to the bornyl chloride solution and to the lithium in the flask just before the reaction was begun. As the halide was added, the initially clear mixture acquired a purple color. In addition, the lithium sand, which initially had a very silvery luster, took on a black coating and sank to the bottom of the flask. When this happened, additional portions of lithium were added, up to a total of about 250% of the theoretically required amount. After completion of the addition of halide, the mixture was held at reflux for 2–10 h. The solution of bornyllithium was then transferred under positive internal flask pressure via the frit and side arm to a graduated addition funnel. The addition funnel was itself attached to another three-necked reaction flask equipped with dry nitrogen inlet, magnetic stirrer, and condenser. The yield of the bornyllithium was then determined by Gilman double titration of an aliquot using 1,2-dibromoethane.[7] The yields given by this method were in the range of 45 to 61%. Following this, the bornyllithium solution was introduced into the second vessel for reaction with an appropriate substrate.

Synthesis of (−)-Bornyldimethylsilane. Bornyllithium was prepared as described above from the reaction of 6.2 g (36 mmol) of (−)-bornyl chloride and ca. 1 g of lithium sand. The bornyl chloride addition took 4 h and the mixture was then held at reflux for 10 h. The bornyllithium solution was then added to 10 g (58 mmol) of chlorodimethylsilane (Petrarch) in 25 mL of anhydrous ether. The reaction solution was stirred for 2 h and then quenched with water. The organic layer was separated and washed with water (4 × 30 mL) and saturated aqueous sodium chloride solution and then dried over anhydrous Na_2SO_4. Pentane and diethyl ether were removed by rotary evaporation. GC analysis (15% FFAP, 155 °C) of the oil remaining showed it to consist of 15% unreacted **2** and 85% of the desired product. Purification by preparative GC (20% Carbowax 20M, 85 °C) gave the final product, an oil, α^{27}_D −20.91° (*l* 1 dm, neat). The IR spectrum (CCl_4) showed prominent absorption of Si-H at 2150 cm^{-1}. The ^1H NMR spectrum showed signals at δ 3.8 (1 SiH, multiplet), 2.0–0.9 (8 H, overlapping signals), 0.8 (9 H, br s), and at 0.05 (6 H, two sets of doublets resulting from the two diastereotopic Me groups on Si). Anal. Calcd for $SiC_{12}H_{24}$: Si, 14.26; C, 73.38; H, 12.32. Found: C, 73.43; H, 12.31.

Synthesis of (−)-Dibornylmethylsilane. Bornyllithium was prepared as described above from the reaction of 30.03 g (170 mmol) of (−)-bornyl chloride and 7.7 g of lithium sand. After the bornyl chloride addition, the mixture was held at reflux for 6 h and then stirred at room temperature for an additional 12 h. Dichloromethylsilane (Petrarch), 10.0 g (87 mmol), was then added dropwise with cooling directly to the bornyllithium solution. The resulting mixture was held at reflux for 1 h and then cautiously quenched with water. The organic layer was separated, washed with water (4 × 65 mL), and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and subsequent Kugelrohr distillation (100–125 °C/0.5 torr) yielded 19.42 g (70%) of the desired product as an oil, $[\alpha]^{24.5}_D$ −32.67° (*c* 10.3, EtOH). The IR spectrum (neat film) showed major absorptions at 2950, 2880, 2100, 1460, 1385, 1365, 1250, 1105, 1090, 1025, 960, 920, 880, 840, 820, and 790 cm^{-1}. The ^1H NMR spectrum showed signals at δ 4.0 (1 SiH, multiplet), 2.18–1.10 (16 H, overlapping signals), 1.0 (18 H, br s), and 0.38 (3 H, d). Anal. Calcd for $SiC_{21}H_{38}$: Si, 8.82; C, 79.16; H, 12.02. Found: C, 79.15; H, 12.07.

