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Preparation of Carbocycles via Base-Catalyzed Endo-Mode Cyclization of Allenes

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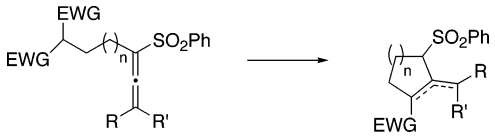

A new and reliable procedure for constructing five- to seven-membered carbocycles via an endo-mode ring-closing reaction of 1-phenylsulfonylallenes with a substituent that has a terminal active methine moiety at the C_1-position has been developed. Trisubstituted 1-phenylsulfonylallenes underwent a similar endo-mode ring-closing reaction to produce the corresponding five- to seven-membered carbocycles, while the formation of six- and seven-membered carbocycles from the corresponding tetrasubstituted allene was not realized. In addition, the introduction of an aromatic ring to the alkyl side chain of the starting allenes made possible the construction not only of normal-sized carbocycles but also an eight-membered framework.

Introduction

The construction of carbocycles is a fundamental and significant process in organic synthesis. Many useful procedures have been developed for preparing mono- as well as multicyclic carbon frameworks. The classical intramolecular Michael-type conjugate addition of carbanion species[1] to activated alkenes and alkynes with an electron-withdrawing group (i.e., Michael acceptors) is still one of the most frequently used methods, despite recent progress in the field of organotransition metal chemistry.[2,3] In contrast to the many examples of intramolecular Michael-type addition of carbanions[1] to alkenes and alkynes possessing an electron-withdrawing group, relatively few examples of the corresponding allene derivatives have been reported.[4−7] In previous papers,[8] we reported a novel and efficient method for the preparation of five- to nine-membered oxacycles **3** (X = O) via the endo-mode intramolecular ring-closing reaction of allenes **2** (X = OH) with a phenylsulfonyl functionality.[9,10] This procedure involves the known [2,3]-sigmatropic rearrangement of the propargyl alcohols **1** with benzenesulfenyl chloride (PhSCl) and oxidation with *m*-chloroperbenzoic acid (*m*-CPBA), followed by a novel base-catalyzed endo-mode ring closure of the resulting allenyl sulfones **2** (R = SO_2Ph) (Scheme 1). A similar

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(1) For leading reviews, see: (a) Winterfeldt, E. *Kontakte (Darmstadt)* **1987**, 37−56; *Chem. Abstr*. **1988**, *109*, 22316d. (b) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Tetrahedron Organic Chemistry Series Vol, 9; Pergamon: Oxford, 1992. (c) Little, R. D.; Masjedizadeh, M. R.; Wallquist, O.; McLoughlin, J. I. *Org. React.* **1995**, *47*, 315−552.

(2) For alkyne, see: (a) Fournet, G.; Balme, G.; Gore, J. *Tetrahedron* **1991**, *47*, 6293−6304. (b) Monteiro, N.; Gore, J.; Balme, G. *Tetrahedron* **1992**, *48*, 10103−10114. (c) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **1993**, 65−68. (d) Cruciani, P.; Aubert, C.; Malacria, M. *Tetrahedron Lett*. **1994**, *35*, 6677−6680. (e) McDonald, F. E.; Olson, T. C. *Tetrahedron Lett*. **1997**, *38*, 7691−7692. (f) Tsukada, N.; Yamamoto, Y. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 2477−2480. (g) Kitagawa, O.; Suzuki, T.; Inoue, T.; Taguchi, T. *Tetrahedron Lett*. **1998**, *39*, 7357−7360. (h) Kadota, I.; Shibuya, A.; Gyoung, Y.; Yamamoto, Y. *J. Am. Chem. Soc*. **1998**, *120*, 10262−10263. (i) Kitagawa, O.; Suzuki, T.; Inoue, T.; Watanabe, Y.; Taguchi, T. *J. Org. Chem*. **1998**, *63*, 9470−9475. (j) Bouyssi, D.; Monteiro, N.; Balme, G. *Tetrahedron Lett*. **1999**, *40*, 1297−1300. (k) Kitagawa, O.; Suzuki, T.; Fujiwara, H.; Fujita, M.; Taguchi, T. *Tetrahedron Lett*. **1999**, *40*, 4585−4588. (l) Kitagawa, O.; Fujiwara, H.; Suzuki, T.; Taguchi, T.; Shiro, M. *J. Org. Chem*. **2000**, *65*, 6819−6825 and references therein.

(3) For allene, see: (a) Besson, L.; Bazin, J.; Gore, J.; Cazes, B. *Tetrahedron Lett*. **1994**, *35*, 2881−2884. (b) Yamamoto, Y.; Al-Masum, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *116*, 6019−6020. (c) Trost, B. M.; Gerusz, V. J. *J. Am. Chem. Soc.* **1995**, *117*, 5156−5157. (d) Meguro, M.; Kamijo, S.; Yamamoto, Y. *Tetrahedron Lett*. **1996**, *37*, 7453−7456 and references therein.

(4) Ma, S. In *Modern Allene Chemistry*; Krause, N., Stephen, A., Hashmi, K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, pp 595−684.

(5) Parsons and co-workers reported the intramolecular Michael-type reaction of allene derivative with a terminal carbanion species. Thus, the ring-closing reaction of dimethyl 4-methyl-6-(phenylsulfinyl)-4,5-hexadiene-1,1-dicarboxylate resulted in the formation of seven-membered oxacycles, instead of the expected carbocycles, presumably due to exo-mode closure by the oxygen atom of the methoxycarbonyl moiety at the sp-hybridized carbon center. The cyclopentane derivative, which would be anticipated by the attack of the terminal carbanion moiety in an exo-mode manner, could not be detected. Pairaudeau, G.; Parsons, P. J.; Underwood, J. M. *Chem. Commun*. **1987**, 1718−1720.

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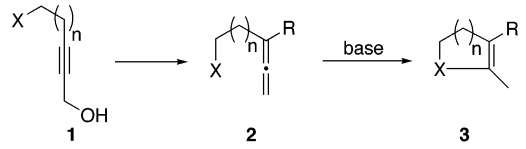
SCHEME 1



R = SO_2Ph, $POPh_2$, $PO(OEt)_2$; X = OH, NHR'; n = 1 ~ 4

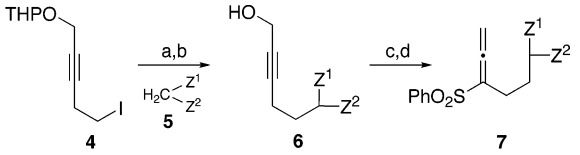
protocol using phosphorus reagents[11] instead of PhSCl provided oxacycles **3** (R = $POPh_2$, $PO(OEt)_2$) with a phosphoryl or a phosphono functionality, which should be very useful for further manipulations.[12,13] Furthermore, this newly developed method was shown to be suitable for the preparation of not only five- to seven-membered monocyclic nitrogen-containing heterocycles, but also azabicyclic systems.[14]

Next, we[15] sought to synthesize carbocycles **3** (X = active methine) using the base-catalyzed endo-mode ring-closing reaction of allenes with a phenylsulfonyl group as well as a terminal active methylene moiety. In this paper, we describe the details of the novel intramolecular ring-closing reaction of allenyl sulfones with suitable internal carbon nucleophiles in an endo-mode manner leading to substituted-cyclopentene, cyclohexene, and cycloheptene derivatives. Preparation of benzocyclohexene, benzocycloheptene, and benzocyclooctene skeletons is also described.

