Versatile [3 + 2] Methylenecyclopentane Annulations of Unactivated and Electron-Rich Olefins with [(Trimethylsilyl)methylene]cyclopropanedicarboxylates

Chad C. Huval and Daniel A. Singleton*

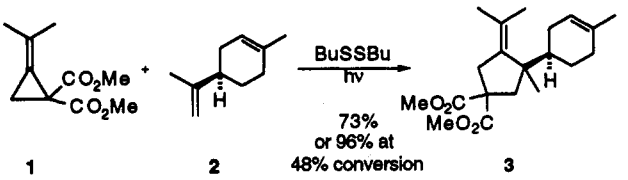
Department of Chemistry, Texas A&M University, College Station, Texas 77843-3255

Received October 26, 1993•

[(Trimethylsilyl)methylene]cyclopropanedicarboxylates **8a-c** are readily available from the cyclopropanation of the silylallenes **7a-c** with dimethyl diazomalonate. The free-radical mediated methylenecyclopentane annulations of unactivated and electron-rich alkenes with **8a-c** proceed in high yield. The product vinylsilanes are set up for diverse secondary conversions, making annulations with **8a-c** highly versatile in the synthesis of cyclopentanes.

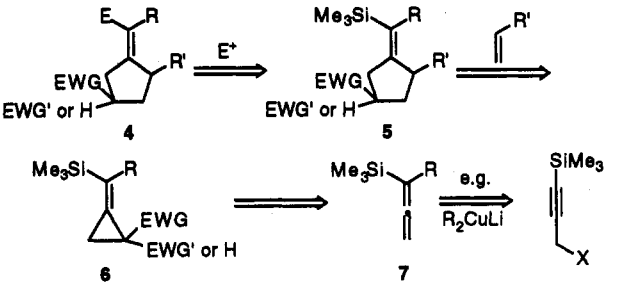
Cycloaddition-type strategies for cyclopentane syntheses allow the most rapid and convergent production of structural complexity.[1] For this reason, there has been considerable interest in the development of single-step [3 atom + 2 atom] ring constructions.[2-4] Many such reactions have been developed in recent years, with diverse applicability and limitations. We have recently reported the free-radical-mediated [3 + 2] methylenecyclopentane annulation of alkenes with methylenecyclopropanes.[5] Unlike most, our annulation works well with unactivated and electron rich alkenes. This regiospecific reaction enjoys the mild conditions and high chemoselectivities of free-radical chain reactions, but unlike many radical reactions, does not require an excess of reacting alkene. Furthermore, the product stereochemistry can be modulated by choice of catalyst.[6]

The most significant limitation on the overall synthetic utility of the annulation is a lack of versatility. Despite the impressive ability of this reaction to annulate complex alkenes selectively, as illustrated by the reaction of dimethyl 2-isopropylidenecyclopropanedicarboxylate (**1**) with limonene (**2**), general access to methylenecyclopropanes related to **1** is limited, less-substituted analogs of **1** do not work satisfactorily in the annulation, and the product **3** is not set up well for further elaboration. Therefore, modestly differing analogs of **3** would not be so easily available.



1 2 3

The approach described in this paper to multiplying the utility of the annulation starts with the ready availability of a variety of silylallenes **7**. If these allenes can be selectively cyclopropanated to give **6**, then free-radical-mediated methylenecyclopentane annulations could serve for the synthesis of a wide variety of cyclopentanes **4** and other products available via the highly pliant[7] vinylsilanes **5**. This would therefore allow the retrosynthetic simplification of various quinanes into one class of simple reagents.



4 5 6 7

Results and Discussion

Synthesis of Methylenecyclopropanes. The synthesis of methylenecyclopropanes by carbene-mediated cyclopropanation of allenes has often suffered from addition of two carbenes to give spiropentanes, C-H insertion, low regioselectivity, or rearrangement of the

• Abstract published in *Advance ACS Abstracts,* March 15, 1994.

(1) Bertz, S. H. *J. Am. Chem. Soc.* **1981**, *103*, 3599. Trost, B. M. Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315.

(2) For some selected examples, see: (a) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6429. (b) Binger, P.; Schuchardt, U. *Angew. Chem., Int. Ed. Eng.* **1977**, *16*, 249. (c) Boger, D. L.; Brotherton, C. E. *J. Am. Chem. Soc.* **1984**, *106*, 805. (d) Danheiser, R. L.; Carini, D. J.; Basak, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604. (e) Herndon, J. W. *J. Am. Chem. Soc.* **1987**, *109*, 3165. (f) Bucheister, A.; Klemarczyk, P.; Rosenblum, M. *Organometallics* **1982**, *1*, 1679. (g) Beak, P.; Burg, D. A. *J. Org. Chem.* **1989**, *54*, 1647. (h) Marino, J. P.; Laborde, E. *J. Am. Chem. Soc.* **1985**, *107*, 734. (i) Tsuji, J.; Shimizu, I.; Ohashi, Y. *Tetrahedron Lett.* **1985**, *26*, 3825. (j) Beal, R. B.; Dombroski, M. A.; Snider, B. B. *J. Org. Chem.* **1986**, *51*, 4391. (k) Berson, J. A.; Duncan, C. D.; Corwin, L. R. *J. Am. Chem. Soc.* **1974**, *96*, 6175. (l) Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1979**, *101*, 7129. (m) Tomioka, H.; Kobayashi, D. Hashimoto, A. Murata, S. *Tetrahedron Lett.* **1989**, *30*, 4685. (n) Miyashi, T.; Kamata, M.; Mukai, T. *J. Am. Chem. Soc.* **1986**, *108*, 2755. (o) Nakamura, E.; Yamago, S.; Ejiri, S.; Dorigo, A. E.; Morokuma, K. *J. Am. Chem. Soc.* **1991**, *113*, 3183. (p) Shimizu, I.; Ohashi, Y.; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 3825. (q) Noyori, R.; Odagi, T.; Takaya, H. *J. Am. Chem. Soc.* **1970**, *92*, 5780.