Tandem Michael Reactions for the Construction of Highly Functionalized Five-Membered Rings

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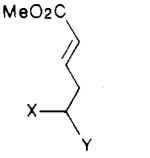
A perpetual goal of synthetic organic chemists is the development of more efficient methods for carrying out multistep transformations. Recently, several groups[2] have reported variants of a Michael–Michael ring closure procedure for the preparation of functionalized cyclohexane derivatives. In light of these reports, we describe an approach to highly functionalized five-membered rings involving a one-pot tandem Michael reaction sequence.

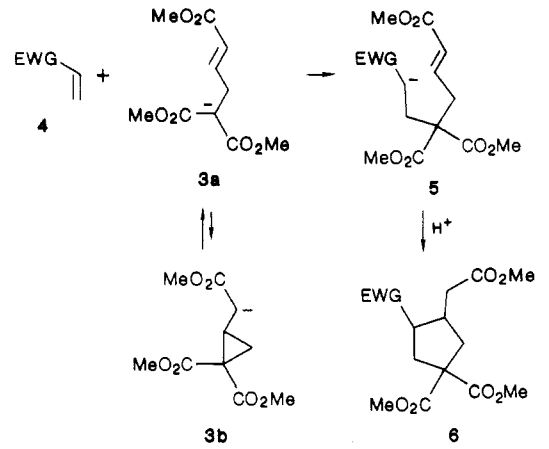
In designing reagents for tandem Michael reactions, it was necessary to position both a Michael donor and an acceptor moiety in the same molecule. To prevent intramolecular closure, the separation of these two subunits must be less than three carbons such that developing ring strain deters cyclization. Considering these criteria, compounds **1** and **2** were sought. Deprotonation of **1** would



1 (X=Y=CO_2Me)
2 (X=Y=SO_2Me)

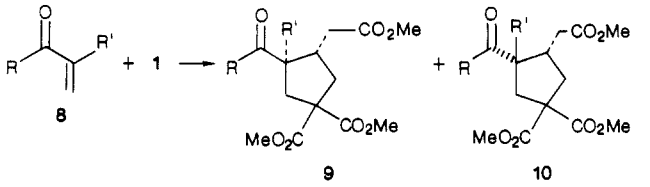
lead to a stabilized anion (**3a**) which would exist in equilibrium[3] with the less stable ring-closed anion **3b** (see

Scheme I[a]



[a] EWG = electron-withdrawing group.

Table I. Addition of 1 to Acyclic Enones



enone	R	R′	9:10[a]	% yield (9 + 10)
8a	CH_3	H	>50:1	65
8b	CH_3	CH_3	5:2	73
8c	Ph	H	>50:1	81
8d	Ph	CH_3	18:1	83

[a] Ratios estimated by GC and NMR integration.

(1) Undergraduate Research Participants: E.J.W. (1985–1986); J.D.P. (Summer 1986); A.J.S. (1984–1986); R.E.D. (1985–1986).

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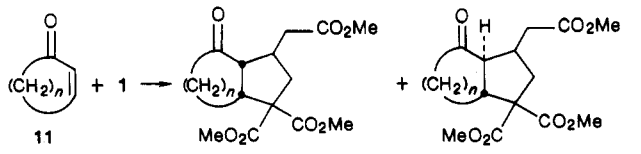
(3) Similar equilibria have been observed and studied previously: (a) Danishefsky, S.; Tsai, M. Y.; Dynak, J. *J. Chem. Soc., Chem. Commum.* **1975**, 7. (b) Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66.

0022-3263/87/1952-0464$01.50/0

Table II. Addition of 1 to Cyclic Enones



enone	n	12:13[a]	% yield (12 + 13)
11a	2	>50:1	62
11b	3	1:9	55

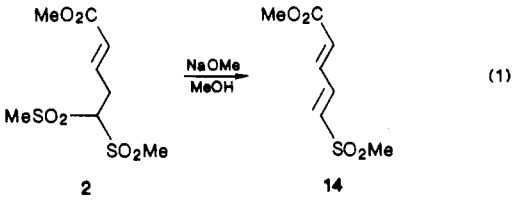
[a] Ratios estimated by GC and NMR integration.

