5 h, HMPA (3 mL) was added, and the mixture was cooled to −78 °C with a dry ice−acetone bath. After 5 min, **2a** (2.86 g, 7.69 mmol) in THF (1.0 mL) was introduced at −78 °C, and then the temperature was raised to room temperature slowly and stirred for additional 5 h. The reaction was quenched with water, extracted with ether, and washed with brine. The combined organic extracts were dried over $MgSO_4$ and evaporated. The crude product was further purified by flash column chromatography (petroleum ether/ethyl acetate = 100:1) to afford **16** (1.72 g, 63%) as a colorless liquid: ^1H NMR δ 5.90−5.55 (m, 2H), 5.40−4.90 (m, 4H), 4.4−3.95 (m, 4H), 3.95−3.65 (m, 2H), 1.24 (d, J = 6.44 Hz, 6H); MS (70 eV, EI) m/z (%) 357 (47.42) [M^+H (2 × ^{81}Br)], 355 (100.00) [M^+H (^{81}Br, ^{79}Br)], 353 (53.77) [M^+H (2 × ^{79}Br)]; IR (neat) 2974, 1614, 1444, 1372,

(33) Still, J. K. In *Chemistry of the Metal−Carbon Bond*; Hartley, F., Ed.; John Wiley & Sons: New York, 1987; Vol. 1.
(34) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121−124.
(35) Stephenson, T. A.; Morehouse, S. M.; Powell, A. R.; Heffer, J. P.; Wilkinson, G. *J. Chem. Soc.* **1965**, 3632−3640.
(36) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253−266.
(37) Oppolzer, W.; Gaudin, J.-M.; Birkinshaw, T. N. *Tetrahedron Lett.* **1988**, *29*, 4705−4708.

Scheme 17



1152, 1086 cm^{-1}; HRMS calcd for $C_{12}H_{19}{}^{79}Br_2O_2$ (M^+H) 352.9752, found 352.9765.

(4) 7-(1′,1′-Dibromomethylene)-5,5-bis(methoxycarbonyl)-1,10-undecadiene (26). Representative Procedure (Procedure D). A solution of **25** (0.50 g, 1.05 mmol) in THF (2 mL) was treated with allylzinc chloride, which was prepared from zinc−copper couple (3.00 g) and allyl chloride (2 mL) in DMSO (10 mL).[14] After being stirred at room temperature for 19 h, the reaction was quenched with water, neutralized with HCl (2 N, 3 mL), extracted with ether (3 × 10 mL), and washed with brine. The combined organic extracts were dried over $MgSO_4$ and evaporated. The crude product was further purified by flash column chromatography (petroleum ether/ethyl acetate = 20:1) to give **26** (0.34 g, 74%) as a colorless liquid together with the recovered **25** (0.10 g). **26**: ^{1}H NMR δ 5.9−5.6 (m, 2H), 5.15−4.80 (m, 4H), 3.72 (s, 6H), 3.05 (s, 2H), 2.4−2.1 (m, 4H), 2.1−1.9 (m, 4H); MS (70 eV, EI) *m*/*z* 441 (0.88) [M^+H (2 × ^{81}Br)], 439 (1.57) [M^+H (^{81}Br, ^{79}Br)], 437 (0.90) [M^+H (2 × ^{79}Br)], 185 (100.00) [CH_2=$CHCH_2CH_2C(COOCH_3)_2{}^+$]; IR (neat) 2950, 1730, 1636, 1438, 1276 cm^{-1}; HRMS calcd for $C_{16}H_{22}{}^{79}Br_2O_4$ (M^+) 435.9885, found 435.9899.

See the Supporting Information for all the experimental details and spectra data of other starting materials.

Carbopalladation Reaction of 2,2-Dibromo-1-phenylstyrene with a Stoichiometric Amount of Pd(PPh$_3$)$_4$. To a degassed solution of 2,2-dibromo-1-phenylstyrene (40 mg, 0.12 mmol), K_2CO_3 (82 mg, 0.59 mmol), and *n*-Bu_4NCl (33 mg, 0.12 mmol) in xylene (2 mL) was added Pd(PPh$_3$)$_4$ (137 mg, 0.12 mmol) under N_2. The reaction mixture was stirred at 80−85 °C for 3 h. The residue was filtered to remove the catalyst and the inorganic salts. The filtrate was submitted directly to GC and GC−MS analysis. 1,2-Diphenylacetylene and 1,1-diphenylethene were formed in 18% and 15% yield, respectively, as determined by GC analysis with authentic samples. The starting material was recovered in 6% GC yield.

A similar procedure was performed for the mixture of 1,1-dibromo-2-phenylpropene (87 mg, 0.32 mmol), Pd(PPh$_3$)$_4$ (366 mg, 0.32 mmol), K_2CO_3 (219 mg, 1.59 mmol), and *n*-Bu_4-NCl (88 mg, 0.32 mmol) in xylene (3 mL) at 80−85 °C for 2.5 h to give α-methylstyrene (15%) and 1-phenylpropyne (35%) together with recovered starting material (16%) by GC analysis.