(3) (a) Curran, D. P.; Chen, M. -H. *J. Am. Chem. Soc.* **1987**, *109*, 6558. (b) Curran, D. P.; Chen, M. -H.; Spletzer, E.; Seong, C. M.; Chang, C. -T *J. Am. Chem. Soc.* **1989**, *111*, 8872. (c) Curran, D. P.; Seong, C. M. *J. Am. Chem. Soc.* **1990**, *112*, 9401. (d) Cekovic, Z.; Saicic, R. *Tetrahedron Lett.* **1986**, *27*, 5893. (e) Clive, D. J.; Angoh, A. G. *J. Chem. Soc., Chem. Commun.* **1985**, 980. (f) Curran, D. P. van Elburg, P. A. *Tetrahedron Lett.* **1989**, *30*, 2501.

(4) (a) Feldman, K. S.; Romanelli, A. L.; Ruckle, R. E., Jr.; Jean, G. *J. Org. Chem.* **1992**, *57*, 100. Feldman, K. S.; Romanelli, A. L.; Ruckle, R. E., Jr.; Miller, R. F. *J. Am. Chem. Soc.* **1988**, *110*, 3300. Feldman, K. S.; Ruckle, R. E., Jr. Romanelli, A. L. *Tetrahedron Lett.* **1989**, *30*, 5845. (b) Miura, K.; Fugami, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 5135.

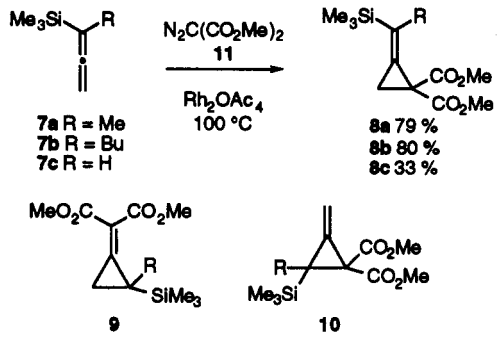
(5) (a) Singleton, D. A.; Church, K. M. *J. Org. Chem.* **1990**, *55*, 4780. (b) Singleton, D. A.; Huval, C. C.; Church, K. M.; Priestley, E. S. *Tetrahedron Lett.* **1991**, *32*, 5765.

(6) Singleton, D. A.; Church, K. M.; Lucero, M. J. *Tetrahedron Lett.* **1990**, *31*, 5551.

(7) (a) Fleming, I.; Dunogue, J.; Smithers, R. *Organic Reactions;* Wiley, New York, 1989; Vol. 37, p 57. (b) Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761.

0022-3263/94/1959-2020$04.50/0

initial methylenecyclopropanes.[8] In the specific case of the synthesis of methylenecyclopropanes **8a-c** from the unsymmetrical allenes **7a-c**,[9] there was particular concern



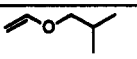
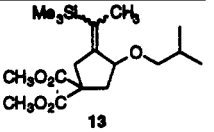
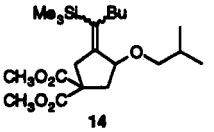
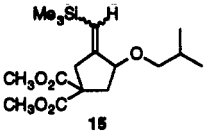
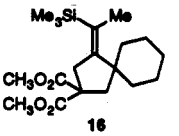
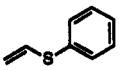
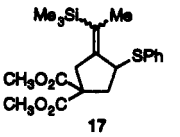
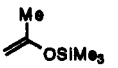
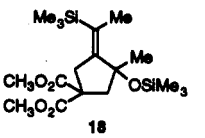
that formation of the isomeric methylenecyclopropanes **9** and **10** would pose a problem. We were therefore pleased to find that the rhodium acetate catalyzed reaction of dimethyl diazomalonate (**11**)[10] with **7a-c** at 100 °C afforded **8a-c** cleanly without forming any **9** or **10**. (The low yield of **8c** appeared due to poor conversion of the starting **7c**.) On the basis of the work of Creary with similar methylenecyclopropanes,[11] the high selectivity in these reactions is likely due to a combination of thermodynamic preference for **8** over **10** and a kinetically slow rearrangement of **8** to **9**.

The stereochemistry of the single isomer **8a** was examined in a ^{1}H NOE experiment. Irradiation of the trimethylsilyl group resulted in an enhancement of the cyclopropane methylene group, in support of the *E* stereochemistry depicted.

Annulations. The methylenecyclopentane annulation of electron-rich or unactivated alkenes with **8a-c** proceeds under conditions which generate either alkylthiyl or trialkylstannyl radicals. These reactions were most efficiently accomplished by irradiation of a neat mixture of alkene, methylenecyclopropane, and 20–30 mol % butyl disulfide or bis(tributyltin) through Pyrex (>300 nm) in a Rayonet photochemical reactor. It was convenient to carry out exploratory reactions in nitrogen-flushed, sealed 3-mm OD capillaries, following the reaction by NMR by placing the capillary within a regular NMR tube. Larger scale reactions were carried out in NMR tubes with no significant difference in yield.

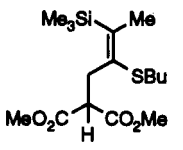
Our results are summarized in Table 1. Butyl disulfide was the best catalyst for **8a** and **8b**, while bis(tributyltin) was best for **8c**. Good yields were obtained both with excess alkene and with a small excess of methylenecyclopropane. The reactions of **8a-c** were significantly slower than the corresponding reactions of **1**.[5b] While the reactions of **1** usually proceeded to completion within a few hours, the reactions of **8a-c** typically required several days. The reactions generally appeared quantitative by NMR at <50% conversions but slowed greatly approaching completion with increasing amounts of byproduct formation. The reaction times could be reduced by increasing the concentration of BuSSBu or by increasing the intensity of the irradiation. However, both of these measures gave

Table 1. Annulations of Alkenes with 8a-c

8a-c	alkene	equiv	% yield (isomer ratio)[a]	product
8a		4.0	89 (53:47)	 **13**
		0.8	54 (62:38)	
8b		3.0	51 (80:20)	 **14**
8c		2.7	70 (83:17)	 **15**
8a		5.4	81 (95:5)	 **16**
		3.9	75 (95:5)	
		2.5	67 (95:5)	
		0.8	55 (95:5)	
8a		3.0	61 (72:28)[b]	 **17**
		0.8	51 (72:28)[b]	
8a		1.8	64[c]	 **18**
		0.5	90[c]	
		0.46	91[c]	

[a] Yields correspond to isolated, purified materials. The ratios of products were obtained from GC and GC/MS analysis of the crude reaction mixture before workup unless otherwise stated. [b] The ratio was obtained from NMR and GC analysis of the product after chromatography. [c] A single isomer was observed by GC and NMR.

significant increases in a byproduct tentatively identified as **12**, as monitored by its characteristic triplet in the ^{1}H NMR at δ 3.88.