Scheme I). The decreased stability of this ester enolate coupled with the ring strain should disfavor the intramolecular closure such that reaction from **3a** predominates (see Scheme I). Intermolecular conjugate addition of **3a** to an acceptor molecule (**4**) would initially generate enolate **5**. Subsequent intramolecular capture of this intermediate by the built-in α,β-unsaturated ester would then lead to the formation of substituted cyclopentane **6**.

The results of tandem Michael additions to a series of enones using compound **1** are summarized in Tables I and II. Both acyclic and cyclic enones were found to react well in the reaction with acyclic cases giving slightly better results. As with the standard Michael process, the success of the current method is highly dependent upon the steric conjestion surrounding the β-position of the acceptor moieties.[4] This may result from the inability of hindered substrates to approach one another or from a facile competing retro-Michael reaction. Surprisingly, alkyl-substituted malonates, which are normally unreactive toward cycloalkenones, were observed to give moderate yields of cyclized products. This suggests that the apparent steric inhibition in these cases may derive more from the competing retro-Michael process since trapping of the initial adduct by subsequent intramolecular addition and protonation of the less stabilized anion would preclude the reverse reaction. Further evidence for the importance of intramolecular trapping of the initial adduct to the success of the hindered Michael addition was found in the attempted tandem reaction of dimethyl (*E* and *Z*)-5-(methoxycarbonyl)-3-methyl-2-hexenedioate (**7**). This substrate, which has a methyl group positioned at the terminus of the tandem acceptor, yielded predominantly starting material and enone self-condensation products when subjected to the reaction conditions (NaOMe, MeOH, 0 °C) employed.

Stereochemistry in the cyclized products appears to reflect the thermodynamic conditions under which the reactions are performed. While unsubstituted enones **8a** and **8c** (R′ = H) were observed to afford almost exclusively the trans product, the α-methyl enones **8b** and **8d** gave less useful product mixtures. This likely results from from reduced steric differentiation (methyl vs. acyl) in the second Michael reaction for the substituted cases. Furthermore, the products from the α-substituted enones cannot equilibrate once ring closure occurs. Stereochemistry in the products derived from cyclic enones was largely dependent upon the ring sizes in the fused bicyclic molecules generated. The 5,5-fused product was, within our limits of detection, entirely cis; the ring junction in the 6,5-product was 9:1 in favor of the trans.[5]

The bis(sulfone) **2** was also synthesized and studied as a tandem Michael substrate. It was hoped that the methanesulfonyl groups would activate C-5 as a Michael donor[6] and then, following cyclization, permit removal of the cumbersome functionality.[7] Treatment of this compound with methanolic sodium methoxide, however, resulted in preferential elimination of a methanesulfonyl unit to give diene **14** in 87% yield. Thus, while such an elimination process may provide an efficient approach to certain 1,4-disubstituted 1,3-butadienes,[8] it precludes the use of sulfone-activated tandem Michael reagents in this synthetic strategy (see eq 1). Evaluation of other carbanion-stabilizing functionality (–CN, –COR) on the Michael donor moiety of these substrates led us to conclude that, in general, the malonate-derived reagents provide the best results under conditions employing alkoxide base. Work is continuing in an effort to expand the scope of the present reaction.