Results and Discussion

The required starting allenes for the ring-closing reaction were prepared by conventional means in a straightforward manner as depicted in Scheme 2. The known propargyl alcohol derivative **4**[16] was treated with the active methylene species **5** in the presence of NaH to give the condensed products, which were subsequently exposed to acidic conditions (*p*-TsOH, MeOH) to afford **6** with a propargyl alcohol moiety. Conversion of **6** into the desired allenes **7** with a phenylsulfonyl group was realized by successive treatment of **6** with PhSCl[17] in THF at −78 °C in the presence of Et_3N and *m*-CPBA in CH_2Cl_2 at 0 °C (Scheme 2).

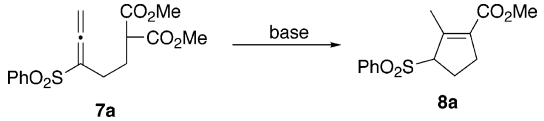
SCHEME 2[a]



a: $Z^1 = Z^2 = CO_2Me$, **b**: $Z^1 = Z^2 = CO_2Et$,
c: $Z^1 = CO_2Et$, $Z^2 = COPh$, **d**: $Z^1 = CO_2Me$, $Z^2 = SO_2Ph$

[a] Reaction conditions: (a) NaH, DMF, 0 °C to rt; (b) *p*-TsOH, MeOH, rt, **6a** (86%), **6b** (86%), **6c** (31%), **6d** (90%); (c) PhSCl, Et_3N, THF, −78 °C; (d) *m*-CPBA, CH_2Cl_2, 0 °C, **7a** (85%), **7b** (81%), **7c** (77%), **7d** (50%).

TABLE 1. Base-Catalyzed Ring-Closing Reaction of 7a[a]



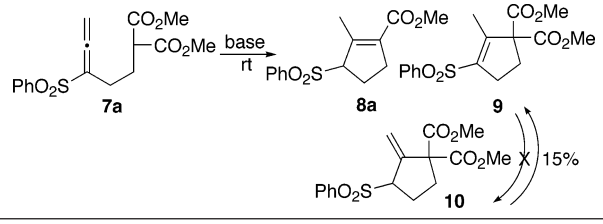
entry	base	equiv	solvent	time	yield (%)
1	^{t}BuOK	1.5	^{t}BuOH	5 min[b]	84
2	^{t}BuONa	1.5	^{t}BuOH	5 min[b]	47
3	^{t}BuOLi	1.5	^{t}BuOH	9 h[c]	96
4	MeOK	4.5[d]	MeOH	2 h[c]	96
5	MeONa	4.5[d]	MeOH	26 h[c]	95
6	MeOLi	4.5[d]	MeOH	5 min[b]	65
7	aq KOH	1.5	^{t}BuOH	5 min[b]	62
8	aq NaOH	1.5	^{t}BuOH	30 min[c]	73
9	aq KOH	1.5	THF	6 h	67
10	aq NaOH	1.5	THF	6 h	65

[a] Reaction was monitored by TLC. Complete consumption of **7a** was observed within 5 min. [b] No other products could be detected on TLC. [c] Three spots gradually converged to **8a**. [d] A longer reaction time was required when 1.5 equiv of base was used.

Initially, we investigated the transformation of **7a** ($Z^1 = Z^2 = CO_2Me$) to the corresponding ring-closed product. The results are summarized in Table 1. The ring-closing reaction of **7a** was first attempted according to the previously optimized conditions[8] for the ring-closing reaction of allenyl sulfones **2** (R = SO_2Ph, X = OH). Thus, exposure of **7a** to ^{t}BuOK (1.5 equiv) in ^{t}BuOH at room temperature for 5 min (consumption of the starting material was monitored by TLC) furnished the unexpected cyclopentene derivatives **8a**[18] in 84% yield (entry 1). When ^{t}BuONa (1.5 equiv) was used instead of ^{t}BuOK, the starting **7a** disappeared within 5 min, the same as entry 1, but the chemical yield of **8a** was much lower (entry 2). Treatment of the allenyl sulfone **7a** with MeOK (4.5 equiv) in MeOH immediately led to not only complete consumption of the starting material as in the case of ^{t}BuOK (entries 1 and 2), but also to the production of three spots on TLC, which after 2 h converged into **8a** in 96% yield (entry 4). A similar result was obtained when

(6) Parsons, P. J.; Stefinovic, M. *Synlett* **1993**, 931−932.
(7) The intermolecular Michael-type reaction between the 1,2-allenyl ketones with the active methine derivatives has been reported. Ma, S.; Yin, S.; Li, L.; Tao, F. *Org. Lett*. **2002**, *4*, 505−507.
(8) Mukai, C.; Yamashita, H.; Hanaoka, M. *Org. Lett*. **2001**, *3*, 3385−3387.
(9) Parsons reported an exo-mode ring-closing reaction of allenyl sulfoxide derivatives; see: (a) Pairaudeau, G.; Parsons, P. J.; Underwood, J. M. *J. Chem. Soc., Chem. Commun*. **1987**, 1718−1720. (b) Gray, M.; Parsons, P. J.; Neary, A. P. *Synlett* **1992**, 597−598. (c) Gray, M.; Parsons, P. J.; Neary, A. P. *Synlett* **1993**, 281−282. (d) Parkes, K.; Penkett, C. S.; Parsons, P. J. *Synlett* **1995**, 709−710. (e) Edwards, N.; Macritchie, J. A.; Parsons, P. J.; Drew, M. G. B.; Jahans, A. W. *Tetrahedron* **1997**, *53*, 12651−12660. (f) Edwards, N.; Macritchie, J. A.; Parsons, P. J. *Tetrahedron Lett*. **1998**, *39*, 3605−3608.
(10) Dai described an exo-mode ring-closing reaction of allenyl sulfones resulting in the formation of five-membered oxacycles: Dai, W.-M.; Lee, M. Y. H. *Tetrahedron* **1998**, *54*, 12497−12512.
(11) Mukai, C.; Ohta, M.; Yamashita, H.; Kitagaki, S. *J. Org. Chem*. **2004**, *69*, 6867−6873.
(12) An endo-mode ring-closing reaction of trisubstituted allenylphosphine oxides, leading to the dihydrofuran skeleton, has been reported: Pravia, K.; White, R.; Fodda, R.; Maynard, D. F. *J. Org. Chem*. **1996**, *61*, 6031−6032.
(13) Brel reported an exo-mode cyclization of the allenylphosphonate derivatives leading to a furan framework: Brel, V. K. *Synthesis* **2001**, 1539−1545.
(14) Mukai, C.; Kobayashi, M.; Kubota, S.; Takahashi, Y.; Kitagaki, S. *J. Org. Chem*. **2004**, *69*, 2128−2136.
(15) Part of this work was published as a preliminary communication: Mukai, C.; Ukon, R.; Kuroda, N. *Tetrahedron Lett*. **2003**, *44*, 1583−1586.
(16) (a) Corey, E. J.; Niwa, H.; Knolle, J. *J. Am. Chem. Soc*. **1978**, *100*, 1942−1943. (b) Mukai, C.; Nomura, I.; Yamanishi, K.; Hanaoka, M. *Org. Lett*. **2002**, *4*, 1755−1758.
(17) Horner, L.; Binder, V. *Liebigs Ann. Chem*. **1972**, *757*, 33−68.
(18) The structure of **8a** was unambiguously established on the basis of its spectral evidence. In particular, the IR spectrum of **8a** showed a carbonyl absorption band at 1712 cm^{-1}, which is in good accordance with that of ethyl 1-cyclopentenecarboxylate (1710 cm^{-1}) rather than that of its regioisomer, ethyl 2-cyclopentenecarboxylate (1730 cm^{-1}).[19]

TABLE 2. Isolation of Compounds 9 and 10



entry	base	equiv	solvent	time	**8a** (%)	**9** (%)	**10** (%)
1	^{t}BuOK	1.5	^{t}BuOH	5 min	84		
2	^{t}BuOK	1.0	^{t}BuOH	5 min	58	30	
3	^{t}BuOK	0.5	^{t}BuOH	5 min	21	36	42
4	^{t}BuOK	0.1	^{t}BuOH	5 min	trace	trace	94
5	Et_3N	6.0	CH_2Cl_2	2 h		24	69

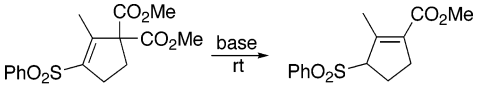
7a was exposed to MeONa (4.5 equiv) in MeOH for a longer reaction time (26 h) (entry 5). Both ^{t}BuOLi and MeOLi were also found to be effective for this ring-closing reaction (entries 3 and 6). Aqueous bases, KOH and NaOH, in ^{t}BuOH and THF could be used for this reaction but gave slightly lower yields (entries 7−10). Thus, ^{t}BuOK was found to be the best base for this transformation with regard to the reaction time and chemical yield.

