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Stereoselective Conjugate Addition of Alkyl Groups to (*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-cyclopentenone Derivatives

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Abstract—Reaction of (*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-2-cyclopentenone (**2**) and a 2-methoxycarbonyl congener (**3**) with R_2CuLi or RMgBr-CuI stereoselectively gave (2*S*,3*R*,4*S*)-3-alkyl-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)cyclopentanone (**4**) and its (2*S*,3*S*,4*S*)-2-methoxycarbonyl derivative (**5**) as a major diastereoisomer. On the other hand, reaction with R_3Al in toluene exclusively gave the corresponding 3,4-*cis*-adducts **6** and **7**.

Introduction

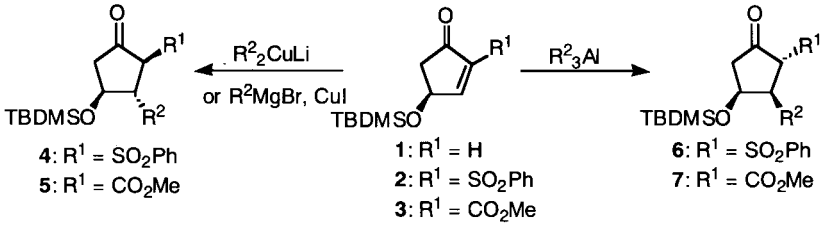
The chiral building block *O*-*tert*-butyldimethylsilyl-(TBDMS)-protected 4-hydroxy-2-cyclopentenone (**1**) has been widely used as a valuable precursor for the synthesis of prostaglandins, endiyne antitumor agents, and other important bioactive compounds in an optically active form.[1–3] Recently, we reported a simple preparation of new (*S*)-4-(TBDMSoxy)-2-cyclopentenone derivatives, (*S*)-2-benzenesulfonyl-4-(TBDMSoxy)-2-cyclopentenone (**2**)[4a,5] and 2-methoxycarbonyl derivative (**3**),[4] starting from (*S*)-malic acid. Since **2** and **3** have an additional functional group at the C-2 position, they are expected to be useful new chiral cyclopentenone building blocks. As a synthetic application of **2** and **3**, we examined the conjugate addition of organocopper and trialkylaluminum reagents to **2** and **3**. We found that the reactions of **2** and **3** with organocopper reagents proceeded cleanly to give 3-alkyl-2-benzenesulfonyl-4-(TBDMSoxy)cyclopentanones **4a**–**d** or 2-methoxycarbonyl derivatives **5a**,**b** with a 3,4-*trans* relationship, whereas **2** and **3** reacted with trialkylaluminums to give the corresponding 3,4-*cis* cyclopentanones **6a**–**c** and **7a**.[6] (Scheme 1)

Results and Discussion

Conjugate addition reaction of organocopper reagents to 2 and 3.

The conjugate addition reaction[7] of carbon nucleophiles to α,β-unsaturated ketones is one of the most important carbon–carbon bond-forming reactions. This reaction is usually carried out using lithium dialkylcuprates or Grignard reagents in the presence of copper(I) salt. (Scheme 2)

We first examined the reaction of organocopper reagents with **2** and **3** (Table 1). Treatment of **2** with lithium dimethylcuprate prepared from methyllithium and copper(I) iodide at −78°C for 15 min gave (2*S*,3*R*,4*S*)-2-benzenesulfonyl-4-(TBDMSoxy)-3-methylcyclopentanone (**4a**) in 90% yield as a sole diastereoisomer, as expected.[8] The relative stereochemistry of the *trans* 2,3-substituents of **4a** was assigned on the basis of the large *J* value between H-2 and H-3 (10.5 Hz).[9,10] The 3,4-*trans*-stereochemistry was confirmed by conversion of **4a** by desulfonylation with samarium(II) iodide (SmI_2)[11] in THF to **8**, which was



Scheme 1.

Keywords: Michael reactions; aluminum and compounds; copper and compounds; cyclopentenones.