Monocyclization Reaction under the Catalysis of Pd(PPh$_3$)$_4$. (a) Synthesis of 1-Bromo-2-methyl-4,4-bis(methoxycarbonyl)-6-methylenecyclohexene (48). Representative Procedure (Condition A). To a degassed solution of compound **35** (160 mg, 0.42 mmol), K_2CO_3 (575 mg, 4.17 mmol), and *n*-Bu_4NCl (231 mg, 0.83 mmol) in xylene (4 mL) was added Pd(PPh$_3$)$_4$ (48 mg, 10 mol %) under N_2. The reaction mixture was stirred at 80−85 °C for 11 h as monitored by TLC (eluent: petroleum ether/ethyl acetate = 10:1). The residue was passed through a short column of silica gel (eluent: ether) to remove the catalyst and inorganic salts. After evaporation of the solvent, the residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 10:1) to afford compounds **48** (40 mg, 32%) and **49** (32 mg, 32%). **48**: liquid; ^{1}H NMR δ 5.33 (s, 1H), 4.95 (s, 1H), 3.64 (s, 6H), 2.90 (s, 2H), 2.70 (s, 2H), 1.93 (s, 3H); MS (70 eV, EI) *m*/*z* 305 (4.24) [M^+H(^{81}Br)], 303 (4.77) [M^+H(^{79}Br)], 245 (100.00) [M^+(^{81}Br) − COOMe], 243 (96.87) [M^+(^{79}Br) − COOMe]; IR (neat) 2952, 1734, 1626, 1438, 1378 cm^{-1}; HRMS calcd for $C_{12}H_{15}{}^{79}BrO_4$ (M^+) 302.0153, found 302.0182.

1-Bromo-2-methyl-4-methoxycarbonyl-6-methylenecyclohexene (49): liquid; ^{1}H NMR δ 5.38 (s, 1H), 4.98 (s, 1H), 3.70 (s, 3H), 2.95−2.35 (m, 5H), 2.0 (s, 3H); MS (70 eV, EI) *m*/*z* 246 (23.07) [M^+(^{81}Br)], 244 (23.56) [M^+(^{79}Br)], 106 (100.00) [M^+ − Br − COOMe]; IR (neat) 2950, 1730, 1626, 1438, 1376, 1272 cm^{-1}; HRMS calcd for $C_{10}H_{13}{}^{79}BrO_2$ (M^+) 244.0099, found 244.0094.

(b) 1-Bromo-2-methyl-4,4-bis(methoxycarbonyl)-6-methylenecyclohexene (48). A mixture of compound **35** (250 mg, 0.65 mmol), Et_3N (0.25 mL), and Pd(PPh$_3$)$_4$ (45 mg, 6 mol %) in CH_3CN (4 mL) was refluxed for 13 h to afford **48** (120 mg, 61%).

(c) 1-Bromo-2-(2′,2′-bis(methoxycarbonyl)-4′-pentenyl)-4,4-bis(methoxycarbonyl)-6-methylenecyclohexene (37). A solution of **10** (500 mg, 0.90 mmol), Et_3N (0.50 mL, 3.60 mmol), and Pd(PPh$_3$)$_4$ (105 mg, 10 mol %) in CH_3CN (6 mL) was stirred at 56 °C for 23 h to afford **37** (320 mg, 75%) as a yellowish liquid: ^{1}H NMR δ 5.95−5.70 (m, 1H), 5.52 (s, 1H), 5.18−4.95 (m, 3H), 3.72 (s, 12H), 3.20 (s, 2H), 2.95 (s, 2H), 2.70 (s, 2H), 2.67 (d, J = 7.61 Hz, 2H); MS (70 eV, EI) *m*/*z* 474 (2.03) [M^+(^{81}Br)], 472 (2.03) [M^+(^{79}Br)], 59 (100.00) [$^+COOCH_3$]; IR (neat) 2934, 1732, 1438, 1260−1230 cm^{-1}; HRMS calcd for $C_{20}H_{25}{}^{79}BrO_8$ (M^+) 472.0733, found 472.0727.

Bicyclization Reaction under the Catalysis of Palladium(0). (a) Synthesis of 2,10-Dimethylene-4,4,8,8-tetrakis(methoxycarbonyl)bicyclo[4.4.0]dec-1(6)-ene (36). Condition A. A degassed solution of compound **10** (52 mg, 0.09 mmol), Pd(PPh$_3$)$_4$ (11 mg, 10 mol %), K_2CO_3 (130 mg, 0.94 mmol), and *n*-Bu_4NCl (52 mg, 0.19 mmol) in xylene (2 mL) was stirred at 80−85 °C for 24 h to afford compound **36** (25 mg, 68%) as a white solid: mp 58−9 °C (ethyl acetate); ^{1}H NMR δ 5.23 (s, 2H), 5.04 (s, 2H), 3.70 (s, 12H), 2.82 (s, 4H), 2.63 (s, 4H); MS (70 eV, EI) *m*/*z* 392 (0.7) [M^+], 43 (100.00) [$C_3H_7{}^+$]; IR (KBr) 2958, 1730, 1428 cm^{-1}. Anal. Calcd for $C_{20}H_{24}O_8$: C, 61.22; H, 6.16. Found: C, 61.03; H, 6.04.