The formation of **8a** from **7a** can tentatively be explained in terms of the intermediacy of the products **9** and/or **10**, both of which would collapse to **8a** through demethoxycarbonylation. To confirm the plausible intermediates **9** and/or **10** for the transformation of **7a** into **8a**, several experiments were carried out (Table 2). Exposure of **7a** to 1.0 equiv of ^{t}BuOK in ^{t}BuOH for 5 min produced a new product **9**, which had a bis(methoxycarbonyl) functionality, in 30% yield together with **8a** (58%) (entry 2). In addition, another cyclopentene derivative **10** possessing a bis(methoxycarbonyl) group was isolated in 42% yield along with **8a** (21%) and **9** (36%) when treated with 0.5 equiv of base for 5 min (entry 3). Finally, the exclusive formation of **10** (94%) was observed upon treatment of **7a** with a catalytic amount of ^{t}BuOK (0.1 equiv) (entry 4). Compounds **9** and **10** were both identical to those observed in the reactions of **7a** with ^{t}BuOLi, MeOM (M = K, Na, Li), and aqueous KOH and NaOH (see Table 1). The 1,2,3-trisubstituted cyclopentene derivatives **9** and **10** were also obtained when **7a** was treated with Et_3N instead of alkoxides in CH_2Cl_2 at room temperature for 2 h (entry 5).

The interconversion between compounds **9** and **10** was studied next. Compound **10** was partially isomerized to **9** (15%) when it exposed to Et_3N in CH_2Cl_2 at room temperature for 48 h, and the starting disubstituted allene **10** was recovered (68%). On the other hand, tetrasubstituted olefin **9** was stable under the same conditions and no isomerization to **10** was detected. These malonate derivatives **9** and **10** readily underwent demethoxycarbonylation with several alkoxides to provide **8a** in the yields shown in Tables 3 and 4.

We next investigated the ring-closing reaction of other allenes **7b**−**d**. Treatment of allene **7b** with 1.5 equiv of ^{t}BuOK in ^{t}BuOH at room temperature afforded the corresponding cyclopentene derivatives **8b** in 93% yield as expected (Table 5, entry 1). Upon treatment with ^{t}BuOK, compound **7c** afforded the debenzylated product

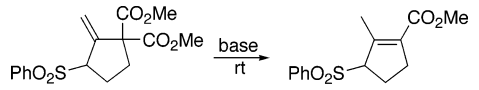
TABLE 3. Transformation of 9 to 8a



entry	base	equiv	solvent	time	**8a** (%)
1	^{t}BuOK	1.5	^{t}BuOH	5 min	63
2	^{t}BuONa	1.5	^{t}BuOH	5 min	64
3	MeONa	4.5[a]	MeOH	20 h	93

[a] A longer reaction time was required when 1.5 equiv of base was used.

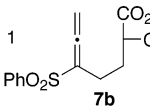
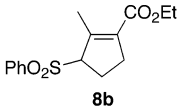
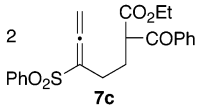
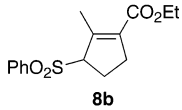
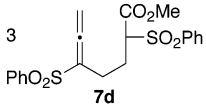
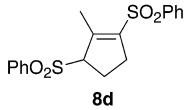
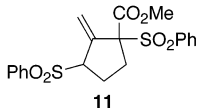
TABLE 4. Transformation of 10 to 8a



entry	base	equiv	solvent	time	**8a** (%)
1	^{t}BuOK	1.5	^{t}BuOH	5 min	79
2	^{t}BuONa	1.5	^{t}BuOH	5 min	76
3	MeONa	4.5[a]	MeOH	24 h	90

[a] A longer reaction time was required when 1.5 equiv of base was used.

TABLE 5. Base-Catalyzed Ring-Closing Reaction of 7b−d[a]

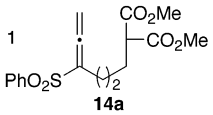
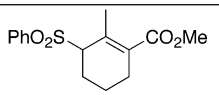
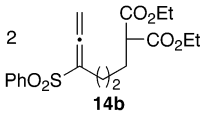
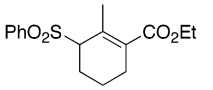
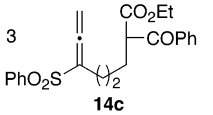
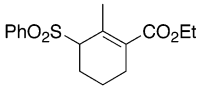
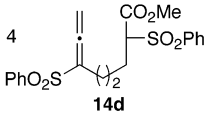
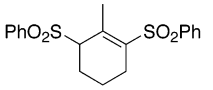
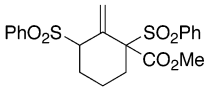
entry	allene	time	product	yield (%)
1		5 min		93
2		5 min		93
3		3 h[b]		98
4				83[c]

[a] Allenes **7b**−**d** were treated with ^{t}BuOK (1.5 equiv) in ^{t}BuOH at rt. [b] The reaction was carried out in a combined solvent of ^{t}BuOH and THF (1:1). [c] When **7d** was exposed to aq KOH in THF at rt for 5 min, compound **11** was obtained as a mixture of two diastereoisomers (95:5).

8b (93%), but not the deethoxycarbonylated one (entry 2). Compound **7d** was rather stable under the standard basic conditions.[20] Thus, the reaction mixture was heated at 60 °C for 3 h to leave the demethoxycarbonylated compound **8d** in 98% yield (entry 3). When aqueous KOH was used instead of ^{t}BuOK, **7d** exclusively provided **11** as a mixture of two diastereoisomers (95:5), the stereochemistry of which was not determined (entry 4). Compound **11** was easily converted into **8d** in 71% yield by exposure to ^{t}BuOK at 60 °C for 3 h.

(19) Scharf, H.-D.; Korte, F. *Chem. Ber.* **1964**, *97*, 2425−2433.
(20) A mixed solvent of ^{t}BuOH and THF (1:1) was used for this compound due to its solubility.

TABLE 6. Base-Catalyzed Ring-Closing Reaction of 12a−d[a]

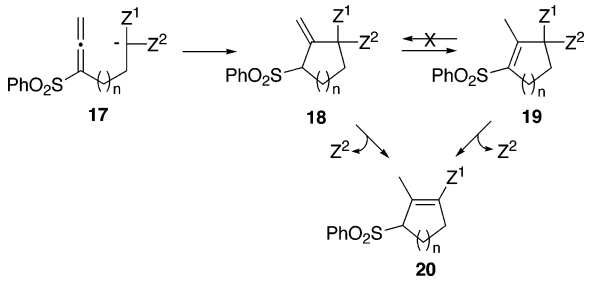
entry	allene	time	product	yield (%)
1	 **14a**	5 min	 **15a**	92
2	 **14b**	5 min	 **15b**	72
3	 **14c**	5 min	 **15b**	83
4	 **14d**	15 h[b]	 **15d**	80
5			 **16**	98[c]

[a] Allenes **12a−d** were treated with ^{t}BuOK (1.5 equiv) in ^{t}BuOH at rt. [b] The reaction was carried out in a combined solvent of ^{t}BuOH and THF (1:1). [c] When **12d** was exposed to aq KOH in THF at rt for 5 min, compound **16** was obtained as a mixture of two diastereoisomers (84:16).