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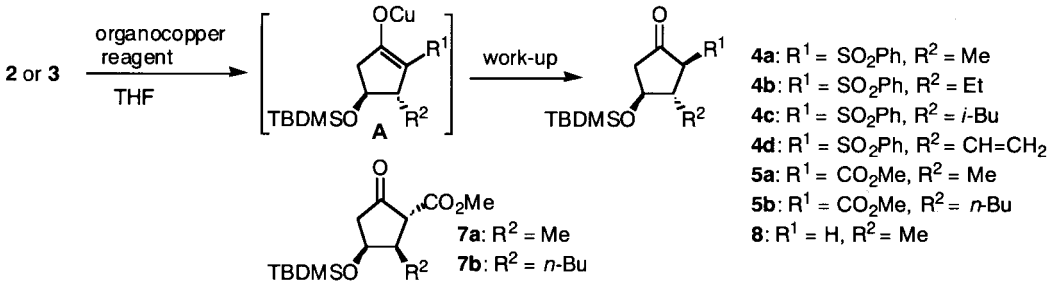


Scheme 2.

Table 1. Conjugate addition of organocopper reagents to **2** and **3** (all reactions were carried out in THF at −78°C.)

Entry	Enone	Reagent	Time (min)	Total yield (%)	Products (ratio)[a]
1	**2**	Me_2CuLi	15	90	**4a**
2	**2**	EtMgBr, CuI	15	85	**4b**
3	**2**	*i*-BuMgBr, CuI	15	82	**4c**
4	**2**	CH_2=CHMgBr, CuI	20	98	**4d**
5[b]	**3**	Me_2CuLi	30	71	**5a**+**7a** (8:1)
6	**3**	*n*-Bu_2CuLi	30	59	**5b**+**7b** (8:1)[c]

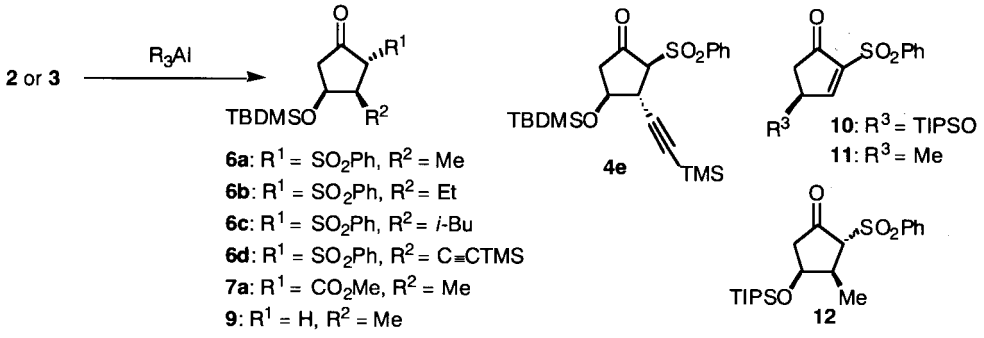
[a] Determined by ^{1}H NMR spectroscopy.
[b] Ref. 4.
[c] 13% of unreacted **3** was recovered.

identical with a racemic authentic sample.[10] Similar reactions of **2** with Grignard reagents in the presence of CuI stereoselectively proceeded to provide **4b–d** in 82–98% yields (Table 1, entries 2–4). The ester congener **3**, upon treatment with Me_2CuLi in THF at −78°C for 30 min, gave an 8:1 mixture of the 3,4-*trans* adduct **5a** and the 3,4-*cis* adduct **7a** in a combined yield of 71%.[4] Similarly, **3** was treated with lithium dibutylcuprate to give a mixture of **5b**[10] and **7b**[10] in a combined yield of 59% in a ratio of 8:1 (determined by ^{1}H NMR spectroscopy) along with 13% of the starting enone **3**. These reactions proceed by the addition of an alkyl group to the C-3 position from the less-hindered α-side to give copper enolates **A**, which are then protonated to produce the thermodynamically stable 2,3-*trans*-3,4-*trans* adduct after work-up.

Conjugate addition reaction of trialkylaluminums to 2 and 3.