(b) Synthesis of 2,10-Dimethylene-4,8-dioxabicyclo[4.4.0]dec-1(6)-ene (52). Condition A. A degassed solution of compound **15** (75 mg, 0.23 mmol), Pd(PPh$_3$)$_4$ (27 mg, 0.02 mmol), K_2CO_3 (317 mg, 2.30 mmol), and *n*-Bu_4NCl (128 mg, 0.46 mmol) in xylene (5 mL) was stirred at 85 °C for 15.5 h to afford **52** (31 mg, 83%) as a white solid: mp 80 °C (acetone); ^{1}H NMR δ 5.40 (s, 2H), 5.12 (s, 2H), 4.21 (s, 4H), 4.15 (s, 4H); MS (70 eV, EI) *m*/*z* 164 (60.45) [M^+], 133 (100.00) [$M^+ - CH_2O$

− H]; IR (KBr) 2922, 1438, 1164, 1094, 1056 cm^{-1}. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.49; H, 7.81.

(c) Synthesis of 2,10-Bis(methylene)-4-oxa-8,8-bis-(methoxycarbonyl)bicyclo[4.4.0] dec-1(6)-ene (53). Condition A. A degassed solution of compound **21** (65 mg, 0.148 mmol), $Pd_2(dba)_3$−$CHCl_3$ (8 mg, 0.08 mmol), K_2CO_3 (103 mg, 0.75 mmol), and dppe (12 mg, 0.03 mmol) in DMF (2 mL) was stirred at 100 °C for 11 h. Flash chromatography (petroleum ether/ethyl acetate = 15:1) provided compound **53** (26 mg, 63%) as a white solid: mp 85−6 °C (acetone−hexane); ^1H NMR δ 5.33 (s, 1H), 5.30 (s, 1H), 5.10 (s, 1H), 5.08 (s, 1H), 4.18 (s, 2H), 4.17 (s, 2H), 3.71 (s, 6H), 2.85 (s, 2H), 2.52 (s, 2H); IR (KBr) 2920, 1731, 1643, 1439, 1083 cm^{-1}; MS (70 eV, EI) *m/z* 278 (45.92) [M^+], 131 (100.00) [M^+H − 2 × COOMe − CH_2O]. Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.51; H, 6.36.

(d) Synthesis of 2-(*E*)-Benzylidene-10-methylene-4-oxa-8,8-bis(methoxycarbonyl)bicyclo[4.4.0]dec-1(6)-ene (54). Condition A. A degassed solution of compound **24** (200 mg, 0.39 mmol), $Pd(PPh_3)_4$ (45 mg, 0.04 mmol), K_2CO_3 (268 mg, 1.94 mmol), and *n*-Bu_4NCl (108 mg, 0.39 mmol) in xylene (2.5 mL) was stirred at 85 °C for 24 h to afford **54** (50 mg, 37%) as a solid: mp 132 °C ($CHCl_3$); ^1H NMR δ 7.45−7.02 (m, 5H), 6.95(s, 1H), 5.36 (s, 1H), 5.16 (s, 1H), 4.50 (s, 2H), 4.19 (s, 2H), 3.73 (s, 6H), 2.91 (s, 2H), 2.57 (s, 2H); IR (KBr) 2926, 1730, 1634, 1540, 1434, 1068 cm^{-1}; MS (70 eV, EI) *m/z* 354 (10.23) [M^+], 91 (100.00) [$PhCH_2^+$]. Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.13; H, 6.22.

(e) Synthesis of 2-Methylene-10-(*E*)-benzylidene-4,4,8,8-tetrakis(methoxy-carbonyl)bicyclo[4.4.0]dec-1(6)-ene (55). Condition A. A degassed solution of compound **30** (58 mg, 0.09 mmol), $Pd(PPh_3)_4$ (10 mg, 0.01 mmol), K_2CO_3 (64 mg, 0.46 mmol), and *n*-Bu_4NCl (26 mg, 0.09 mmol) in xylene (1.5 mL) was stirred at 90 °C for 22 h to afford **55** (20 mg, 46%) as a liquid: ^1H NMR δ 7.4−7.1 (m, 5H), 6.83 (s, 1H), 5.29 (s, 1H), 5.09 (s, 1H), 3.69 (s, 6H), 3.52 (s, 6H), 3.12 (s, 2H), 2.88 (s, 2H), 2.67 (s, 2H), 2.63 (s, 2H); MS (70 eV, EI) *m/z* 468 (100.00) [M^+]; IR (neat) 2952, 1732, 1436 cm^{-1}; HRMS calcd for $C_{26}H_{28}O_8$ (M^+) 468.1784, found 468.1783.

(f) Synthesis of 2,10-Bis((*E*)-benzylidene)-4,4,8,8-tetrakis(methoxycarbonyl)bicyclo[4.4.0]dec-1(6)-ene (56). Conditions A. A degassed solution of compound **12** (71 mg, 0.11 mmol), $Pd(PPh_3)_4$ (11 mg, 0.01 mmol), K_2CO_3 (69 mg, 0.50 mmol), and *n*-Bu_4NCl (28 mg, 0.10 mmol) in xylene (2 mL) was stirred at 85 °C for 22.5 h to afford **56** (21 mg, 39%) and **57** (5 mg, 9%). **56**: mp 168−170 °C (ethyl acetate−hexane); ^1H NMR δ 7.35−7.00 (m, 10H), 6.82 (s, 2H), 3.47 (s, 12H), 3.13 (s, 4H), 2.61 (s, 4H); IR (KBr) 2952, 1732, 1438 cm^{-1}; MS (70 eV, EI) *m/z* 544 (0.23) [M^+], 45 (100.00) [$COOH^+$]. Anal. Calcd for $C_{32}H_{32}O_8$: C, 70.58; H, 5.92. Found: C, 70.62; H, 5.97.