The ring-closing reaction of the C_1-homologated allenes **14**[21] under the standard conditions (^{t}BuOK in ^{t}BuOH at room temperature) was examined next. The results are summarized in Table 6. Allenes **14a**,**b** gave the corresponding 1-alkoxycarbonyl-2-methyl-3-phenylsulfonyl-2-cyclohexene derivatives **15a**,**b** (entries 1 and 2). Preferential debenzoylation over deethoxycarbonylation was observed in the reaction of **14c** (entry 3). Allene **14d**[20] behaved the same as **7d** toward base leading to the formation of **15d** and **16** (entries 4 and 5). Thus, this novel endo-mode ring-closing reaction of allenes, accompanied with deacylation, could be suitable for constructing a cyclopentene skeleton as well as a cyclohexene framework.

Easy dealkoxycarbonylation and debenzoylation were observed during the base-catalyzed endo-mode ring-closing reaction of allenes **7** and **14** and resulted in the exclusive formation of 1-alkoxycarbonyl (or phenylsulfonyl)-2-methyl-3-phenylsulfonyl-2-cycloalkene derivatives **8** and **15**. Considering both the results in Table 2 and those in the base-catalyzed transformation of **9** and **10** into **8a** (Tables 3 and 4), it can be concluded that the Michael-type endo-mode ring-closing reaction of allenyl sulfones **17** under basic conditions first occurred at the sp-hybridized carbon center of the allenyl moiety, resulting in the formation of the *exo*-methylene derivative **18**, which might be in part susceptible to base-catalyzed isomerization to the endo-olefin derivative **19**, which has a 1,3-diacyl moiety. The final step of this transformation must be the deacylation of **18** and/or **19** with the aid of

SCHEME 3



alkoxy species, which leads to the exclusive production of **20** (Scheme 3). The simple explanation for dealkoxycarbonylation and/or debenzoylation might involve initial nucleophilic attack of the alkoxide on the carbonyl center. In the cases of **7c** and **14c**, a more cationic carbonyl moiety (benzoyl group) of two carbonyl functionalities was attacked by *tert*-butoxide (Tables 5 and 6). Thus, debenzoylation preferentially occurred over deethoxycarbonylation (Table 5, entry 2, and Table 6, entry 3). On the basis of these observations, the other plausible mechanism for decarbonylation of the 1,3-dicarbonyl functionality, which would involve the attack of the alkoxide at the alkyl group of the ester functionality with liberation of carbon dioxide, can be ruled out. Balme and co-workers[2b] reported similar demethoxycarbonylation as well as preferential deacetylation over demethoxycarbonylation in their investigation of the palladium-catalyzed exo-mode ring-closing reaction of alkyne derivatives with 1,3-diacyl functionalities.

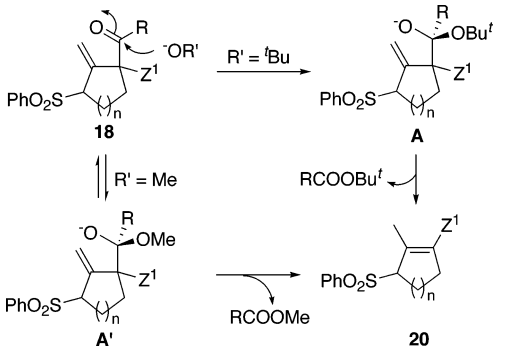
In addition, a more sterically hindered alkoxide (*tert*-butoxide) reacted much faster than a sterically less-hindered methoxide and hydroxide (Table 1). These observations were in contrast to our prediction. Presumably, the addition of *tert*-butoxide to a cationic carbonyl moiety of **18** as a first step would result in the simultaneous formation of intermediate **A**, and serious nonbonding steric congestion due to changing of hybridization from sp2 to sp3 (120° to ca. 109°) might be encountered. This inherent instability of **A** would irreversibly be released by elimination of a bulky alkoxide moiety leading to products **20**. In the case of a sterically smaller methoxide, for example, addition to a carbonyl group of **18** must be faster than that of *tert*-butoxide. However, under less sterically congested conditions, intermediate **A′** might be stable enough, compared to **A**, and be in equilibrium with the starting carbonyl compound **18**. As a result, collapse of intermediate **A′** to the final products **20** would be much slower than that of intermediate **A** (Scheme 4). A similar explanation might be possible for the transformation of **19** into **20**.

To obtain more information on the conversion of **18** and/or **19** into **20** under basic conditions, additional experiments were performed. Two allenes **7e** and **14e**[22] with a fairly bulky ester group could be anticipated to prevent the attack of bulky *tert*-butoxide. Thus, allenes **7e** and **14e** were exposed to the standard ring-closing conditions (^{t}BuOK (1.5 equiv) in ^{t}BuOH at room temperature for 5 min), and this led to the isolation of **21** and **22** in respective yields of 88% and 99% (Scheme 5).

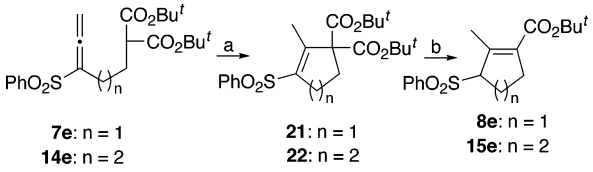
(21) Allenes **14** were prepared from the hexynyl iodide derivatives **12** via the corresponding active methine derivatives **13** (see the Supporting Information).

(22) Compounds **7e** and **14e** were prepared according to the general procedure (see the Supporting Information).

SCHEME 4

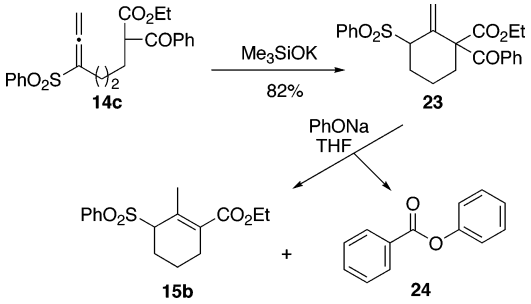


SCHEME 5[a]



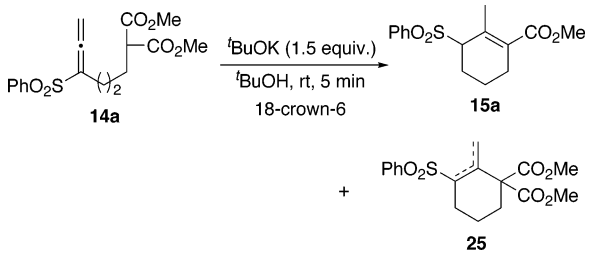
[a] Reaction conditions: (a) ^{t}BuOK, ^{t}BuOH, rt, 5 min, **21** (88%) **22** (99%); (b) ^{t}BuOK, ^{t}BuOH, rt, 24 h, **8e** (11%).