Organoaluminum reagents are used as nucleophiles and offer some advantages such as the availability of lower alkyl ligands, ease of handling, and low toxicity.[12] Trialkylaluminums are known to be less reactive than organocopper reagents for conjugate addition reactions to α,β-unsaturated ketones, so that the reactions require an additive such as a radical initiator,[13] Ni(I),[14] or Cu(I) salt,[15] or a doubly activated alkene as an electrophile.[16] We anticipated that **2** and **3** could react with trialkylaluminums, since these are activated as β-ketosulfone or β-ketoester (Scheme 3).

A solution of 2.2 equiv. of Me_3Al in hexane was added to a solution of **2** in toluene at −78°C and the mixture was stirred at the same temperature for 30 min to give (2*R*,3*S*,4*S*)-2-benzenesulfonyl-4-(TBDMSoxy)-3-methylcyclopentanone (**6a**) in 86% yield as a sole diastereoisomer (Table 2, entry 1). The 2,3-*trans*- and 3,4-*cis*-stereochemistries of **6a** were determined by the *J* value between H-2 and H-3 (10.0 Hz) in ^{1}H NMR spectroscopy and its desulfonylation with SmI_2 to **9**[10] (72%). When 1 equiv. of Me_3Al was used, the reaction was not completed even after stirring for 1.5 h; **6a** was obtained in 49% yield along with 49% of unreacted **2** (Table 2, entry 2). Solvent effects were observed in this reaction: the reaction in dichloromethane



Scheme 3.

Table 2. Conjugate addition of organoaluminum reagents to **2**, **3**, **10**, and **11**

Entry	Enone	Reagent (equiv.)	Solvent	Conditions	Total yield (%)	Products (ratio)
1	**2**	Me_3Al (2.2)	Toluene	−78°C, 30 min	86	**6a**
2	**2**	Me_3Al (1)	Toluene	−78°C, 1.5 h	49[a]	**6a**
3	**2**	Me_3Al (2.2)	CH_2Cl_2	−78°C, 30 min	74	**6a**
4	**2**	Me_3Al (2.2)	Et_2O	−78°C, 3 h	0[b]	–
5	**2**	Et_3Al (2.2)	Toluene	−78°C, 30 min	65	**6b**
6	**2**	*i*-Bu_3Al (2.2)	Toluene	−78°C, 30 min	32	**6c**
7	**2**	Et_2Al–C≡CTMS (2.2)	Toluene	−78°C, 30 min	Quant.	**4e**+**6d**+**6b** (51:31:18)[c]
8	**10**	Me_3Al (2.2)	Toluene	−78°C, 30 min	62[d]	**12**
9	**11**	Me_3Al (2.2)	Toluene	−78°C, 30 min	0[e]	–
10	**3**	Me_3Al (2.2)	Toluene	−78°C, 30 min	22[f]	**7a**
11	**3**	Me_3Al (4)	Toluene	−78°C, 30 min	66	**7a**

[a] 49% of unreacted **1b** was recovered.
[b] 81% of unreacted **1b** was recovered.
[c] Determined by ^1H NMR spectroscopy.
[d] 24% of unreacted **10** was recovered.
[e] 22% of unreacted **11** was recovered.
[f] 22% of unreacted **3** was recovered.

gave **6a** in a slightly lower yield (74%), while ether was not effective; only unreacted **2** (81%) was recovered (Table 2, entries 3 and 4).

A similar reaction of **2** with 2.2 equiv. of triethylaluminum proceeded exclusively to provide **6b** in 65% yield. The reaction of **2** with triisobutylaluminum gave **6c** in 32% yield as a sole stereoisomer. The stereochemistry of the products **6b** and **6c** was determined by a comparison of the coupling constants of H-2 and H-3, and H-3 and H-4 ($J_{2,3}$=9.6, 9.8 Hz and $J_{3,4}$=3.6, 3.7 Hz, respectively) in the ^1H NMR spectra with those of **6a** ($J_{2,3}$=10.0 Hz and $J_{3,4}$=3.7 Hz). In contrast, a similar reaction of diethyl(trimethylsilylethynyl)aluminum[17] in toluene gave an inseparable 51:31:18 mixture of **4e**, **6d** and **6b** in quantitative yield (see Experimental).