12

The stereochemistry of the major isomer of **16** was assigned as shown (*E*) after protodesilylation afforded **23** (*vide infra*), since protodesilylation proceeds with retention of configuration.[12] In the ^{13}C NMR of **13-15** and **17**, the trimethylsilyl group carbons of the major isomers were shifted upfield from the minor isomers. This led to the tentative assignment of the major isomers as *E*, based on trends in simpler vinylsilanes.[12] Since a second isomer of **18** could not be detected, its stereochemistry could only be assigned highly tentatively by analogy with **16**.

We previously proposed a free-radical chain mechanism for the annulation (Scheme 1).[5a,13] However, these reactions usually do not go to completion when catalyzed by diphenyl disulfide/AIBN, even when a full equivalent of diphenyl disulfide/AIBN is used, and the low rate of these

(8) Binger, P.; Büch, H. M. *Topics in Current Chemistry*, Springer-Verlag, New York, 1987; Vol. 135, pp. 77–151. For older methods, see: Rahman, W.; Kuivila, H. G. *J. Org. Chem.* **1966**, *31*, 772. For synthesies of allenes, see: *The Chemistry of the Allenes*, Vol 1; Landor, S. R. ed.; Academic: New York, 1982.

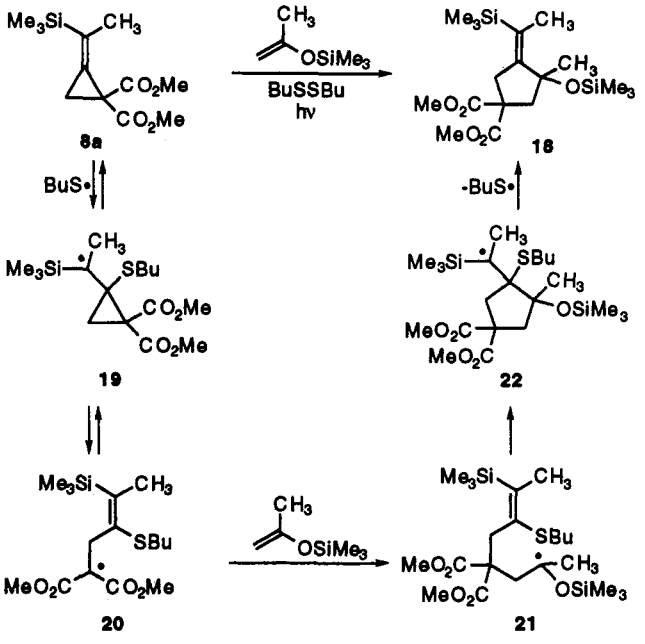
(9) Danheiser, R. L.; Tsai, Y. -M.; Fink, D. M. *Organic Synthesis*; Wiley, New York, 1987; Vol. 66, p 1.

(10) Peace, P. W.; Carman, F.; Wulfman, D. S. *Synthesis* **1971**, 658.

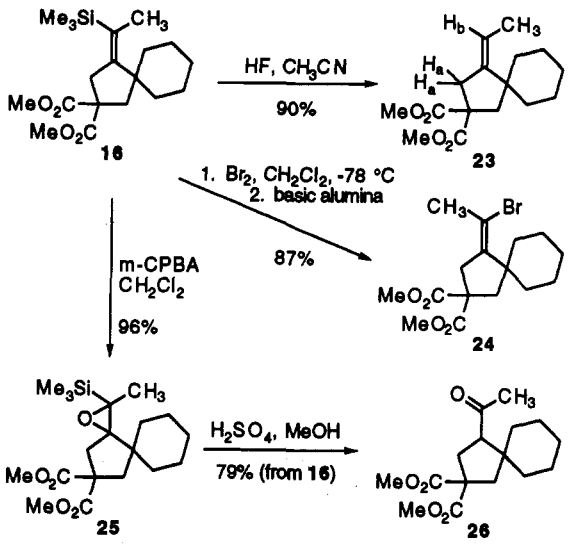
(11) Creary, X. *J. Org. Chem.* **1978**, *43*, 1777.

(12) Colvin, E. *Silicon in Organic Synthesis*; Butterworths: Boston, MA, 1981; pp 60–63.

Scheme 1



Scheme 2



reactions is consistent with a very low quantum yield.[14] This suggests a nonchain process. A possible explanation is that the addition of thiyl radicals to the methylenecyclopropanes is slow or highly reversible and that the chain-transfer step is interrupted by thiyl radical–thiyl radical recombination. The starting methylenecyclopropanes react only extremely slowly in the absence of a reactive alkene,[15] suggesting that the formation of **20** is reversible.

In attempted reactions of **8a** with cyclohexene, cyclopentadiene, 1-(trimethylsiloxy)cyclohexene, and 1-methoxy-1-(trimethylsiloxy)-2-methyl-1-propene, no annulated products could be isolated, and only the very slow formation of **12** was observed. The apparent failure of **20** to add to these alkenes is in line with previous observations; additions of malonate radicals to alkenes are quite sensitive to steric effects, and additions to 1,2-disubstituted alkenes have often been low yielding.[3c]

Product Transformations. The versatility of the annulation depends on the transformations available for the product vinylsilanes. To explore the utility of the annulation products in this regard, some typical vinylsilane transformations were carried out with **16** (Scheme 2). Protodesilylation with HF in acetonitrile afforded **23** in high yield. The stereochemistry of **23** was assigned from NOE studies. Irradiation of the cyclopentane ring protons H_a resulted in an enhancement of the vinylic proton H_b, while irradiation of the allylic methyl hydrogens resulted in an enhancement of a resonance assigned to the cyclohexane ring. These results establish the stereochemistry of both **23** and **16**.