SCHEME 6



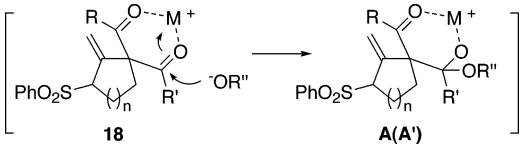
No de(*tert*-butoxy)carbonyl products **8e** and **15e** were detected in the reaction mixture. When **21** was treated with ^{t}BuOK for 24 h, de(*tert*-butoxy)carbonyl compound **8e** was obtained in 11% yield as a minor product together with recovery of the starting material **21** in 68% yield. On the other hand, compound **22** was stable under these conditions and **22** was completely recovered intact. These experiments indirectly supported the proposed reaction pathway in Scheme 4. Despite many efforts to isolate RCO_2Bu^t and RCO_2Me, both of which should be byproducts of the base-catalyzed endo-mode ring-closing reaction of **7** and **14** if the deacylation step proceeded as depicted in Scheme 4, these byproducts could not be isolated. The ring-closing reaction of **14c** with the use of other bases such NaOPh and NaSPh was examined because we envisaged that the resulting *tert*-butyl benzoate and *tert*-butyl benzothioate would be much easier to monitor by TLC. However, independent treatment of **14c** with NaOPh and NaSPh brought an intractable mixture presumably due to intermolecular Michael-type addition of these bases to the allene **14c**. When **14c** was exposed to Me_3SiOK, the ring-closed product **23** with a 1,3-diacyl moiety was obtained in 82% yield (Scheme 6). The resulting **23** was subsequently treated with excess amounts of NaOPh in THF at room temperature to fortunately give the desired phenyl benzoate (**24**) in 12% yield along with the cyclohexene derivative **15b** in quantitative yield. This observation strongly suggested that the mechanism for the deacylation step involves the attack of alkoxides, used as a base, as depicted in Scheme 4.

TABLE 7. Ring-Closing Reaction of 14a in the Presence of 18-Crown-6



entry	18-crown-6 (equiv)	**15a** (%)	**25** (%) (exo:endo)
1		92	
2	1.5	51	24 (1:2)
3	6.0	58	41 (1:3)

As described in Table 7, entry 1, the cyclohexene derivative **15a** was exclusively formed from **14a** by treatment with 1.5 equiv of ^{t}BuOK in ^{t}BuOH at room temperature. When a similar reaction was carried out in the presence of 1.5 equiv of 18-crown-6, **15a** was isolated in 51% yield along with the cyclohexene derivatives **25**, which have a 1,3-bismethoxycarbonyl functionality, in 24% yield (Table 7, entry 2). Interestingly, an increase in the amount of 18-crown-6 from 1.5 to 6.0 equiv changed the ratio of **15a** to **25** (**15a**: 58%, **25**: 41%) (entry 3). The effect of 18-crown-6 on deacylation was uncertain at this stage, but these results might be tentatively interpreted in terms of the six-membered cyclic intermediate **18** mediated by countercationic species, which would help deacylation.

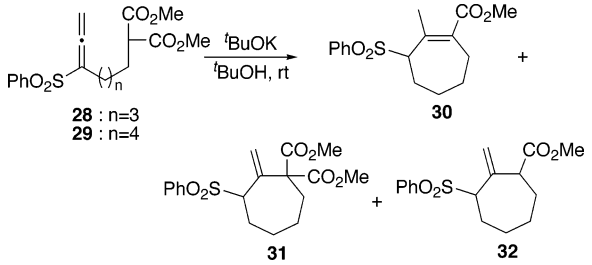


The next phase of this study involved the application of the endo-mode ring-closing reaction to the construction of larger carbocycles. The allene **28**[23] was then exposed to 1.5 equiv of ^{t}BuOK in ^{t}BuOH at rt for 20 min (Table 8, entry 1) to provide the seven-membered compound **30** (37%) and **32** (29%), accompanied with demethoxycarbonylation, although the chemical yield (66%) was somewhat lower than in the formation of cyclopentene and cyclohexene frameworks (see Tables 5 and 6). The malonate derivative **31** was obtained in 53% yield (entry 2) when **28** was treated with a catalytic amount of ^{t}BuOK for 12 h (0.5 equiv). The *exo*-methylene derivative **32**, which should have been derived from **31**, was formed in 34% yield as a mixture of *cis*- and *trans*-isomers in a ratio of 4 to 1[24] along with **31** (38%) upon treatment with 1.0 equiv of ^{t}BuOK for 1 h (entry 3). It was shown that a mixture of *cis*- and *trans*-**32** underwent base-catalyzed

(23) Compound **28** was prepared from the known dimethyl malonate derivative **26** (see the Supporting Information).

(24) The ratio of *cis*- and *trans*-**32** was determined by ^{1}H NMR spectral analysis.

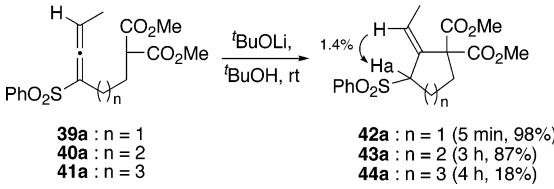
TABLE 8. Base-Catalyzed Ring-Closing Reaction of 28



entry	base (equiv)	time	product (%)
1	1.5	20 min	**30** (37), **32** (29)
2	1.0	1 h	**31** (38), **32** (34)[a]
3	0.5	12 h	**31** (53)

[a] A mixture of *cis*- and *trans*-**32** was obtained in a ratio of 4:1.

SCHEME 7

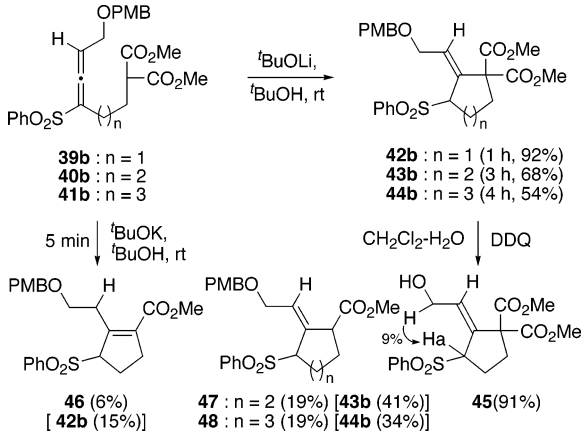


isomerization to furnish a mixture of *cis*-**32** and the *endo*-methylene derivative **30** in 40% yield (*cis*-**32**/**30** = ca. 3:2).[25] The stereochemistry of *cis*-**32** was determined by a NOE experiment, which revealed 1.0% enhancement between two allylic protons. This result should reflect the fact that thermodynamically less stable *trans*-**32** predominantly isomerized to more stable endo-olefin derivative **30**, while the isomerization of rather stable *cis*-**32** to **30**, in comparison with the *trans*-congener, might be much slower under the basic conditions used. In the case of compound **29**, no eight-membered carbocycles could be detected in the reaction mixture under various basic conditions.

We next looked at the scope and limitations of the newly developed method for constructing carbocycles based on the endo-mode ring-closing reaction. As shown in Table 8, cycloheptene derivatives could be prepared by the endo-mode ring-closing reaction of allenes, although the chemical yields are moderate or lower, compared to those for the preparation of cyclopentene and cyclohexene congeners. However, we clarified that the C_1-homologated allene **29**[26] could not produce the corresponding eight-membered derivatives at all.