To study the reaction mechanism, the TBDMSO group at the C-4 position was replaced by triisopropylsilyl(TIPS)oxy and methyl groups. Thus, 2-benzenesulfonyl-4-(TIPSoxy)-2-cyclopentenone (**10**) and 2-benzenesulfonyl-4-methyl-2-cyclopentenone (**11**) were treated with Me_3Al (Table 2, entries 8 and 9). Reaction of **10** with 2.2 equiv. of Me_3Al in toluene for 30 min gave the 3,4-*cis* adduct **12** in 62% yield as a sole diastereoisomer along with 24% of unreacted **10**. The ^1H NMR spectrum of **12** indicated the 2,3-*trans* and 3,4-*cis* relationships ($J_{2,3}$=9.5 Hz and $J_{3,4}$=4.0 Hz). On the other hand, the conjugate addition reaction of compound **11** with 4 equiv. of Me_3Al completely failed; 22% of unreacted **11** and complex mixtures were isolated. These results indicate that the presence of the silyloxy group at the C-4 position is important for both the reactivity and high stereoselectivity.

The ester congener **3**, upon treatment with 2.2 equiv. of Me_3Al in toluene at −78°C for 30 min, gave the 3,4-*cis* adduct **7a** as a single diastereoisomer but in only 22% yield, along with 22% of unreacted **3**. The spectroscopic data of **7a** were identical to those of a racemic authentic sample.[10] The use of 4 equiv. of Me_3Al increased the yield to 66%. In contrast, no reaction took place when the cyclopentenone **1** was treated with Me_3Al under the same conditions. These results show that an additional electron-withdrawing group at the C-2 position is necessary for the reaction.

One possible explanation for the high diastereoselectivity in the reaction of **2** and **3** with R_3Al is based on the assumption of a 1:2 complex of **B** and **C**, respectively. Thus, the first alane combines with the keto and sulfonyl or ester groups as a Lewis acid to activate the enone **2** or **3**. The second R_3Al chelates an oxygen atom of the TBDMSO group to form the intermediate **B** or **C**.[18] The alkyl group is then transferred intramolecularly from the chelated R_3Al to give the 3,4-*cis* adducts **6a**–**d** and **7a**. The nucleophilicity of the alkyl group of the resulting ate-complex is higher than that for a noncoordinated R_3Al.[13a,19] A bulky alane such as triisobutylaluminum and/or a bulky silyloxy group such as a TIPSO group at the C-4 position would retard the formation of the intermediate **B** to reduce the yield of the conjugate addition. The high reactivity of diethyl(trimethylsilylethynyl)aluminum to enones[20] would allow the reaction

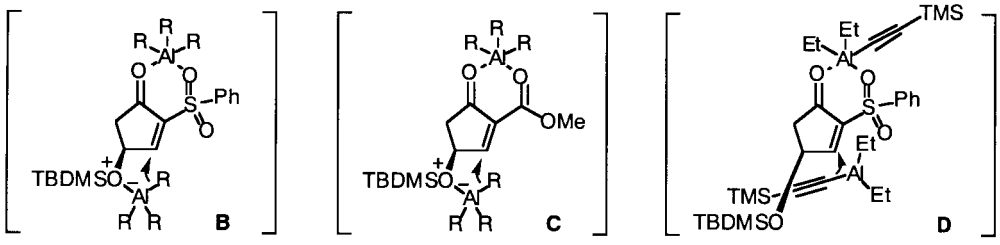


Figure 1.

to proceed through a non-chelated intermediate **D**, in which the nucleophile attacks from the less-hindered side to give the 3,4-*trans* isomer **3**. In ether, complexation of R_3Al with ether would make it unable to form intermediate **B**.

In summary, this study revealed the stereoselective conjugate addition of alkyl groups to optically active (*S*)-4-(TBDMSoxy)-2-cyclopentenone derivatives **2** and **3** by means of organocopper reagents and trialkylaluminums. Reaction of **2** and **3** with organocopper reagents stereoselectively gave the corresponding 3,4-*trans* adduct, while trialkylaluminum led to the 3,4-*cis* adduct as a single diastereoisomer. (Fig. 1)