The annulation products are also readily converted to vinyl bromides and ketones. Bromination of **16** followed by elimination of Me_3SiBr with basic alumina afforded **24** in 87% yield. The use of this two-step bromodesilylation procedure is assumed to give inversion of configuration based on literature precedent.[16] Epoxidation of **16** followed by direct acid-catalyzed rearrangement of the product mixture afforded the ketone **26** in good yield. Vinyl bromides like **24** and α,β-epoxy silanes like **25** should be intermediates valuable in their own right, which further increases the utility of the methylenecyclopentane annulation.

Conclusion. The [3 + 2] methylenecyclopentane annulations with methylenecyclopropanes are mechanistically most parallel to Feldman's annulations with vinylcyclopropanes[4] and synthetically most parallel to Curran's atom-transfer cycloadditions with homopropargyl iodides.[3a-c] In each case a highly complex process is possible because the annulation mechanism controls the fate of the intermediate radicals. The reactions are complementary; for example, *exo*-disubstituted methylenecyclopentanes like **13–18** are unobtainable from the related annulations. The combination of the ready availability of (silylmethylene)cyclopropanes like **8a-c**, their efficient annulations of electron rich and unactivated 1,1-disubstituted alkenes, and the array of electrophilic substitutions possible on the resulting vinylsilanes should make these reactions competitive with the other methodologies and attractive to organic synthesis.

Experimental Section

All reactions were carried out in dry glassware under a nitrogen atmosphere using solvents dried by standard techniques. Flash chromatography was performed using 230–400-mesh Kieselgel 60 silica gel from E. Merck. ^1H and ^{13}C NMR spectra were observed at 200 and 50 MHz, respectively, as solutions in $CDCl_3$ unless otherwise indicated. Dimethyl diazomalonate and **7a-c** were prepared by known methods.[17] The alkenes were used as received from commercial suppliers unless otherwise noted.

Cyclopropanation of Allenes with Dimethyl Diazomalonate; General Procedure. *CAUTION: These reactions evolve N_2 and can develop high pressures.* A mixture of the allene, dimethyl diazomalonate, and Rh_2OAc_4 in a pressure tube was heated to 100 °C overnight. The pressure tube was cooled to −78 °C before opening, and the reaction mixture was poured into 100 mL of H_2O and extracted with diethyl ether (3 × 40 mL).

(13) For the photochemical generation of thiyl radicals from disulfides, see: (a) Schmidt, U.; Muller, A.; Markau, K. *Chem. Ber.* **1964**, *97*, 405. (b) Calvert, J. G.; Pitts, J. N. *Photochemistry*; Wiley: New York, 1961; p 490. (c) Rao, P. M.; Knight, A. R. *Can. J. Chem.* **1968**, *46*, 2462. For the addition of electrophilic radicals to methylenecyclopropane, see: Marti, V. P. J.; Paul, V.; Roberts, B. P. *J. Chem. Soc. Perkin Trans. 2* **1986**, 481.

(14)) No quantum yield measurements were undertaken. However, under nearly identical experimental conditions a sensitized diene dimerization (with an expected quantum yield of ≤1) was complete in 25 min.

(15) After 8 days, by ^1H and ^{13}C NMR and GC/MS analysis of the crude reaction mixture of a typical setup in the absence of alkene, 84% of **8a** remained with the presence of 16% of **12**. Irradiation for 12 days of a mixture of 1.1 molar equivalent of butyl disulfide, **8a**, and no olefin, returned 52% of **8a** along with 44% of **12**.

(16) Miller, R. B.; McGarvey, G. *Synth. Commun.* **1979**, *9*, 831.

(17) 1,1-Dimethylallene: Bailey, W. J.; Pfeifer, C. R. *J. Org. Chem.* **1955**, *20*, 95. Silylsubstituted allenes: Danheiser, R. L.; Tsai, Y.-M.; Fink, D. M. *Organic Synthesis*; Wiley, New York, 1987; Vol. 66, p 1.

The combined ethereal extracts were washed (brine), dried (Na_2SO_4), and concentrated on a rotary evaporator. The methylenecyclopropanes were then isolated by flash chromatography (12-in. × 0.5-in. silica gel column) of the residue using 3–5% EtOAc in 30–60 °C petroleum ether as eluent.

Dimethyl 2-(1-methylethylidene)-1,1-cyclopropanedicarboxylate (1). The general procedure was followed using 2.0 mL (1.39 g, 20.4 mmol) of 1,1-dimethylallene, 0.74 g (4.7 mmol) of dimethyl diazomalonate, and 10 mg (0.023 mmol) of Rh_2OAc_4 to afford 0.79 g (85%) of 1 as a clear oil: ^1H NMR δ 3.66 (s, 6 H), 2.05 (m, 2 H), 1.80 (t, 3 H), 1.76 (t, 3 H); ^{13}C NMR δ 168.80, 125.38, 116.26, 52.36, 32.29, 21.96, 21.54, 18.50; HRMS calcd for $C_{10}H_{14}O_4$ 198.08920, found 198.08876. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 59.94; H, 7.03.

Dimethyl 2-[1-(Trimethylsilyl)ethylidene]-1,1-cyclopropanedicarboxylate (8a). The general procedure was followed using 2.30 g (18.2 mmol) of 1-methyl-1-(trimethylsilyl)allene, 2.04 g (12.9 mmol) of freshly prepared dimethyl diazomalonate, and 22.4 mg (0.051 mmol) of Rh_2OAc_4 to afford 2.60 g (79%) of the clear liquid 8a: ^1H NMR δ 3.68 (s, 6 H), 2.19 (q, 2 H), 1.80 (t, 3 H), 0.083 (s, 9 H); ^{13}C NMR δ 168.58, 128.69, 126.70, 52.42, 30.53, 19.38, 18.56, 2.15; IR (neat) 2957, 1738, 1732, 1437, 1307, 1286, 1251, 1107, 860, 839 cm^{-1}; MS *m/e* 256 (M^+). Anal. Calcd for $C_{12}H_{20}O_4Si$: C, 56.22; H, 7.86. Found: C, 56.33; H, 7.66.