Our next efforts focused on the effect of substituents at the allenic terminus (tri- and tetrasubstituted 1-phenylsulfonylallenes) in the ring-closing step. According to the standard procedure, **39a**[27] was treated with ^{t}BuOK in ^{t}BuOH at room temperature for 10 min to unexpectedly give an intractable mixture (Scheme 7). The desired ring-closed product **42a** was obtained in 98% yield when treated with ^{t}BuOLi instead of ^{t}BuOK for 10 min. No demethoxycarbonylation was observed in contrast to the

SCHEME 8



case of disubstituted allenes **7**, and the resulting ring-closed product **42a** had an (*E*)-ethylidene group.[28] Similarly, **40a**[27] furnished the six-membered product **43a** in high yield (87%),[29] although it took a prolonged reaction time (3 h) until the starting material was completely consumed. In contrast to these results, the seven-membered carbocycle **44a** was formed in a low yield (18%).[30] By analogy to the ring-closing reaction of **39a**, **40a**, and **41a**, the (*p*-methoxybenzyl)oxymethyl derivatives **39b** and **40b**[27] provided the corresponding five-and six-membered carbocycles **42b** and **43b** in respective yields of 92% and 68%, with a (*Z*)-(*p*-methoxybenzyl)-oxyethylidene moiety[31] when treated with ^{t}BuOLi (Scheme 8). Notably, the seven-membered product **44b** was also formed in moderate yield (53%). This result is different from that of the simpler trisubstituted allene **41a**, which provided the corresponding seven-membered product **44a** in a rather lower yield (18%). Compounds **42b**, **43b**, and **44b** have (*Z*)-stereochemistry,[31] while **42a**, **43a**, and **44a** have (*E*)-stereochemistry.[28] The difference in the stereochemistry of these compounds would presumably reflect the thermodynamic stability of each compound. Upon exposure of allenes **39b**, **40b**, and **41b** to the most standard conditions (1.5 equiv of ^{t}BuOK in ^{t}BuOH at room temperature), the ring-closing reaction proceeded to afford the corresponding (*Z*)-(*p*-methoxybenzyl)oxyethylidene derivatives **42b**, **43b**, and **44b** along with the demethoxycarbonylated compounds **46**−**48**.[32] An efficient ring-closing reaction was also observed when tetrasubstituted allene **39c**[27] was exposed to basic conditions (Scheme 9). However, this method was ineffective for the ring-closing reaction of the tetrasubstituted allenes **40c** and **41c**[27] resulting in the formation of intractable mixtures. In fact, the ring-closed products **43c** and **44c** could never be detected in these reaction mixtures. Several reaction conditions were used to attempt to

(25) No peaks due to *trans*-**32** could be detected by ^{1}H NMR. The ratio of *cis*-**32** to **30** was determined by ^{1}H NMR spectral analysis.

(26) Compound **29** was prepared from the known dimethyl malonate derivative **27** (see the Supporting Information).

(27) Allenes **39**−**41** were prepared from the corresponding alkynes **33**−**35** via compounds **36**−**38** (see the Supporting Information).

(28) The (*E*)-stereochemistry of **42a**, **43a**, and **44a** was determined by an NOE experiment. For instance, 1.4% enhancement of Ha of **43a** was observed upon irradiation of a vinyl proton.

(29) Compound **43a** was obtained in 65% yield when **40a** was exposed to ^{t}BuOK instead of ^{t}BuOLi for 5 min.

(30) Compound **44a** was obtained in 30% yield when **41a** was exposed to ^{t}BuOK instead of ^{t}BuOLi for 5 min.

(31) The (*Z*)-stereochemistry of **42b**, **43b**, and **44b** was confirmed as follows. Treatment of **42b**, for example, with DDQ afforded the allylic alcohol derivative **45** in 91% yield. An NOE experiment of **45** revealed a 9% enhancement of Ha when allylic protons were irradiated.

(32) Compounds **47** and **48** were obtained as a mixture of two diastereoisomers in a ratio of ca. 1:1.

SCHEME 9

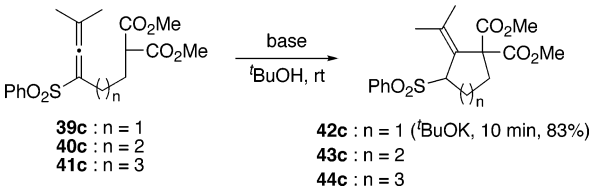
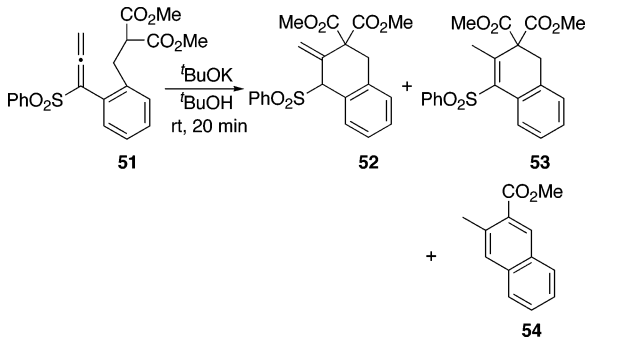


TABLE 9. Ring-Closing Reaction of 51



entry	^{t}BuOK (equiv)	**52** (%)	**53** (%)	**54** (%)
1	2.0	10	9	58
2	1.5	23	15	53
3	0.1	86	14	

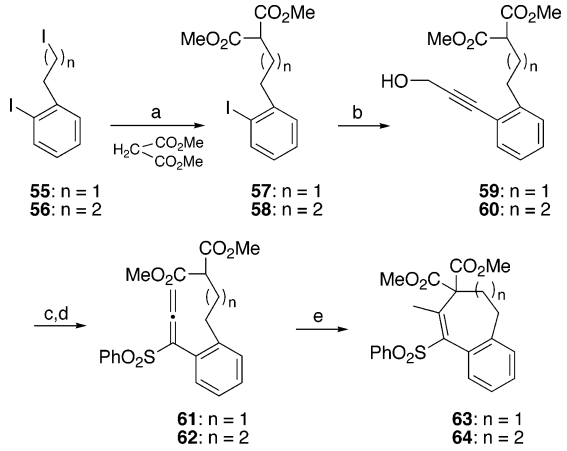
overcome the difficulty encountered in the formation of six- and seven-membered products by changing the solvent, base, reaction temperature, and/or concentration; however, no improvement was made.

In summary, the endo-mode ring-closing reaction of 1,1-disubstituted phenylsulfonylallenes possessing a terminal active methine moiety produced five- to seven-membered carbocycles, accompanied by deacylation, in high yields. The efficient construction of cyclopentane and cyclohexane skeletons from the corresponding tri- and tetra-substituted allenes was also realized. This procedure was not necessarily suitable for constructing seven-membered carbocycles, although **41b** afforded the corresponding seven-membered framework in moderate yields (Scheme 8).

Our endeavors were then turned to application of this endo-mode ring-closing reaction to 1-alkyl (with a terminal active methine moiety)-2-allenylbenzene derivatives in which the template effect of the aromatic ring would be expected to facilitate the ring-closing step. Thus, upon exposure to ^{t}BuOK (1.5 equiv) in ^{t}BuOH at room temperature for 20 min, **51**[33] underwent a ring-closing reaction to give the two predictable products **52** and **53** in respective yields of 23% and 15%, in addition to the unexpected naphthalene derivative **54** in 53% yield as a major product (Table 9, entry 2). An increase in the amount of ^{t}BuOK (2.0 equiv) brought a slightly high yield of **54** (58%) as well as lower yields of **52** (10%) and **53** (9%) (entry 1). On the other hand, a catalytic amount of ^{t}BuOK (0.1 equiv) provided **52** as a major product (86%) along with **53** (14%) (entry 3). In this case, no formation of the desulfonylated product **54** was observed. Compound **54** must be derived from **52** and/or **53** via succes-

(33) Compound **51** was prepared form the known iodobenzene derivative **49** via the propargyl alcohol derivative **50** (see the Supporting Information).

SCHEME 10[a]



[a] Reaction conditions: (a) NaH, THF, rt, **57** (67%), **58** (77%); (b) propargyl alcohol, $PdCl_2(PPh_3)_2$, $^i Pr_2NH$, CuI, AcOEt, rt, **59** (87%), **60** (88%); (c) PhS(O)Cl, Et_3N, CH_2Cl_2, −78 °C; (d) toluene reflux, **61** (88%), **62** (88%); (e) ^{t}BuOK (1.0 equiv), ^{t}BuOH, rt, **63** (5 min, 66%), **64** (2 h, 29%).

sive demethoxycarbonylation and dephenylsulfinic acid. In fact, when **52** was treated with ^{t}BuOK for 5 min, the naphthalene derivative **54** was obtained in 52% yield together with double bond-isomerized product **53** (18%) and recovery of the starting material **52** (27%). The dihydronaphthalene framework **53** was rather stable, compared to the *exo*-methylene framework **52**, and afforded **54** in only 17% yield along with **52** (22%) and the recovery of **53** (46%) under basic conditions.