Experimental

All melting points are uncorrected. IR spectra were recorded using a JASCO IR-1 spectrophotometer. ^{1}H NMR spectra were determined with a Varian XL-300 (300 MHz) spectrometer using $CDCl_3$ as a solvent and tetramethylsilane as an internal standard. Specific rotations were recorded on a JASCO DIP-360 polarimeter. High-resolution mass spectra (Exact FAB-MS) were obtained with a JEOL JMS-SX 102A instrument. Column chromatography was carried out on Silica gel 60 PF_{254} (Nacalai Tesque, Inc.) under pressure. Known cyclpentenone **3** was prepared according to the reported procedure.[4b]

(*S*)-2-Benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-2-cyclopentenone (2). A solution of methyl phenyl sulfone (1.28 g, 8.19 mmol) in THF (10 mL) was added to a solution of LDA in THF (20 mL), prepared from diisopropylamine (954 mg, 9.43 mmol) and butyllithium (1.6 M in hexane, 5.38 mL, 8.60 mmol), at −78°C under a nitrogen atmosphere and the mixture was stirred for 1 h. Then a solution of methyl (*S*)-3,4-bis(*tert*-butyldimethylsilyloxy)-butanoate[4b] (1.49 g, 4.10 mmol) in THF (16 mL) was added to the solution of the anion at the same temperature. The whole mixture was stirred for 10 min, and then aq. NH_4Cl was added. The organic layer was separated, and the aqueous layer was extracted with EtOAc and the combined extracts were washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 20:1) to give (*S*)-1-benzenesulfonyl-4,5-bis(*tert*-butyldimethylsilyloxy)-2-pentanone (1.46 g, 75%) as a pale yellow oil: $[\alpha]_D^{24}=-19.1$ (*c* 1.01, $CHCl_3$); IR (CCl_4) ν 1720, 1320, 1150 cm^{-1}; ^{1}H NMR δ: 0.015, 0.024, 0.03, 0.06 (all 3H, s), 0.84, 0.87 (both 9H, s), 2.78 (1H, d of ABq, *J*=6.9, 15.6 Hz), 2.94 (1H, d of ABq, *J*=4.9, 15.6 Hz), 3.38 (1H, dd, *J*=10.0, 6.9 Hz), 3.55 (1H, dd, *J*=10.0, 4.8 Hz), 4.06–4.16 (1H, m), 4.20, 4.26 (each 1H, ABq, *J*=13.5 Hz), 7.53–7.61 (2H, m), 7.64–7.71 (1H, m), 7.87–7.92 (2H, m). HRMS (FAB) Calcd for $C_{23}H_{43}O_5SSi_2$ [$(M+H)^+$]: 487.2370. Found: 487.2361. The mixture of the ketosulfone (716 mg, 1.47 mmol), *p*-toluenesulfonyl azide (304 mg, 1.54 mmol) and Et_3N (521 mg, 5.15 mmol) in MeCN (15 mL) was stirred at room temperature for 1 h. The solution was concentrated and the residue was diluted with Et_2O (30 mL). The solution was washed with 9% KOH and brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 20:1) to give (*S*)-1-benzenesulfonyl-4,5-bis(*tert*-butyldimethylsilyloxy)-1-diazo-2-pentanone (720 mg, 95%) as a pale yellow oil: $[\alpha]_D^{26}=-48.2$ (*c* 1.00, $CHCl_3$); IR (CCl_4) ν 2120, 1670, 1340, 1150 cm^{-1}; ^{1}H NMR δ: −0.16, −0.02, 0.01, 0.02 (all 3H, s), 0.75, 0.85 (both 9H, s), 2.68 (1H, d of ABq, *J*=7.8, 14.5 Hz), 2.75 (1H, d of ABq, *J*=4.4, 14.5 Hz), 3.34 (1H, dd, *J*=10.1, 6.9 Hz), 3.53 (1H, dd, *J*=10.1, 4.6 Hz), 4.07–4.17 (1H, m), 7.52–7.59 (2H, m), 7.61–7.68 (1H, m), 8.00–8.06 (2H, m). Anal. Calcd for $C_{23}H_{40}N_2O_5SSi_2$: C, 53.87; H, 7.86; N, 5.46. Found: C, 53.57; H, 7.27; N, 5.87. A solution of the diazoketosulfone (890 mg, 1.74 mmol) in CH_2Cl_2 (2 mL) was added to a boiling solution of $Rh_2(OAc)_4$ (8 mg, 0.017 mmol) in CH_2Cl_2 (15 mL), and the mixture was refluxed for 15 min. After evaporation of the solvent, the crude material was chromatographed on silica gel (hexane/EtOAc, 7:1) to give **2** (443 mg, 72%) as colorless crystals: mp 90–91.5°C (hexane/EtOAc); $[\alpha]_D^{26}=-80.1$ (*c* 1.02, $CHCl_3$); IR (CCl_4) ν 1740, 1630, 1320, 1150 cm^{-1}; ^{1}H NMR δ: 0.12, 0.14 (both 3H, s), 0.90 (9H, s), 2.43 (1H, dd, *J*=18.5, 2.6 Hz), 2.88 (1H, dd, *J*=18.5, 6.2 Hz), 5.00 (1H, dt, *J*=6.2, 2.4 Hz), 7.52–7.61 (2H, m), 7.63–7.70 (1H, m), 8.05–8.10 (2H, m), 8.13 (1H, d, *J*=2.3 Hz). Anal. Calcd for $C_{17}H_{24}O_4SSi$: C, 57.92; H, 6.86. Found: C, 57.82; H, 6.94.