3-(*E*)-Benzylidiene-5,5-bis(methoxycarbonyl)-1-(2′,2′-bis(methoxycarbonyl)-5′-phenyl-4′(*E*)-pentenyl)cyclohexene (57): liquid; ^1H NMR δ 7.45−7.1 (m, 10H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.28 (s, 1H), 6.07 (dt, *J* = 15.64, 7.36 Hz, 1H), 5.68 (s, 1H), 3.71 (s, 4H), 3.69 (s, 12H), 3.02 (s, 2H), 2.74 (d, *J* = 7.45 Hz, 2H); IR (neat) 2952, 1728, 1438, 1264−1098 cm^{-1}; MS (70 eV, EI) *m/z* 531 (0.23) [M^+ − CH_3], 45 (100) [^+COOH]; HRMS calcd for $C_{32}H_{34}O_8$ (M^+) 546.2254, found 546.2226.

(g) Synthesis of 2,10-Bis((*E*)-benzylidene)-4,8-dioxabicyclo[4.4.0]dec-1(6)-ene (59). Conditions A. A degassed solution of compound **17** (250 mg, 0.52 mmol), $Pd(PPh_3)_4$ (30 mg, 0.03 mmol), K_2CO_3 (362 mg, 2.62 mmol), and *n*-Bu_4NCl (145 mg, 0.52 mmol) in xylene (3 mL) was stirred at 85 °C for 23.5 h to afford **59** (31 mg, 19%), **60** (40 mg, 20%), and **61** (20 mg, 12%). **59**: mp 110−112 °C (hexane); ^1H NMR δ 7.45−7.05 (m, 10H), 7.00 (s, 2H), 4.52 (s, 4H), 4.13 (s, 4H); IR (KBr) 2920, 1446, 1378, 1118 cm^{-1}; MS (70 eV, EI) *m/z* 316 (28.69) [M^+], 91(100.00) [$PhCH_2^+$]; HRMS calcd for $C_{22}H_{20}O_2$ (M^+) 316.1463, found 316.1455.

1-Bromo-2-(2′-oxa-5′-phenyl-4′(*E*)-pentenyl)-4-oxa-6(*E*)-benzylidenecyclohexene (60): liquid; ^1H NMR δ 7.6−7.1 (m, 10H), 7.02 (s, 1H), 6.65 (d, *J* = 15.98 Hz, 1H), 6.29 (dt, *J* = 15.9, 6.03 Hz, 1H), 4.63 (s, 2H), 4.44 (s, 2H), 4.40 (s, 2H), 4.18 (dd, *J* = 6.0, 1.42 Hz, 2H); IR (neat) 2924, 2850, 1672, 1624, 1492, 1448, 1358, 1080 cm^{-1}; MS (70 eV, EI) *m/z* 398 (0.9) [$M^+(^{81}Br)$], 396 (0.95) [$M^+(^{79}Br)$], 117 (100.00) [$PhC_3H_4^+$]; HRMS calcd for $C_{22}H_{21}{}^{79}BrO_2$ (M^+) 396.0725, found 396.0753.

3-(*E*)-Benzylidene-5-oxa-1-(2′-oxa-5′-phenyl-4′(*E*)-pentenyl)cyclohexene (61): mp 50−51 °C (hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50−7.10 (m, 10H), 6.54 (d, *J* = 16.0 Hz, 1H), 6.25−6.05 (m, 3H), 4.57 (d, *J* = 1.56 Hz, 2H), 4.21 (s, 2H), 4.09 (dd, *J* = 6.1, 1.4 Hz, 2H), 4.02 (s, 2H); IR (KBr) 2922, 2842, 1670, 1596, 1492, 1446, 1078 cm^{-1}; MS (70 eV, EI) *m/z* 318 (1.66) [M^+], 105 (100.00) [$PhC_2H_4^+$]; HRMS calcd for $C_{22}H_{22}O_2$ (M^+) 318.1620, found 318.1596.