Dimethyl 2-[1-(Trimethylsilyl)pentylidene]-1,1-cyclopropanedicarboxylate (8b). The general procedure was followed using 3.56 g (21.1 mmol) of 1-butyl-1-(trimethylsilyl)allene, 4.40 g (27.8 mmol) of freshly prepared dimethyl diazomalonate, and 22 mg (0.05 mmol) of Rh_2OAc_4 to afford 4.95 g (78%) of the clear liquid 8b: ^1H NMR δ 3.65 (s, 6 H), 2.17 (m, 4 H), 1.3–1.05 (m, 4 H), 0.79 (t, 3 H), 0.078 (s, 9 H); ^{13}C NMR δ 168.82, 131.16, 129.38, 52.21, 33.95, 31.20, 30.46, 22.32, 18.92, 13.62, 1.58; MS *m/e* 298 (M^+); HRMS calcd for $C_{15}H_{26}O_4Si$ 298.16004, found 298.15873. Anal. Calcd for $C_{15}H_{26}O_4Si$: C, 60.37; H, 8.78. Found: C, 60.05; H, 8.75.

Dimethyl 2-[1-(Trimethylsilyl)methylidene]-1,1-cyclopropanedicarboxylate (8c). The general procedure was followed using 2.00 g (17.8 mmol) of (trimethylsilyl)allene, 1.50 g (9.49 mmol) of freshly prepared dimethyl diazomalonate, and 20.0 mg (0.045 mmol) of Rh_2OAc_4 to afford 750 mg (33%) of the clear liquid 8c: ^1H NMR δ 6.11 (t, 1 H), 3.71 (s, 6 H), 2.23 (d, 2 H), 0.12 (s, 9 H); ^{13}C δ 168.50, 136.28, 118.49, 52.60, 31.36, 18.59, −1.44; IR (neat) 2957, 1739, 1436, 1295, 1140, 843 cm^{-1}; MS *m/e* 242 (M^+). Anal. Calcd for $C_{11}H_{18}O_4Si$: C, 54.52; H, 7.49. Found: C, 54.68; H, 7.58.

Annulation of Alkenes with Methylenecyclopropanes; General Procedure. An oven-dried 3-mm o.d. standard wall Pyrex tube, flame sealed at one end and capped with a septum wrapped with parafilm at the other, was dried with a heat gun under a N_2 flush. The reagents were added under an N_2 atmosphere using standard syringe techniques, and the tube was again flushed with N_2 for approximately 15 min and flame sealed under N_2. After being shook to ensure homogeneity, the reaction was photolyzed in a Rayonet photochemical reactor. The progress of these reactions was most easily followed by NMR by placing the resulting capillary within an NMR tube and referencing approximately using the external $CDCl_3$. The methylenecyclopentanes were isolated by direct flash chromatography (18-in. × 0.25-in. silica gel column) using 3% EtOAc in 30–60 °C petroleum ether as eluent.

Dimethyl 3-Methyl-3-(4-methyl-3-cyclohexen-1-yl)-4-(1-methylethylidene)-1,1-cyclopentanedicarboxylate ((R*,R*)- and (R*, S*)-3). A. The general annulation procedure was followed using 53.8 mg (0.27 mmol) of 1, 17.2 mg (0.13 mmol) of freshly distilled (*R*)-(+)-limonene, 14.3 mg (0.08 mmol) of butyl disulfide, and 48 h of irradiation (16–300-nm lamps) to give 30.9 mg (73% based on limonene) of a 6:4 mixture of diastereomers of **3** as a viscous oil: ^1H NMR δ 5.40–5.26 (m, 1 H), 3.70 (s, 3 H), 3.67 (s, 3 H), 3.28 (m, 1 H), 2.50–2.30 (m, 2 H), 2.1–1.5 (m, 16 H), 1.20 (m, 1 H), 1.11 (d, 3 H); ^{13}C NMR δ 172.88, 172.81, 138.16, 137.62, 133.99, 133.69, 123.99, 123.90, 121.12, 121.02, 57.39, 57.32, 52.69, 52.56, 48.03, 47.52, 43.75, 43.62, 42.27, 42.01, 41.57, 31.25, 31.18, 27.18, 26.48, 25.42, 24.06, 23.50, 23.41, 23.35, 23.27, 20.64, 20.54; IR (neat) 2957, 2920, 1755, 1738, 1732, 1435, 1263, 1238, 1201, 1169 cm^{-1}. Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.99; H, 9.00.

B. The general annulation procedure was followed using 53.6 mg (0.27 mmol) of 1, 27.6 mg (0.20 mmol) of freshly distilled (*R*)-(+)-limonene, 7.9 mg (0.04 mmol) of butyl disulfide, and 40 h of irradiation (16–300 nm lamps) to afford 14.3 mg of limonene (52%), and 31.3 mg (96% based on recovered limonene) of a 6:4 mixture of diastereomers of **3** as a viscous oil.

Dimethyl 3-[1-(Trimethylsilyl)ethylidene]-4-(2-methylpropoxy)-1,1-cyclopentanedicarboxylate (13). A. The general annulation procedure was followed using 48.0 mg (0.19 mmol) of **8a**, 76 mg (0.76 mmol) of freshly distilled isobutyl vinyl ether, 9.3 mg (0.052 mmol) of butyl disulfide, and 10 d of irradiation (4–300-nm lamps) to afford 59.6 mg (89%) of a 53:47 mixture of trans and cis isomers of **13** as an oil: ^1H NMR δ 4.40 and 4.20 (m, 1 H), 3.70, 3.70, 3.69, and 3.68 (s, 6 H), 3.38–2.90 (m, 3 H), 2.78–1.19 (m, 3 H), 1.82–1.62 (m, 3 H), 0.90–0.78 (m, 6 H), 0.16 and 0.11 (s, 9 H); ^{13}C NMR δ 172.90, 172.29, 171.68, 171.59, 148.86, 147.45, 134.07, 133.64, 79.70, 78.25, 75.97, 74.57, 58.47, 57.51, 52.80, 52.62, 39.50, 38.96, 38.78, 37.86, 28.74, 28.61, 22.30, 19.74, 19.68, 19.61, 19.54, 19.08, 18.69, −0.26, −0.69; IR (neat) 2955, 2874, 1738, 1435, 1277, 1250, 1201, 1170, 1116, 1082, 850, 837, 756 cm^{-1}; MS *m/z* 341 ($M^+ - CH_3$). Anal. Calcd for $C_{18}H_{32}O_5Si$: C, 60.64; H, 9.05. Found: C, 60.72; H, 9.11.