Conjugate addition of lithium dimethylcuprate to 2. A solution of methyllithium in Et_2O (1.14 M, 1.1 mL, 1.19 mmol) was added to a suspension of CuI (113 mg, 0.59 mmol) in THF (5 mL) at −78°C under a nitrogen atmosphere and the mixture was stirred at −20°C for 5 min. The mixture was recooled to −78°C, a solution of **2** (100 mg, 0.30 mmol) in THF (2 mL) was added to the cold mixture. The whole was stirred for further 15 min, and then aq. NH_4Cl was added. The organic layer was separated, and the aqueous layer was extracted with Et_2O and the combined extracts were washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 20:1) to give (2*S*,3*R*,4*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-3-methylcyclopentanone (**4a**) (99 mg, 90%) as colorless crystals: mp 107–108°C (hexane); $[\alpha]_D^{23}=+144.4$ (*c* 1.09, $CHCl_3$); IR (CCl_4) ν 1760, 1320, 1150 cm^{-1}; ^{1}H NMR δ: 0.04, 0.08 (both 3H, s), 0.89 (9H, s), 1.31 (3H, d, *J*=6.6 Hz), 2.43 (1H, dd, *J*=17.1, 10.3 Hz), 2.57 (1H, ddd, *J*=17.1, 6.6, 1.0 Hz), 2.78 (1H, ddq, *J*=10.5, 8.5, 6.6 Hz), 3.40 (1H, br d, *J*=10.5 Hz), 3.79 (1H, ddd, *J*=10.3, 8.5, 6.6 Hz), 7.75–7.62 (2H, m), 7.66–7.73 (1H, m), 7.87–7.92 (2H, m). Anal. Calcd for $C_{18}H_{28}O_4SSi$: C, 58.66; H, 7.66. Found: C, 58.40; H, 7.56.

(3*S*,4*S*)-3-(*tert*-Butyldimethylsilyloxy)-4-methylcyclopentanone (8). According to the procedure of Molander and Hahn,[11] a solution of SmI_2 in THF (0.1 M, 3.3 mL, 0.33 mmol) was added to a solution of **4a** (40 mg, 0.11 mmol) in THF (1 mL) and MeOH (0.5 mL) at −78°C under a nitrogen atmosphere and the mixture was stirred at the same temperature for 10 min and at room temperature for 30 min. The mixture was poured into sat. aq. K_2CO_3 (10 mL), and extracted with Et_2O. The extract was dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 20:1) to give **8** (22 mg, 88%) as a colorless oil, whose spectroscopic data were identical with those of an authentic sample.[10]