(1)

Experimental Section[9]

General Procedure for Tandem Michael Additions. Sodium methoxide was generated on a 5.50-mmol scale by reacting 0.13 g of sodium metal in 15 mL of dry methanol under nitrogen atmosphere. To this solution at 0 °C was added a 10-mL methanol solution of 1.27 g (5.50 mmol) of dimethyl (*E*)-5-(methoxycarbonyl)-2-hexenedioate dropwise with stirring. The resulting yellow solution was stirred for 15 min at 0 °C before 5.50 mmol

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(5) Based upon previously reported spectral correlations in 4-hydrindanones, we have tentatively assigned the major isomer as trans. The stereochemistry of the adjacent stereocenter is unknown. See: (a) Cicero, B. L.; Weisbuch, F.; Dana, G. *J. Org. Chem.* **1981**, *46*, 914. (b) Fuchs, B. In *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. L., Eds.; Wiley: New York, 1978; Vol. 10, p 1.

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(8) Elimination was also observed in the reaction of dimethyl (*E*)-5-(phenylsulfonyl)-2-hexenedioate with methanolic sodium methoxide; the product was 2,4-hexadienedioate in 73% yield.

(9) IR spectra were recorded with a PE-681 instrument and are referenced to polystyrene. ^{1}H NMR spectra were measured in $CDCl_3$ at 300 MHz on a Varian XL-300 superconducting FT instrument or at 60 MHz on a Hitachi Perkin-Elmer R-24B spectrometer; chemical shifts are reported in δ units relative to internal Me_4Si. ^{13}C NMR spectra were measured at 75 MHz on the Varian XL-300; chemical shifts are reported in ppm relative to internal Me_4Si. Mass spectra were recorded at 70 eV on a CEC double focusing mass spectrometer. All reactions were run under an atmosphere of dry nitrogen in oven-dried glassware. Reactions were monitored by TLC or GC (Varian 3400, 0.25 mm × 3 m DB-1 column). Preparative thick layer chromatography was performed on silica gel using Analtech (No. 02015) preparative plates with fluorescent indicator. Methanol for cyclization reactions was distilled from sodium metal prior to each run. Methyl vinyl ketone (Aldrich) was dried over $CaCl_2$ and distilled prior to use. 3-Methyl-3-buten-2-one,[10] 1-phenyl-2-propen-1-one,[11] 2-methyl-1-phenyl-2-propen-1-one,[11] dimethyl (*E*)-5-methoxycarbonyl-2-hexenedioate,[12] and dimethyl (*E* and *Z*)-5-(methoxycarbonyl)-3-methyl-2-hexenedioate[13] were prepared and purified by literature methods or slight modifications thereof.

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of the enone was added in 10 mL of methanol. The reaction was stirred for 1 h at 0 °C and for 6–12 h at 20 °C; the reaction was monitored by TLC or GC until the starting materials were totally consumed. The reaction mixture was poured into 50 mL of 0.5 M HCl and ether extracted twice. The combined ether extracts were were washed with saturated NaCl, dried over anhydrous $MgSO_4$, concentrated in vacuo, and purified by preparative thick layer chromatography on four 20 cm × 20 cm plates. The following new compounds were prepared.

Dimethyl *trans*-3-Acetyl-4-[(methoxycarbonyl)methyl]-1,1-cyclopentanedicarboxylate (9a): 65%; bp 140–146 °C (0.5 mmHg, Kugelrohr); IR (thin film) 1740, 1715, 1365 cm^{-1}; ^1H NMR (300 MHz) δ 3.77 (br s, 6 H) 3.67 (s, 3 H), 2.78 (m, 1 H), 2.68 (m, 2 H), 2.40 (m, 4 H), 2.22 (s, 3 H), 1.96 (m, 1 H); ^{13}C NMR (75 MHz) 208.3, 172.1, 172.0, 171.5, 58.7, 56.4, 52.7, 52.3, 51.4, 39.4, 38.1, 37.9, 37.2, 36.9, 35.6, 34.3, 28.9 ppm; MS, *m/z* (relative intensity) 300 (M^+, 7), 269 (24), 208 (34), 185 (22), 145 (43), 137 (28), 125 (21), 59 (38), 43 (100); exact mass calcd for $C_{14}H_{20}O_7$ *m/z* 300.1207, found *m/z* 300.1212.