We next focused on preparing larger benzocycloheptene and benzocyclooctene skeletons. Condensation of the diiodo derivative **55**[34] with dimethyl malonate gave the condensed product **57** in 67% yield, which was subsequently converted into the propargyl alcohol derivative **59** in 87% yield by the Sonogashira coupling reaction. Unexpectedly, the transformation of **59** into the allenyl sulfone derivative **61** via [2,3]-sigmatropic rearrangement of the sulfenic ester derivative was troublesome, and the allene **61** was isolated in only 10% yield upon treatment with PhSCl and *m*-CPBA. After we screened several reagents and conditions, we found that benzenesulfinyl chloride (PhS(O)Cl)[35] instead of PhSCl was effective for this transformation. As a result, **59** was reacted with PhS(O)Cl in the presence of Et_3N at −78°C to provide the corresponding sulfinic ester derivative, which was subsequently refluxed in toluene for 4.5 h to produce the desired **61** in 88% yield. A similar protocol was applied for the diiodo derivative **56**[34] to provide the C_1-homologated allene derivative **62**, via **58** and **60**, in acceptable yields (Scheme 10). Easy transformation of the allene **61** into benzocycloheptene derivative **63** under the standard basic conditions (5 min) was realized in 66% yield, as expected. The efficient formation of the seven-membered ring of **63** may be attributed to the template effect of an aromatic ring. However, the formation of an eight-membered formation did not proceed as efficiently as we had anticipated. In fact, exposure of the allene **62** to

(34) Ripa, L.; Hallberg, A. *J. Org. Chem*. **1996**, *61*, 7147−7155.

(35) (a) Stirling, C. J. M. *J. Chem. Soc., Chem Commun*. **1967**, 131−131. (b) Smith, G.; Stirling, C. J. M. *J. Chem. Soc. C* **1971**, 1530−1535.

^{t}BuOK produced benzocyclooctene derivative **64** in a rather lower yield (29%).

In summary, we have developed a new and reliable procedure for constructing of five- to seven-membered carbocycles via an endo-mode ring-closing reaction of 1-phenylsulfonylallenes with an alkyl side chain, possessing a terminal active methine moiety, at the C_1-position. The resulting carbocycles readily underwent deacylation under basic conditions. Trisubstituted 1-phenylsulfonylallenes underwent a similar endo-mode ring-closing reaction to produce the corresponding five- to seven-membered carbocycles, although the formation of the seven-membered frameworks was inefficient. In the case of tetrasubstituted allenes, five-membered carbocycle was constructed in high yields, but the corresponding six- and seven-membered compounds could not be obtained. In addition, the introduction of an aromatic ring to the alkyl side chain of the starting allenes made possible the formation of not only normal-sized carbocycles (six-and seven-membered ones), but also an eight-membered framework, although the yield of the latter was rather low.

Experimental Section

Dimethyl 6-Hydroxy-4-hexyne-1,1-dicarboxylate (6a). To a solution of dimethyl malonate (0.18 mL, 1.59 mmol) in DMF (9.0 mL) was added NaH (60% in oil, 50.4 mg, 1.27 mmol) at 0 °C. After the mixture was stirred for 15 min at rt, a solution of **4** (310 mg, 1.06 mmol) in DMF (1.0 mL) was added to the mixture. The reaction mixture was stirred for 6 h, quenched by addition of saturated aqueous NH_4Cl, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. *p*-TsOH (37.9 mg, 0.22 mmol) was added to a solution of the crude adduct in MeOH (10 mL) at rt, and the mixture was stirred at the same time for 24 h. The reaction mixture was concentrated to leave the residue, which was chromatographed with hexane−AcOEt (2:1) to give **6a**[36] (195 mg, 86%) as a colorless oil: IR 3609, 3462, 2224, 1747 (sh), 1732 cm^{-1}; ^{1}H NMR δ 4.23 (2H, t, J = 2.0 Hz), 3.74 (6H, s), 3.58 (1H, t, J = 7.3 Hz), 2.34 (1H, t, J = 2.0 Hz), 2.32 (2H, tt, J = 2.0, 6.9 Hz), 2.16−2.05 (2H, m); ^{13}C NMR δ 169.4, 83.6, 79.1, 52.5, 50.9, 50.2, 27.4, 16.6; FABMS *m/z* 215 ($M^+ + 1$, 100). FABHRMS calcd for $C_{10}H_{15}O_5$ 215.0919, found 215.0914.

Dimethyl 4-(Phenylsulfonyl)-4,5-hexadiene-1,1-dicarboxylate (7a). To a solution of **6a** (270 mg, 1.26 mmol) in THF (20 mL) was added Et_3N (0.53 mL, 3.78 mmol) at −78 °C, and the reaction mixture was stirred for 15 min. PhSCl (546 mg, 3.78 mmol) was added to the reaction mixture, which was stirred for 3 h, quenched by addition of water, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane-AcOEt (2:1) to give the crude sulfoxide derivative. *m*-CPBA (261 mg, 1.51 mmol) was added to a solution of the crude sulfoxide in CH_2Cl_2 (13 mL) at 0 °C, and the mixture was stirred for 2.5 h. The reaction mixture was quenched by addition of water and extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane−AcOEt (2:1) to give **7a** (363 mg, 85%) as a colorless oil: IR 1969, 1938, 1747 (sh), 1732 cm^{-1}; ^{1}H NMR δ 7.91−7.50 (5H, m), 5.41 (2H, t, J = 3.3 Hz), 3.71 (6H, s), 3.36 (1H, t, J = 7.6 Hz) 2.37−2.26 (2H, m), 2.11−1.99 (2H, m); ^{13}C NMR δ 207.5, 169.1, 139.8, 133.5, 129.1, 128.0, 112.1, 85.1, 52.6, 50.3, 26.5, 24.4; MS *m/z* 338 (M^+, 48). Anal. Calcd for $C_{16}H_{18}O_6S$: C, 56.79; H, 5.36. Found: C, 56.49; H, 5.47.

(36) Brillon, D.; Deslongchamps, P.*Can. J. Chem.* **1987**, *65*, 43−55.

General Procedure for Ring-Closing Reaction of Compounds 7 and 14. Typical Procedure. To a solution of **7a** (27.2 mg, 0.08 mmol) in ^{t}BuOH (0.8 mL) was added ^{t}BuOK (13.5 mg, 0.12 mmol), and the mixture was stirred for 5 min at rt. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane−AcOEt (3:1) to give **methyl 2-methyl-3-(phenylsulfonyl)-1-cyclopentene-1-carboxylate (8a)** (18.8 mg, 84%). Chemical yields are summarized in Tables 1, 2, and 5−7 and Scheme 5.

Methyl 2-methyl-3-(phenylsulfonyl)-1-cyclopentene-1-carboxylate (8a): colorless solid; mp 104−107 °C (from Et_2O); IR 1712, 1647 cm^{-1}; ^{1}H NMR 7.88−7.51 (5H, m), 4.19−4.16 (1H, m), 3.70 (3H, s), 2.47−2.02 (4H, m), 2.28 (3H, br-s); ^{13}C NMR δ 165.3, 145.5, 137.3, 135.6, 134.0, 129.0, 128.9, 77.2, 51.4, 31.5, 25.0, 16.1; MS *m/z* 280 (M^+, 0.5). Anal. Calcd for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 59.74; H, 5.87.