(h) Synthesis of 1-Bromo-2-(2′,2′,5′-tris(methoxycarbonyl)-4′(*E*)-pentenyl)-4,4-bis(methoxycarbonyl)-6-((*E*)-methoxycarbonylmethylene)cyclohexene (62). Condition A. A degassed solution of compound **13** (70 mg, 0.10 mmol), $Pd_2(dba)_3$−$CHCl_3$ (6 mg, 0.06 mmol), Ag_2CO_3 (86 mg, 0.31 mmol), and PPh_3 (12 mg, 0.05 mmol) in xylene (2 mL) was stirred at 90 °C for 14 h to afford **62** (58 mg, 94%) as a white solid: mp 90−1 °C (ethyl acetate); ^1H NMR δ 6.89 (dt, *J* = 15.27, 7.71 Hz, 1H), 6.44 (s, 1H), 5.88 (d, *J* = 15.5 Hz, 1H), 3.76 (s, 3H), 3.75(s, 6H), 3.73(s, 3H), 3.72 (s, 6H), 3.57 (s, 2H), 3.28(s, 2H), 2.83 (s, 2H), 2.82 (d, *J* = 6.43 Hz, 2H); IR (KBr) 2952, 1732, 1610, 1436, 1366 cm^{-1}; MS (70 eV, EI) *m/z* 591 (6.49) [$M^+H(^{81}Br)$], 589 (6.29) [$M^+H(^{79}Br)$], 59 (100.00) [$COOCH_3^+$]; HRMS calcd for $C_{24}H_{30}{}^{79}BrO_{12}$ (M^+H) 589.0921, found 589.0974.

(i) Synthesis of 2,10-Dimethylene-3,9-dimethyl-4,8-dioxabicyclo[4.4.0]dec-1(6)-ene (63). Condition A. A degassed solution of compound **16** (100 mg, 0.28 mmol), $Pd(PPh_3)_4$ (16 mg, 5 mol %), K_2CO_3 (196 mg, 1.42 mmol), and *n*-Bu_4NCl (78 mg, 0.28 mmol) in xylene (1.5 mL) was stirred at 85 °C for 20 h. Flash chromatography (petroleum ether/ethyl acetate = 40:1) afforded **63** (30 mg, 55%) as a white solid, mp 50−2 °C (acetone−hexane). *meso*-**63**: ^1H NMR δ 5.31 (s, 2H), 5.15 (s, 2H), 4.19 (dd, *J* = 45.93, 18.32 Hz, 4H), 4.14 (q, *J* = 6.02 Hz, 2H), 1.38 (d, *J* = 6.40 Hz, 6H); (R*, R*)-**63**: ^1H NMR δ 5.36 (s, 2H), 5.20 (s, 2H), 4.19 (dd, *J* = 45.93, 18.32 Hz, 4H), 4.14 (q, *J* = 6.02 Hz, 2H), 1.41 (d, *J* = 6.35 Hz, 6H); MS (70 eV, EI) *m/z* 192 (21.37) [M^+], 147 (100.00) [M^+ − OC_2H_5]; IR (KBr) 2976, 1446, 1408, 1062 cm^{-1}; HRMS calcd for $C_{12}H_{16}O_2$ (M^+) 192.1150, found 192.1154.

(j) Synthesis of 2,10-Dimethylene-3(*S*),9(*S*)-dimethyl-4,8-dioxabicyclo[4.4.0]dec-1(6)-ene ((*S*,*S*)-63). Condition A. A degassed solution of compound (*S*,*S*)-**16** (50 mg, 0.14 mmol), $Pd(PPh_3)_4$ (8 mg, 5 mol %), K_2CO_3 (98 mg, 0.71 mmol), and *n*-Bu_4NCl (40 mg, 0.14 mmol) in xylene (1.5 mL) was stirred at 85 °C for 21 h. Flash chromatography (petroleum ether/ethyl acetate = 40:1) afforded (*S*,*S*)-**63** (15 mg, 55%) as a white solid: mp 50−2 °C (acetone−hexane); ^1H NMR δ 5.36 (s, 2H), 5.20 (s, 2H), 4.18 (dd, *J* = 45.56, 17.7 Hz, 4H), 4.15 (q *J* = 6.02 Hz, 2H), 1.41 (d, *J* = 6.29 Hz, 6H); IR (KBr) 2976, 1446, 1408, 1062 cm^{-1}; $[\alpha]^{20}{}_D$ = +83.0° (*c* 0.2, chloroform).

(k) Synthesis of 2,10-Dimethylene-3-methyl-4-oxa-8,8-bis(methoxycarbonyl)bicyclo[4.4.0]dec-1(6)-ene (64). Condition A. A degassed solution of compound **23** (150 mg, 0.33 mmol), $Pd(PPh_3)_4$ (19 mg, 5 mol %), K_2CO_3 (229 mg, 1.66 mmol), and *n*-Bu_4NBr (107 mg, 0.33 mmol) in xylene (2 mL) was stirred at 85 °C. After the mixture was stirred for 18 h, another portion of $Pd(PPh_3)_4$ (19 mg, 5 mol %) was added under N_2, and then the mixture was stirred for an additional 8 h at 85 °C. Flash chromatography afford **64** (66 mg, 67%) as a white solid: mp 50−1 °C (acetone); ^1H NMR δ 5.30 (s, 1H), 5.28 (s, 1H), 5.15 (s, 1H), 5.09 (s, 1H), 4.45−4.0 (m, 3H), 3.71 (s, 3H), 3.70 (s, 3H), 2.86 (dd, *J* = 22.30, 13.22 Hz, 2H), 2.50 (dd, *J* = 42.24, 17.89 Hz, 2H), 1.36 (d, *J* = 6.4 Hz, 3H); MS (70 eV, EI) *m/z* 292 (22.61) [M^+], 43 (100.00) [$C_3H_7^+$]; IR (KBr) 2954, 1732, 1436, 1082 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.50; H 7.02.