B. The general annulation procedure was followed using 50.6 mg (0.20 mmol) of **8a**, 14.6 mg (0.15 mmol) of freshly distilled isobutyl vinyl ether, 10.7 mg (0.060 mmol) of butyl disulfide, and 11 d of irradiation (4–300-nm lamps) to afford 27.9 mg (54%) of a 62:38 mixture of trans and cis isomers of **13**.

Dimethyl 3-[1-(Trimethylsilylpentylidene]-4-(2-methylpropoxy)-1,1-cyclopentanedicarboxylate (14). The general annulation procedure was followed using 49.9 mg (0.17 mmol) of **8b**, 51.0 mg (0.51 mmol) of freshly distilled isobutyl vinyl ether, 11.2 mg (0.063 mmol) of butyl disulfide, and 12 d of irradiation (9–300-nm lamps) to afford 34.0 mg (51%) of a 57:43 mixture of trans and cis isomers of **14** as an oil: ^1H NMR δ 4.37 and 4.20 (m, 1 H), 3.70, 3.69 and 3.67 (s, 6 H), 3.35–2.90 (m, 3 H), 2.80–1.90 (m, 5 H), 1.77 (m, 1 H), 1.40–1.05 (m, 4 H), 0.95–0.80 (m, 9 H), 0.12 (s, 9 H); ^{13}C NMR δ 175.43, 147.86, 139.55, 79.84, 78.05, 75.46, 74.58, 58.38, 52.82, 52.67, 39.53, 39.01, 38.59, 37.12, 33.66, 33.03, 32.80, 31.36, 28.70, 28.65, 23.10, 19.75, 19.64, 13.99, 0.43, −0.21; MS *m/e* 398 (M^+), 383 ($M^+ - CH_3$); HRMS calcd for $C_{21}H_{38}O_5Si$ 398.24885, found 398.24698. Anal. Calcd for $C_{21}H_{38}O_5Si$: C, 63.28; H, 9.62. Found: C, 63.01; H, 9.51.

Dimethyl 3-[1-(Trimethylsilyl)methylidene]-4-(2-methylpropoxy)-1,1-cyclopentanedicarboxylate (15). The general annulation procedure was followed using 56.2 mg (0.23 mmol) of **8c**, 60.9 mg (0.61 mmol) of isobutyl vinyl ether, 23.5 mg (0.04 mmol) of bis(tributyltin), 250 μL of C_6D_6, a standard NMR tube, and 5 d of irradiation (9–300-nm lamps) to afford 56.0 mg (70%) of an 83:17 mixture of isomers of **15** as an oil: ^1H NMR δ 5.65–5.55 (m, 1 H), 3.98 (m, 1 H), 3.70 and 3.68 (s, 6 H), 3.21–3.05 (m, 3 H), 2.80–2.10 (m, 3 H), 1.77 (m, 1 H), 0.85 (d, 3 H), 0.82 (d, 3 H), 0.09 and 0.06 (s, 9 H); ^{13}C NMR (major isomer) δ 172.75, 171.92, 155.79, 124.46, 82.86, 75.75, 57.50, 52.77, 52.65, 39.02, 37.39, 28.39, 19.33, 19.19, −0.76; MS *m/z* 342 (M^+), 327 ($M^+ - CH_3$). Anal. Calcd for $C_{17}H_{30}O_5Si$: C, 59.62; H, 8.83. Found: C, 59.15; H, 8.78.

Dimethyl 4-(1-Methylethylidene)spiro[4.5]decane-2,2-dicarboxylate (16). A. The general annulation procedure was followed using 51.6 mg (0.20 mmol) of **8a**, 60 μL (48 mg, 0.50 mmol) of methylenecyclohexane, 7.6 μL (7.1 mg, 0.040 mmol) of butyl disulfide, and 3 d of irradiation (16–300-nm lamps) to give 16.5 mg (32%) of **8a** and 47.7 mg (67% or 99% based on recovered **8a**) of a 95:5 mixture of trans and cis isomers of **16** as an oil. The spectroscopic properties of the major isomer are: ^1H NMR δ 3.69 (s, 6 H), 2.96 (q, 2 H), 2.39 (s, 2 H), 1.84 (t, 3 H), 2.05–1.10 (m, 10 H), 0.12 (s, 9 H); ^{13}C NMR δ 172.58, 155.34, 127.53, 58.31, 52.58, 47.99, 44.54, 42.65, 34.76, 25.68, 23.25, 17.83, −0.09; IR (neat) 2951, 2860, 1734, 1600, 1252, 1201, 1182, 1167, 849, 837 cm^{-1}. Anal. Calcd for $C_{19}H_{32}O_4Si$: C, 64.73; H, 8.91. Found: C, 65.00; H, 8.91.

B. The general annulation procedure was followed using 50.4 mg (0.20 mmol) of **8a**, 14.1 mg (0.15 mmol) of methylenecyclohexane, 10.3 mg (0.058 mmol) of butyl disulfide, and 11 d of irradiation (4–300-nm lamps) to afford 28.6 mg (55%) of a 95:5 mixture of trans and cis isomers of **16**.

C. The general annulation procedure was followed using 490 g (1.9 mmol) of **8a**, 720 mg (7.5 mmol) of methylenecyclohexane,

101.5 mg (0.57 mmol) of butyl disulfide, a standard NMR tube, and 12 d of irradiation (4–300-nm lamps) to afford 505 mg (75%) of **16**.