Conversion of 7a into 9 and 10. A solution of **7a** (51.5 mg, 0.15 mmol) and Et_3N (0.13 mL, 0.91 mmol) in CH_2Cl_2 (1.5 mL) was stirred for 2 h. The reaction mixture was concentrated to leave the residue, which was chromatographed with hexane−AcOEt (3:1) to give **dimethyl 2-methyl-3-(phenylsulfonyl)-2-cyclopentene-1,1-dicarboxylate (9)** (12.5 mg, 24%) and **dimethyl 2-methylene-3-(phenylsulfonyl)cyclopentane-1,1-dicarboxylate (10)** (32.7 mg, 69%).

Dimethyl 2-methyl-3-(phenylsulfonyl)-2-cyclopentene-1,1-dicarboxylate (9): colorless oil; IR 1732, 1634 cm^{-1}; ^{1}H NMR δ 7.93−7.50 (5H, m), 3.74 (6H, s), 2.69−2.59 (2H, m), 2.49−2.41(2H, m), 2.29 (3H, t, J = 2.0 Hz); ^{13}C NMR δ 169.5, 148.7, 140.3, 140.3, 133.5, 129.2, 127.3, 70.5, 53.0, 31.8, 31.4, 13.6; MS *m/z* 338 (M^+, 10). Anal. Calcd for $C_{16}H_{18}O_6S$: C, 56.79; H, 5.36. Found: C, 56.46; H, 5.43.

Dimethyl 2-methylene-3-(phenylsulfonyl)cyclopentane-1,1-dicarboxylate (10): colorless solid; mp 96−98 °C (from Et_2O); IR 1734 cm^{-1}; ^{1}H NMR δ 7.91−7.50 (5H, m), 5.73 (1H, d, J = 1.7 Hz), 5.44 (1H, d, J = 1.7 Hz), 4.11−4.03 (1H, m), 3.71 (3H, s), 3.70 (3H, s), 2.55−2.10 (4H, m); ^{13}C NMR δ 170.6, 169.1, 139.6, 136.8, 133.9, 129.7, 128.9, 122.6, 69.3, 63.7, 53.1, 53.0, 33.4, 26.4; MS *m/z* 338 (M^+, 0.2). Anal. Calcd for $C_{16}H_{18}O_6S$: C, 56.79; H, 5.36. Found: C, 56.70; H, 5.48.

Isomerization of 10 into 9. A solution of **10** (43.0 mg, 0.13 mmol) and Et_3N (0.05 mL, 0.39 mmol) in CH_2Cl_2 (1.3 mL) was stirred for 48 h. The reaction mixture was concentrated to leave the residue, which was chromatographed with hexane−AcOEt (3:1) to give **9** (6.6 mg, 15%) along with recovery of **10** (29.2 mg, 68%).

Dimethyl (2*Z*)-(2-Hydroxyethylidene)-3-(phenylsulfonyl)cyclopentane-1,1-dicarboxylate (45). DDQ (59.0 mg, 0.26 mmol) was added to a solution of **42b** (61.9 mg, 0.13 mmol) in CH_2Cl_2 and H_2O (1.3 mL, 20:1) and vigorously stirred at rt for 1 h. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane-AcOEt (1:1) to give **45** (42.3 mg, 91%) as a colorless oil: IR 3605, 3526, 1732 cm^{-1}; ^{1}H NMR δ 7.94−7.53 (5H, m), 6.43 (1H, dt, J = 1.3, 6.3 Hz), 4.54−4.47 (1H, m), 4.24−3.98 (2H, m), 3.78 (3H, s), 3.72 (3H, s), 2.73 (1H, br-s), 2.58−2.04 (4H, m); ^{13}C NMR δ 171.2, 169.5, 138.3, 137.4, 134.1, 131.7, 129.4, 129.1, 67.2, 63.8, 61.3, 53.2, 53.0, 32.4, 27.5; MS *m/z* 368 (M^+, 0.1); FABHRMS calcd for $C_{17}H_{21}O_7S$ 369.1008, found 369.1020.

Dimethyl 3-(*o*-Iodophenyl)propane-1,1-dicarboxylate (57). To a solution of dimethyl malonate (55.4 mg, 0.42 mmol) in THF (1.0 mL) was added NaH (60% in oil, 11.2 mg, 0.28 mmol) at 0 °C, and the mixture was stirred for 30 min at rt. A solution of **55** (49.7 mg, 0.14 mmol) in THF (1.0 mL) was added to the mixture. The reaction mixture was stirred for 12 h, quenched by addition of saturated aqueous NH_4Cl, and extracted with AcOEt. The extract was washed with water and

brine, dried, and concentrated to dryness. The residue was chromatographed with hexane−AcOEt (8:1) to give **57** (33.7 mg, 67%) as a colorless oil: IR 1749 (sh), 1732 cm^{-1}; ^1H NMR δ 7.83−6.84 (4H, m), 3.75 (6H, s), 3.44 (1H, t, J = 7.6 Hz), 2.81−2.71 (2H, m), 2.25−2.15 (2H, m); ^{13}C NMR δ 169.4, 143.1, 139.4, 129.4, 128.3, 128.0, 100.3, 52.5, 50.8, 38.0, 28.9; MS *m/z* 362 (M^+, 41); FABHRMS calcd for $C_{13}H_{16}IO_4$ 363.0093, found 363.0088.

Dimethyl 3-[2-{1-(Phenylsulfonyl)-1,2-propadienyl}-phenyl]propane-1,1-dicarboxylate (61). To a solution of sodium benzenesulfinate (400 mg, 2.40 mmol) was added a solution of oxalyl chloride (0.25 M benzene solution, 8.00 mL, 2.00 mmol) at 0 °C. After being stirred for 1 h at rt, the reaction mixture (2.80 mL, 0.70 mmol) was added to a solution of **59** (100 mg, 0.35 mmol) and Et_3N (0.48 mL, 3.50 mmol) in CH_2Cl_2 at −78 °C. The reaction mixture was stirred for 10 min, quenched by addition of water, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The crude sulfinic ester in toluene was heated under reflux for 4 h. The reaction mixture was concentrated, and the residue was chromatographed with hexane−AcOEt (3:1) to give **61** (126 mg, 88%) as a colorless oil: IR 1967, 1931, 1749 (sh), 1732 cm^{-1}; ^1H NMR δ 7.75−7.08 (9H, m), 5.50 (2H, s), 3.74 (6H, s), 3.33 (1H, t, J = 7.3 Hz), 2.48−2.39 (2H, m), 2.03−1.96 (2H, m); ^{13}C NMR δ 208.9, 169.4, 141.1, 139.5, 133.5, 131.2, 129.7, 129.5, 128.8, 128.6, 127.7, 126.2, 112.2, 83.0, 52.5, 51.4, 30.9, 30.1; MS *m/z* 414 (M^+, 4.7); FABHRMS calcd for $C_{22}H_{23}O_6S$ 415.1215, found 415.1207.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds **6a**−**e**, **12**, **13b**−**e**, **36a**−**c**, **37a**−**c**, **38a**−**c**, **39b**, **40a**−**c**, **41b**,**c**, **42b**, **43b**, **44a**,**b**, **46**−**48**, **50**−**53**, **57**−**62**, and **64**, characterization data for compounds **6b**−**e**, **7b**−**e**, **8b**−**e**, **11**, **13b**−**e**, **14a**−**e**, **15a**−**d**, **16**, **21**−**23**, **25**, **28**−**32**, **36b**,**c**, **37a**−**c**, **38a**−**c**, **39a**−**c**, **40a**−**c**, **41a**−**c**, **42a**−**c**, **43a**,**b**, **44a**,**b**, **46**−**48**, **51**−**54**, **58**−**60**, and **62**−**64** and preparation of compounds **12**, **36a**, and **50**. This material is available free of charge via the Internet at http://pubs.acs.org.

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