(l) Synthesis of 2,10-Dimethylene-3(*S*)-methyl-4-oxa-8,8-bis(methoxycarbonyl)bicyclo[4.4.0]dec-1(6)-ene ((*S*)-64). Condition A. A degassed solution of compound (*S*)-**23**

(30 mg, 0.07 mmol), $Pd(PPh_3)_4$ (4 mg, 5 mmol %), K_2CO_3 (46 mg, 0.33 mmol), and *n*-Bu_4NBr (22 mg, 0.07 mmol) in xylene (1 mL) was stirred at 85 °C. After the mixture was stirred for 11.5 h, another portion of $Pd(PPh_3)_4$ (4 mg, 5 mol %) was added under N_2, and then the mixture was stirred for an additional 3 h at 85 °C. Flash chromatography afforded (*S*)-**64** (13 mg, 67%) as a colorless liquid: ^{1}H NMR data are the same as those for **64**; $[\alpha]^{20}_D = +23.2°$ (*c* 0.466, chloroform).

(m) Synthesis of 2,9-Bis(methylene)-4,4-bis(methoxycarbonyl)bicyclo[4.3.0]non-1(5)-ene (65). Conditions A. A degassed solution of compound **28** (400 mg, 0.94 mmol), $Pd(PPh_3)_4$ (54 mg, 5 mol %), K_2CO_3 (654 mg, 4.74 mmol), and *n*-Bu_4NCl (262 mg, 0.95 mmol) in xylene (2 mL) was stirred at 85 °C for 13.5 h to afford **65** (80 mg, 33%), **66** (24 mg, 8%), and **67** (10 mg, 3%). **65**: liquid; ^{1}H NMR δ 5.35 (s, 1H), 5.09 (s, 1H), 5.03 (s, 1H), 4.86 (s, 1H), 3.70 (s, 6H), 2.85 (s, 2H), 2.77 (s, 2H), 2.70−2.50 (m, 2H), 2.50−2.30 (m, 2H); MS (70 eV, EI) *m*/*z* 262 (19.91) [M^+], 203 (100.00) [$M^+ - COOCH_3$]; IR (neat) 2952, 1732, 1638, 1436 cm^{-1}; HRMS calcd for $C_{15}H_{18}O_4$ (M^+) 262.1205, found 262.1219.

2-Bromo-1-(2′,2′-bis(methoxycarbonyl)-4′-pentenyl)-3-methylenecyclopentene (66): liquid; ^{1}H NMR δ 5.90−5.65 (m, 1H), 5.18−4.95 (m, 3H), 4.85 (s, 1H), 3.70 (s, 6H), 3.03 (s, 2H), 2.62 (s, 2H), 2.60 (s, 2H), 2.45−2.25 (m, 2H); MS (70 eV, EI) *m*/*z* 343 (1.43) [$M^+(^{81}Br) - H$], 341 (1.51) [$M^+(^{79}Br) - H$], 203 (100.00) [$M^+ - Br - COOCH_3 - H$]; IR (neat) 2950, 1732, 1630, 1438 cm^{-1}; HRMS calcd for $C_{15}H_{19}{}^{79}BrO_4$ (M^+) 342.0467, found 342.0461.

2-Bromo-1-(3′-butenyl)-5,5-bis(methoxycarbonyl)-3-methylenecyclohexene (67): liquid; ^{1}H NMR δ 5.95−5.70 (m, 1H), 5.44 (s, 1H), 5.65−4.90 (m, 3H), 3.70 (s, 6H), 2.98 (s, 2H), 2.79 (s, 2H), 2.55−2.32 (m, 2H), 2.32−2.10 (m, 2H); MS (70 eV, EI) *m*/*z* 343 (1.83) [$M^+(^{81}Br) - H$], 341 (1.97) [$M^+(^{79}Br) - H$], 243 (100.00) [$M^+(^{81}Br) - COOMe - C_3H_6$], 241 (92.72) [$M^+(^{81}Br) - COOMe - C_3H_6$]; IR (neat) 2950, 1734, 1614, 1438, 1256 cm^{-1}; HRMS for $C_{15}H_{19}{}^{79}BrO_4$ (M^+) calcd 342.0467, found 342.0490.

(n) Synthesis of 2-Bromo-1-(2′,2′-bis(methoxycarbonyl)-5′-hexenyl)-3-methylenecyclopentene (68). Condition A. A degassed solution of compound **26** (54 mg, 0.12 mmol), $Pd(PPh_3)_4$ (14 mg, 10 mol %), K_2CO_3 (170 mg, 1.23 mmol), and *n*-Bu_4NCl (68 mg, 2.45 mmol) in xylene (1 mL) was stirred at 85 °C for 23 h to afford **68** (26 mg, 60%) as a liquid: ^{1}H NMR δ 5.95−5.5 (m, 1H), 5.2−4.90 (m, 3H), 4.85 (s, 1H), 3.72 (s, 6H), 3.05 (s, 2H), 2.75−2.45 (m, 2H), 2.4−2.15 (m, 2H), 2.15−1.75 (m, 4H); IR (neat) 2950, 1730, 1632, 1436, 1276 cm^{-1}; MS (70 eV, EI) *m*/*z* 358 (9.22) [$M^+(^{81}Br)$], 356 (9.48) [$M^+(^{79}Br)$], 217 (100.00) [$M^+ - Br - COOCH_3 - H$]; HRMS calcd for $C_{16}H_{21}{}^{79}BrO_4$ (M^+) 356.0623, found 356.0596.