D. The general annulation procedure was followed using 475 g (1.9 mmol) of **8a**, 985 mg (10.2 mmol) of methylenecyclohexane, 135.0 mg (0.76 mmol) of butyl disulfide, a standard NMR tube, and 12 d of irradiation (4–300-nm lamps) to afford 526 mg (81%) of **16**.

Dimethyl3-(Phenylthio)-4-[1-(trimethylsilyl)ethylidene]-cyclopentane-1,1-dicarboxylate (17). A. The general annulation procedure was followed using 50.9 mg (0.20 mmol) of **8a**, 80 μL (83.4 mg, 0.61 mmol) of phenyl vinyl sulfide, 7.6 μL (7.1 mg, 0.040 mmol) of butyl disulfide, and 3 d of irradiation (16–300-nm lamps) to afford 47.8 mg (61%) of a 72:28 mixture of isomers of **17** as an oil: ^{1}H NMR δ 7.40–7.10 (m, 5 H), 5.04 and 4.38 (m, 1 H), 3.73, 3.72, and 3.67 (s, 6 H), 3.50–2.37 (m, 4 H), 1.74 and 1.26 (s, 3 H), 0.14 and 0.11 (s, 9 H); ^{13}C NMR (major isomer) δ 172.73, 172.59, 145.63, 134.48, 128.80, 128.26, 127.46, 121.66, 59.04, 52.77, 52.52, 43.21, 40.55, 22.12, 22.08, -2.79; IR (neat) 3060, 2955, 1738, 1600, 1437, 1271, 1251, 1219, 1197, 1167, 1105, 844 cm^{-1}; MS *m/z* 392 (M$^+$). Anal. Calcd for $C_{20}H_{28}O_4SSi$: C, 61.19; H, 7.19. Found: C, 61.37; H, 6.98.

B. The general annulation procedure was followed using 50.2 mg (0.20 mmol) of **8a**, 21.4 mg (0.16 mmol) of phenyl vinyl sulfide, 10.3 mg (0.16 mmol) of butyl disulfide, and 3 d of irradiation (4–300-nm lamps) to afford 31.4 mg (51%) of a 72:28 mixture of trans and cis isomers of **17** as an oil.

Dimethyl 3-Methyl-3-(trimethylsiloxy)-4-[(1-(trimethylsilyl)ethylidene]cyclopentane-1,1-dicarboxylate (18). A. The general annulation procedure was followed using 51.0 mg (0.20 mmol) of **8a**, 70 mg (0.35 mmol based on 70% purity[18]) of isopropenoxytrimethylsilane, 9.3 mg (0.052 mmol) of butyl disulfide, and 12 d of irradiation (4–300-nm lamps) to give 49.0 mg (64%) of a single isomer of **18** as an oil, contaminated with 1–2% of an unidentifiable impurity: ^{1}H NMR δ 3.71 (s, 3 H), 3.70 (s, 3 H), 3.07–2.88 (m, 2 H), 2.65 (d, 1 H), 2.40 (dd, 1 H), 1.86 (t, 3 H), 1.37 (s, 3 H), 0.12 (s, 9 H), 0.10 (s, 9 H); ^{13}C NMR δ 172.33, 171.97, 151.74, 130.56, 81.48, 57.08, 52.78, 52.74, 50.17, 40.47, 28.91, 16.88, 2.13, -0.61; IR (neat) 2955, 2901, 1743, 1435, 1257, 1203, 1172, 1126, 841, 756 cm^{-1}; MS *m/z* 371 (M$^+$ - CH_3). Anal. Calcd for $C_{18}H_{34}O_5Si_2$: C, 55.92; H, 8.86. Found: C, 56.46; H, 8.79.

B. The general annulation procedure was followed using 51.0 mg (0.20 mmol) of **8a**, 20.0 mg (0.10 mmol based on 70% purity) of isopropenoxytrimethylsilane, 9.1 mg (0.051 mmol) of butyl disulfide, and 12 d of irradiation (4–300-nm lamps) to afford 34.9 mg (90%) of a single isomer of **18**. Upon further elution, 7.2 mg (2.1%) of the trapped intermediate **12** was isolated: ^{1}H NMR δ 3.88 (t, 1 H), 3.70 (s, 6 H), 2.93 (d, 2 H), 2.53 (t, 2 H), 1.76 (s, 3 H), 1.52–1.15 (m), 0.95–0.78 (m) (the signals at 1.52–1.15 and 0.95–0.78 overintegrate by ~50% from the expected 4 H and 3 H, respectively), 0.16 (s, 9 H); ^{13}C δ 169.66, 144.99, 139.69, 52.44, 50.41, 32.34, 31.49, 30.24, 22.21, 19.36, 13.65, 0.72; MS *m/z* 346 (M$^+$). In a separate procedure, irradiation of a mixture of 122.4 mg (0.48 mmol) of **8a** and 95.7 mg (0.54 mmol) of butyl disulfide for 12 d afforded 74.5 mg (0.21 mmol, 44%) of **12** and 63.6 mg (0.25 mmol, 52%) of **8a** after chromatography over silica gel eluting with EtOAc (0–3%) in 30–60 °C petroleum ether.

C. The general procedure was followed using 165 mg (0.64 mmol) of **8a**, 57.9 mg (0.29 mmol based on 70% purity) of isopropenoxytrimethylsilane, 28.1 mg (0.16 mmol) of butyl disulfide, and 12 d of irradiation (4–300-nm lamps) to afford 34.9 mg (90%) of **18**.