Conjugate addition of ethylmagnesium bromide and copper(I) iodide to 2. A solution of ethylmagnesium bromide in THF (0.96 M, 0.83 mL, 0.8 mmol) was added to a solution of CuI (76 mg, 0.4 mmol) in THF (4 mL) at −78°C under a nitrogen atmosphere and the mixture was stirred at −20°C for 10 min. The mixture was recooled to −78°C, and a solution of **2** (67 mg, 0.2 mmol) in THF (2 mL) was added to the cold mixture. The whole was stirred for further 15 min, and then aq. NH_4Cl was added. The organic layer was separated, and the aqueous layer was extracted with EtOAc and the combined extracts were washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 10:1) to give (2*S*,3*R*,4*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-3-ethylcyclopentanone (**4b**) (65 mg, 85%) as colorless crystals: mp 118–120°C (hexane/EtOAc); $[\alpha]_D^{27}=-27.6$ (*c* 0.21 $CHCl_3$); IR (KBr) ν 1750, 1320, 1140 cm^{-1}; ^1H NMR δ: 0.03, 0.08 (both 3H, s), 0.89 (9H, s), 0.99 (3H, t, *J*=7.5 Hz), 1.73 (2H, qd, *J*=7.5, 5.9 Hz), 2.50 (1H, dd, *J*=16.9, 9.2 Hz), 2.57 (1H, ddd, *J*=16.9, 6.6, 1.0 Hz), 2.85 (1H, ddt, *J*=9.2, 7.3, 5.9 Hz), 3.73 (1H, br d, *J*=9.2 Hz), 3.99 (1H, dt, *J*=9.2, 7.0 Hz), 7.52–7.61 (2H, m), 7.64–7.71 (1H, m), 7.85–7.91 (2H, m). HRMS (FAB) Calcd for $C_{19}H_{31}O_4SSi$ $[(M+H)^+]$: 383.1712. Found: 383.1707.

Conjugate addition of isobutylmagnesium bromide and copper(I) iodide to 2. According to a procedure similar to that described for the reaction of **2** with EtMgBr and CuI, treatment of **2** (67 mg, 0.2 mmol) with isobutylmagnesium bromide in Et_2O (2.0 M, 0.4 mL, 0.8 mmol) and CuI (67 mg, 0.4 mmol) gave (2*S*,3*R*,4*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-3-(2-methylpropyl)cyclopentanone (**4c**) (67 mg, 82%) as colorless crystals: mp 69–72°C (hexane); $[\alpha]_D^{27}=+13.2$ (*c* 0.41 $CHCl_3$); IR (KBr) ν 1755, 1310, 1140 cm^{-1}; ^1H NMR δ: 0.03, 0.08 (both 3H, s), 0.89 (9H, s), 0.66 (3H, d, *J*= 6.6 Hz), 0.96 (3H, d, *J*=6.4 Hz), 1.35–1.57 (2H, m), 1.79–1.96 (1H, m), 2.51 (1H, dd, *J*=16.9, 8.3 Hz), 2.59 (1H, dd, *J*=17.1, 6.6 Hz), 2.89–3.01 (1H, m), 3.41 (1H, d, *J*=7.7 Hz), 3.95 (1H, dt, *J*=8.4, 6.6 Hz), 7.53–7.62 (2H, m), 7.64–7.72 (1H, m), 7.85–7.92 (2H, m). HRMS (FAB) Calcd for $C_{21}H_{35}O_4SSi$ $[(M+H)^+]$: 411.2025. Found: 411.2020.

Conjugate addition of vinylmagnesium bromide and copper(I) iodide to 2. According to a procedure similar to that described for the reaction of **2** with EtMgBr and CuI, treatment of **2** (94 mg, 0.28 mmol) with vinylmagnesium bromide in Et_2O (1.14 M, 1.1 mL, 1.12 mmol) and CuI (106 mg, 0.56 mmol) gave (2*S*,3*R*,4*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-3-vinylcyclopentanone (**4d**) (100 mg, 98%) as colorless crystals: mp 85–86°C (hexane); $[\alpha]_D^{23}=+147.7$ (*c* 1.00, $CHCl_3$); IR (CCl_4) ν 1760, 1320, 1150 cm^{-1}; ^1H NMR δ: 0.02, 0.03 (both 3H, s), 0.87 (9H, s), 2.54 (1H, dd, *J*=17.1, 10.0 Hz), 2.64 (1H, ddd, *J*=17.1, 7.0, 0.9 Hz), 3.33 (1H, dt, *J*=10.0, 8.0 Hz), 3.68 (1H, dd, *J*=10.2, 0.9 Hz), 3.98 (1H, ddd, *J*=10.1, 8.2, 6.9 Hz), 5.13 (1H, dt, *J*=10.2, 1.0 Hz), 5.17 (1H, dt, *J*=17.0, 1.0 Hz), 5.69 (1H, ddd, *J*=17.1, 10.2, 7.8 Hz), 7.53–7.61 (2H, m, ArH), 7.64–7.71 (1H, m, ArH), 7.85–7.90 (2H, m, ArH). Anal. Calcd for $C_{19}H_{28}O_4SSi$: C, 59.96; H, 7.42. Found: C, 59.60; H, 7.45.