(o) Synthesis of 2,11-Bis(methylene)-9-oxa-5,5-bis(methoxycarbonyl)bicyclo[5.4.0]undec-1(7)-ene (69). Condition A. A degassed solution of compound **22** (52 mg, 0.12 mmol), $Pd(PPh_3)_4$ (14 mg, 10 mol %), K_2CO_3 (160 mg, 1.16 mmol), and *n*-Bu_4NCl (64 mg, 0.23 mmol) in xylene (3 mL) was stirred at 83 °C for 15 h. Flash chromatography (petroleum ether/dichloromathane = 1.5:1) afforded **69** (19 mg, 57%) as a liquid: ^{1}H NMR δ 5.31 (s, 1H), 5.07 (s, 1H), 4.85 (s, 1H), 4.79 (s, 1H), 4.21 (s, 4H), 3.72 (s, 6H), 2.55 (s, 2H), 2.45−2.15 (m, 4H); MS (70 eV, EI) *m*/*z* 292 (100.00) [M^+]; IR (neat) 2952, 1728, 1448, 1106 cm^{-1}; HRMS calcd for $C_{16}H_{20}O_5$ (M^+) 292.1311, found 292.1311.

(p) Synthesis of 2,11-Bis(methylene)-5,5,9,9-tetrakis(methoxycarbonyl)bicyclo[5.4.0]undec-1(7)-ene (70). Condition A. A degassed solution of compound **29** (80 mg, 0.14 mmol), $Pd(PPh_3)_4$ (16 mg, 10 mol %), K_2CO_3 (190 mg, 1.38 mmol), and *n*-Bu_4NCl (85 mg, 0.31 mmol) in xylene (4 mL) was stirred at 85 °C for 11 h. After purification (petroleum ether/dichloromathane = 1.5:1), the reaction afforded **70** (32 mg, 56%) as a solid: mp 90−2 °C (ethyl acetate); ^{1}H NMR δ 5.24 (s, 1H), 5.07 (s, 1H), 4.87 (s, 1H), 4.74 (s, 1H), 3.73 (s, 6H), 3.69 (s, 6H), 2.82 (s, 2H), 2.75 (s, 2H), 2.72 (s, 2H), 2.40−2.22 (m, 2H), 2.20−2.15 (m, 2H); MS (70 eV, EI) *m*/*z* 406 (2.15) [M^+], 227 (100.00) [$M^+H - 2 \times COOCH_3 - 2 \times OCH_3$]; IR (KBr) 2932, 1738, 1436 cm^{-1}; HRMS calcd for $C_{21}H_{26}O_8$ (M^+) 406.1628, found 406.1628.

(q) Synthesis of 2,12-Bis(methylene)-5,5,9,9-tetrakis(methoxycarbonyl)bicyclo[5.5.0]dodec-1(7)-ene (71). Condition A. A degassed solution of compound **11** (100 mg, 0.17 mmol), $Pd(PPh_3)_4$ (20 mg, 10 mol %), Ag_2CO_3 (115 mg, 0.42 mmol), and *n*-Bu_4NCl (95 mg, 0.34 mmol) in xylene (4.5 mL) was stirred at 80 °C for 5 h. After purification (petroleum ether/dichloromathane = 1.5:1), the reaction afforded **71** (27 mg, 38%) as a liquid: ^{1}H NMR δ 5.05 (s, 2H), 4.79 (s, 2H), 3.72 (s, 12H), 2.83 (s, 4H), 2.50−2.35 (m, 4H), 2.25−2.10 (m, 4H); MS (70 eV, EI) *m*/*z* 420 (5.95) [M^+], 241 (100.00) [$M^+H - 2 \times COOCH_3 - 2 \times OCH_3$]; IR (neat) 2954, 1728, 1496 cm^{-1}; HRMS calcd for $C_{22}H_{28}O_8$ (M^+) 420.1784, found 420.1778.

(r) Synthesis of 2-Bromo-1-(2′,2′,9′,9′-tetrakis(methoxycarbonyl)-19′-eicosenyl)-5,5-bis(methoxycarbonyl)-3-methylenecyclohexene (72). Condition A. A degassed solution of compound **31** (132 mg, 0.15 mmol), $Pd(PPh_3)_4$ (9 mg, 5 mol %), K_2CO_3 (104 mg, 0.75 mmol), and *n*-Bu_4NCl (42 mg, 0.15 mmol) in xylene (1.5 mL) was stirred at 85 °C for 12 h. After purification (petroleum ether/ethyl acetate = 6:1), the reaction afforded **72** (73 mg, 61%) as a liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.9−5.65 (m, 1H), 5.45 (s, 1H), 5.05 (s, 1H), 5.05−4.75 (m, 2H), 3.64 (s, 6H), 3.63 (s, 6H), 3.62 (s, 6H), 3.11 (s, 2H), 2.88 (s, 2H), 2.60 (s, 2H), 2.05−1.85 (m, 2H), 1.85−1.60 (m, 6H), 1.40−1.15 (m, 18H), 1.15−0.85 (m, 4H); MS (70 eV, EI) *m*/*z* 719 (74.27) [$M^+ - Br$], 145 (100.00) [$^+CH_3C(COOMe)_2$]; IR (neat) 2926, 1730, 1436 cm^{-1}; HRMS calcd for $C_{39}H_{59}{}^{79}BrO_{12}$ (M^+) 798.3190, found 798.3179.