Dimethyl 4-Ethylidenespiro[4.5]decane-2,2-dicarboxylate (23). A solution of 83.5 mg (0.24 mmol) of a 16:1 mixture of isomers of **16** and 130 μL of 48% HF in 125 μL of CH_3CN was stirred at 25 °C for 18 h. The mixture was then poured into 20 mL of H_2O, extracted with three 10-mL portions of diethyl ether, rinsed with 10 mL of brine, dried (Na_2SO_4), and concentrated using a rotary evaporator. The residue was chromatographed on silica using 5% EtOAc in 30–60 °C petroleum ether as eluent to afford 60.4 mg (90%) of a 16:1 mixture of isomers of **23** as an oil. The spectral properties of the major isomer were as follows: ^{1}H NMR δ 5.32 (q of t, 1 H), 3.68 (s, 6 H), 2.88 (m, 2 H), 2.39 (s, 2 H), 1.69 (d of t, 3 H), 1.90–1.00 (m, 10 H); ^{13}C NMR δ 172.79, 147.00, 116.96, 57.89, 52.51, 45.13, 44.67, 43.21, 35.23, 25.63, 22.96, 13.70; IR (neat) 2932, 2858, 1736, 1435, 1288, 1250, 1199, 1176 cm^{-1}; MS (both isomers) *m/z* 280 (M$^+$). Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: C, 68.44; H, 8.56. The structure of **23** was probed further by difference NOE. Low-power irradiation of the methylene group of the major isomer at δ 2.88 resulted in a large enhancement of the vinylic proton at δ 5.32. Low-power irradiation of the allylic methyl protons of the major isomer at δ 1.69 resulted in an enhancement of the cyclohexane protons near δ 1.39. The observable spectral properties of the minor isomer of **23** were as follows: ^{1}H NMR δ 3.69 (s, 3 H), 2.98 (m, 2 H), 2.33 (s, 2 H).

Dimethyl 4-(1-Bromoethylidene)spiro[4.5]decane-2,2-dicarboxylate (24). To a solution of 63.7 mg (0.18 mmol) of vinylsilane **16** in 3 mL of CH_2Cl_2, cooled to -78 °C, was slowly added a solution of Br_2 (50 μL) in 2 mL of CH_2Cl_2. To the red-orange solution was added 3 mL of MeOH saturated with Na_2SO_3, and the resulting mixture was vigorously stirred until the mixture became light yellow (10 min). While still cold (-78 °C), the reaction mixture was quickly extracted with 10% Na_2SO_3 until all of the color had disappeared. After separation, the aqueous layer was thoroughly extracted with CH_2Cl_2 (50 mL). The combined organic extracts were allowed to stand overnight at 25 °C with excess Al_2O_3. The mixture was then filtered and concentrated to afford 63.0 mg (87% based on 90% purity) of **24** as colorless crystals. These crystals were further purified for analytical purposes by flash chromatography over silica gel, eluting with 2% EtOAc in 30–60 °C petroleum ether, to give 45 mg (69%) of **24**: ^{1}H NMR δ 3.70 (s, 6 H), 3.12 (q, 2 H), 2.54 (s, 2 H), 2.44 (t, 3 H), 1.8–1.0 (m, 10 H); ^{13}C NMR δ 172.41, 145.80, 116.56, 57.11, 52.76, 47.31, 45.27, 45.08, 35.03, 26.05, 25.37, 22.75; IR (neat) 2930, 1739, 1254 cm^{-1}; MS *m/z* 358, 360 (M$^+$); HRMS calcd for $C_{16}H_{23}O_4Br$ 358.07797, found 358.07820.

Dimethyl 4-Acetylspiro[4.5]decane-2,2-dicarboxylate (26). A solution of 62.9 mg (0.18 mmol) of vinylsilane **16**, 150 mg (1.79 mmol) of $NaHCO_3$, and 66.0 mg (0.38 mmol) of *m*-CPBA in 4 mL of CH_2Cl_2 was stirred at 25 °C overnight. An additional 63 mg (0.37 mmol) of *m*-CPBA was added, and the resulting slurry was again stirred overnight. The reaction was then poured into saturated Na_2SO_3, extracted thoroughly with CH_2Cl_2 (120 mL), washed with saturated $NaHCO_3$ and then brine, and dried (Na_2SO_4). Concentration on a rotary evaporator followed by drying under high vacuum afforded 63.1 mg (96%) of **25** as an oil: ^{1}H NMR δ 3.70 (s, 3 H), 3.70 (s, 3 H), 2.76 (d, 1 H), 2.59 (d, 1 H), 2.16 (d, 1 H), 2.12 (dd, 1 H), 1.7–1.0 (m, 10 H), 1.38 (s, 3 H), 0.079 (s, 9 H); ^{13}C NMR δ 173.03, 172.17, 74.80, 57.38, 57.34, 52.70, 52.56, 45.36, 43.68, 41.09, 34.05, 32.73, 25.72, 23.43, 21.95, 16.83, -2.03; IR (neat) 2953, 1739, 1435, 1253, 1216, 1178, 843, 733 cm^{-1}; HRMS calcd for $C_{19}H_{32}O_5Si$ 368.20190, found 368.20240. A solution of the crude silyl epoxide from the epoxidation of 110.8 mg (0.31 mmol) of vinylsilane **16** as described above and 5 mL of 20% H_2SO_4 in 5 mL of MeOH was stirred at 25 °C overnight. It was then quenched with 25 mL of H_2O and extracted completely with CH_2Cl_2 (50 mL), concentrated on a rotary evaporator, and purified by flash chromatography eluting with 3% EtOAc in 30–60 °C petroleum ether to afford 66.5 mg (79%) of **26**: ^{1}H NMR δ 3.71 (s, 3 H), 3.70 (s, 3 H), 2.74 (dd, 1 H), 2.61–2.33 (m, 3 H), 2.15 (s, 3 H), 2.09 (d, 1 H), 1.70–0.80 (m, 10 H); ^{13}C NMR δ 209.28, 173.43, 172.65, 61.82, 57.72, 52.79, 52.74, 46.44, 42.62, 38.53, 34.85, 32.28, 32.18, 25.71, 23.72, 22.22; IR (neat) 2932, 2856, 1738, 1704, 1434, 1253 cm^{-1}; MS *m/z* 296 (M$^+$); HRMS calcd for $C_{16}H_{24}O_5$ 296.16237, found 296.16170. Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.14; H, 8.29.

(18) The commercial isopropenoxytrimethylsilane was contaminated with 30% of hexamethyldisiloxane.

Acknowledgment. We thank the Institute of General Medical Sciences of the National Institutes of Health for support of this research.

Supplementary Material Available: ^{1}H NMR spectra for **8a-c**, **12-18**, and **23-26** (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.