Dimethyl (3*R,4*S**)- and (3*S**,4*S**)-3-Acetyl-4-[(methoxycarbonyl)methyl]-3-methyl-1,1-cyclopentanedicarboxylate (9b and 10b).** A 5:2 diastereomeric mixture (NMR, GC) was obtained in 73% yield. The physical properties and spectral data for the mixture are as follows: bp 165–172 °C (0.5 mmHg, Kugelrohr); IR (thin film) 1740, 1712, 1365 cm^{-1}; ^1H NMR (300 MHz) δ 3.78 (br s, 6 H), 3.60 and 3.57 (2s, 3 H), 2.92–2.03 (complex, 7 H), 2.12 and 2.09 (2s, 3 H), 1.36 and 1.12 (2s, 3 H); MS, *m/z* (relative intensity) 314 (M^+, 3), 43 (100); exact mass calcd for $C_{15}H_{22}O_7$ *m/z* 314.1365, found *m/z* 314.1369.

Dimethyl *trans*-3-Benzoyl-4-[(methoxycarbonyl)methyl]-1,1-cyclopentanedicarboxylate (9c): 81%; IR (thin film) 3060, 1738, 1680, 1599, 1580 cm^{-1}; ^1H NMR (300 MHz) δ 7.82 (m, 2 H), 7.41 (m, 3 H), 3.78 (s, 3 H), 3.73 (s, 3 H), 3.54 (s, 3 H), 3.20–1.88 (complex, 8 H); MS, *m/z* (relative intensity) 362 (M^+, 4), 331 (7), 105 (100), 77 (21); exact mass calcd for $C_{19}H_{22}O_7$ *m/z* 362.1365, found *m/z* 362.1362.

Dimethyl (3*R,4*S**)-3-Benzoyl-4-[(methoxycarbonyl)methyl]-3-methyl-1,1-cyclopentanedicarboxylate (9d).** This compound was obtained essentially pure (NMR, GC) in 83% yield. The spectral data are as follows: IR (thin film) 3080, 1742, 1682, 1602, 1582, 1390 cm^{-1}; ^1H NMR (60 MHz) δ 7.75 (m, 2 H), 7.38 (m, 3 H), 3.71 (s, 3 H), 3.65 (s, 6 H), 3.30–1.75 (complex, 7 H), 1.30 (s, 3 H); MS, *m/z* (relative intensity) 376 (M^+, 3), 105 (100), 77 (28); exact mass calcd for $C_{20}H_{24}O_7$ *m/z* 376.1522, found *m/z* 376,1528.

***cis*-6,6-Bis(methoxycarbonyl)-8-[(methoxycarbonyl)methyl]bicyclo[3.3.0]octan-2-one (12a)**: 62%; IR (thin film) 1740 cm^{-1}; ^1H NMR (300 MHz) δ 3.78 (s, 6 H), 3.70 (s, 3 H), 3.56 (m, 1 H), 2.93 (m, 1 H), 2.63 (m, 2 H), 2.41–1.98 (complex, 6 H), 1.49 (m, 1 H); ^{13}C NMR (75 MHz) 217.9, 171.9, 171.0, 169.2, 63.2, 52.4, 52.0, 51.1, 50.9, 45.9, 38.8, 37.3, 35.1, 34.1, 23.7 ppm; MS, *m/z* (relative intensity) 312 (M^+, 12), 281 (48), 192 (52), 168 (46), 145 (59), 136 (39), 105 (51), 91 (48), 77 (42), 59 (100); exact mass calcd for $C_{15}H_{20}O_7$, *m/z* 312.1209, found *m/z* 312.1219.