(s) Synthesis of 2-Bromo-1-(2′,2′-bis(methoxycarbonyl)-12′-tridecenyl)-5,5-bis(methoxycarbonyl)-3-methylenecyclohexene (73). Condition A. A degassed solution of compound **33** (200 mg, 0.30 mmol), $Pd(PPh_3)_4$ (17 mg, 5 mol %), K_2CO_3 (208 mg, 1.51 mmol), and *n*-Bu_4NCl (83 mg, 0.30 mmol) in xylene (2 mL) was stirred at 85 °C for 12 h to afford **73** (0.10 g, 57%) as a liquid: ^{1}H NMR δ 5.91−5.69 (m, 1H), 5.51 (s, 1H), 5.12 (s, 1H), 5.05−4.80 (m, 2H), 3.70 (s, 6H), 3.69 (s, 6H), 3.19 (s, 2H), 2.94 (s, 2H), 2.66 (s, 2H), 2.10−1.94 (m, 2H), 1.94−1.70 (m, 2H), 1.50−0.95 (m, 14H); MS (70 eV, EI) *m*/*z* 586 (0.3) [M^+ (^{81}Br)], 584 (0.3) [M^+ (^{79}Br)], 445 (100.00) [$M^+ - Br - COOCH_3 - H$]; IR (neat) 2924, 2854, 1732, 1436 cm^{-1}; HRMS calcd for $C_{28}H_{41}{}^{79}BrO_8$ (M^+) 584.1985, found 584.1998.

Bicyclization of Compound 10 in the Presence of Diphenylmethane. Condition A. A degassed solution of compound **10** (60 mg, 0.11 mmol), $Pd(PPh_3)_4$ (13 mg, 10 mol %), K_2CO_3 (150 mg, 1.09 mmol), *n*-Bu_4NCl (60 mg, 0.22 mmol), and diphenylmethane (18 mg, 0.11 mmol) in xylene (2 mL) was stirred at 83 °C for 16 h to afford compounds **36** (26 mg, 62%) and **40** (3 mg, 9%). Diphenylmethane was recovered in 90% NMR yield.

2,10-Dimethylene-4,4,8-tris(methoxycarbonyl)bicyclo-[4.4.0]dec-1(6)-ene (40): liquid; ^{1}H NMR δ 5.26 (s, 1H), 5.20 (s, 1H), 5.06 (s, 1H), 5.04 (s, 1H), 3.72 (s, 3H), 3.69 (s, 6H), 3.05−2.10 (m, 9H); MS (70 eV, EI) *m*/*z* 334 (0.95) [M^+], 155 (100.00) [$M^+H - 2 \times COOCH_3 - 2 \times OCH_3$]; IR (neat) 2920, 1732, 1436 cm^{-1}; HRMS calcd for $C_{18}H_{22}O_6$ (M^+) 334.1417, found 334.1407.

Carbopalladation Reaction of a Mixture of 10 and 14 under Catalysis of $Pd(PPh_3)_4$. Condition A. A degassed solution of compounds **10** (50 mg, 0.09 mmol) and **14** (50 mg, 0.11 mmol), $Pd(PPh_3)_4$ (25 mg, 10 mol %), K_2CO_3 (273 mg, 1.98 mmol), and *n*-Bu_4NCl (110 mg, 0.40 mmol) in xylene (4 mL) was stirred at 80 °C for 13 h. After evaporation of the solvent, methylene bromide (35 μL) was added as the internal reference. **37** was afforded in 64% NMR yield, and **14** was recovered in 98% NMR yield.

Monocyclization Reaction of 10 under the Catalysis of $Pd(PPh_3)_4$. Condition A. A degassed solution of compound **10** (300 mg, 0.54 mmol), $Pd(PPh_3)_4$ (62 mg, 10 mol %), K_2CO_3 (747 mg, 5.41 mmol), and *n*-Bu_4NCl (300 mg, 1.08 mmol) in xylene (5 mL) was stirred at 80−85 °C for 0.5 h to afford **37** (0.201 g, 79%) and recovered **10** (4 mg).

Bicyclization Reaction of 42 under Catalysis of Pd(PPh$_3$)$_4$. Condition A. A degassed solution of compound **37** (40 mg, 0.09 mmol), Pd(PPh$_3$)$_4$ (10 mg, 10 mol %), K_2CO_3 (117 mg, 0.85 mmol), and *n*-Bu$_4$NCl (47 mg, 0.17 mmol) in xylene (2 mL) was stirred at 85 °C for 16 h. After evaporation of the solvent, methylene bromide was added as the internal reference. **36** was afforded in 92% NMR yield.

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Supporting Information Available: The Experimental details of starting materials not listed in the text, the ORTEP presentation of compound **36**, and a set of ^{1}H NMR spectra of all the new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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