***trans*-7,7-Bis(methoxycarbonyl)-9-[(methoxycarbonyl)methyl]bicyclo[4.3.0]nonan-2-one (13b)**: 55%; mp 95–96 °C; IR (thin film) 1738, 1720 cm^{-1}; ^1H NMR (300 MHz) δ 3.78 (s, 3 H), 3.74 (s, 3 H), 3.66 (s, 3 H), 2.72 (dd, 1 H, *J* = 3, 14 Hz), 2.61 (m, 1 H), 2.37 (m, 5 H), 2.18 (m, 1 H), 1.68 (m, 1 H), 1.30 (m, 1 H); ^{13}C NMR (75 MHz) 208.7, 172.4, 171.3, 61.0, 58.2, 52.3, 52.1, 51.3, 41.1, 38.4, 38.1, 32.4, 27.5, 26.6 ppm; MS, *m/z* (relative intensity) 326 (M^+, 12), 295 (44), 59 (100); exact mass calcd for $C_{16}H_{22}O_7$ *m/z* 326.1365, found *m/z* 326.1359.

Methyl (*E*)-5,5-Bis(methylsulfonyl)-2-pentenoate (2). The sodium salt of bis(methylsulfonyl)methane was prepared, isolated and dried on a 100-mmol scale according to the procedure of Cronyn[14] for the sodium salt of bis(ethanesulfonyl)methane. The dried salt (14.5 g, 75.0 mmol) was added portionwise to a stirred solution of 13.4 g (8.80 mL, 75.0 mmol) of methyl (*E*)-4-bromo-2-butenoate in anhydrous DMF keeping the temperature below 50 °C. The mixture was stirred for 24 h, poured into saturated NaCl, and ether extracted twice. The combined ether extracts were washed with water and saturated NaCl, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The resulting white solid was washed with ether and filtered to afford 9.77 g (36.2 mmol, 48.2%) of methyl (*E*)-5,5-bis(methylsulfonyl)-2-pentenoate: mp 105–106 °C; IR ($CHCl_3$) 1720, 1662, 1360, 1320, 1130 cm^{-1}; ^1H NMR (60 MHz) δ 6.80 (dt, 1 H, *J* = 7, 17 Hz), 5.95 (d, 1 H, *J* = 17 Hz), 4.21 (t, 1 H, *J* = 7 Hz), 3.68 (s, 3 H), 3.18 (s, 6 H); MS, *m/z* (relative intensity) 270 (M^+, 6), 239 (10), 191 (28), 41 (100); exact mass calcd for $C_8H_{14}O_6S_2$ *m/z* 270.0232, found *m/z* 270.0245.

Methyl (*E*,*E*)-5-(Methylsulfonyl)-2,4-pentadienoate (14). Treatment of 1.48 g (5.50 mmol) of methyl (*E*)-5,5-bis(methylsulfonyl)-2-pentenoate according to the standard tandem Michael protocol yielded 0.91 g (4.79 mmol, 87.0%) of methyl (*E*,*E*)-5-(methylsulfonyl)-2,4-pentadienoate: mp 135–136 °C; IR ($CHCl_3$) 1720, 1642, 1600, 1592, 1584, 1328, 1140 cm^{-1}; ^1H NMR (60 MHz) δ 7.30 (dd, 2 H, *J* = 4, 14 Hz), 6.73 (dd, 1 H, *J* = 4, 14 Hz), 6.28 (dd, 1 H, *J* = 4, 14 Hz), 3.79 (s, 3 H), 3.00 (s, 3 H); ^{13}C NMR (75 MHz) 165.7, 139.7, 138.1, 135.5, 130.7, 52.2, 42.8 ppm; MS, *m/z* (relative intensity) 190 (M^+, 4), 175 (3), 159 (28), 127 (31), 111 (67), 99 (52), 96 (21), 79 (100), 69 (64), 59 (35); exact mass calcd for $C_7H_{10}O_4S$ *m/z* 190.0299, found *m/z* 190.0292.

Acknowledgment. We thank the Oklahoma State University Center for Energy Research and the OSU College of Arts and Sciences for support of this work. R.E.D. is also grateful for support in the form of a Lew Wentz Scholarship administered by the College of Arts and Sciences at OSU.

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