Conjugate addition of lithium dibutylcuprate to 3. According to a procedure similar to that described for the reaction of **2** with lithium dimethylcuprate, treatment of **3** (119 mg, 0.44 mmol) with lithium dibutylcuprate prepared by butyllithium (1.6 M, 1.1 mL, 1.76 mmol) and CuI (168 mg, 0.88 mmol) gave an oily mixture of **5b** and **7b** (total 85 mg, 59%). The ratio of **5b** and **7b** was estimated to be 8:1 by an integrated intensity of the peak heights of the signals due to the methine proton at the 1-position appeared at δ 2.88 (d) and 3.15 (d), respectively.[8] The mixture was rechromatographed on silica gel (hexane/EtOAc, 50:1). The first fraction gave methyl (1*S*,2*S*,3*S*)-3-(*tert*-butyldimethylsilyloxy)-2-butyl-5-oxocyclopentanecarboxylate (**5b**) as an oil, whose spectroscopic data were identical with those of an authentic sample.[10] The second fraction gave methyl (1*R*,2*R*,3*S*)-3-(*tert*-butyldimethylsilyloxy)-2-butyl-5-oxocyclopentanecarboxylate (**7b**) as an oil, whose spectroscopic data were identical with those of an authentic sample.[10]

Conjugate addition of trimethylaluminum to 2. General procedure. A 1.0 M solution of Me_3Al in hexane (0.63 mL, 0.63 mmol) was added to a solution of **2** (100 mg, 0.28 mmol) in toluene (6 mL) at −78°C under a nitrogen atmosphere. The mixture was stirred at the same temperature for 30 min and quenched with sat. aq. NH_4Cl. The mixture was allowed to warm to room temperature and extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 10:1) to give (2*R*,3*S*,4*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-3-methylcyclopentanone (**6a**) (89 mg, 86%) as colorless crystals: mp 111–113.5°C (hexane); $[\alpha]_D^{24}=-96.9$ (*c* 1.08, $CHCl_3$); IR (CCl_4) ν 1760, 1320, 1140 cm^{-1}; ^1H NMR δ: 0.02, 0.05 (both 3H, s), 0.82 (9H, s), 1.30 (3H, d, *J*=6.8 Hz), 2.31 (1H, dt, *J*=16.8, 1.0 Hz), 2.54 (1H, dd, *J*=16.8, 3.9 Hz), 2.96 (1H, dqd, *J*=10.0, 6.8, 3.5 Hz), 3.48 (1H, d, *J*=10.0 Hz), 4.31 (1H, t, *J*=3.7 Hz), 7.54–7.61 (2H, m), 7.65–7.71 (1H, m), 7.86–7.91 (2H, m). Anal. Calcd for $C_{18}H_{28}O_4SSi$: C, 58.66; H, 7.66. Found: C, 58.87; H, 7.51.

Use of CH_2Cl_2 as a solvent: Compound **2** (100 mg, 0.28 mmol) was treated with Me_3Al (1.0 M solution in hexane, 0.63 mL, 0.63 mmol) in CH_2Cl_2 (6 mL) to give **6a** (77 mg, 74%).

(3*S*,4*R*)-3-(*tert*-Butyldimethylsilyloxy)-4-methylcyclopentanone (9). According to a procedure similar to that described for the preparation of **8**, treatment of **6a** (40 mg, 0.11 mmol) with SmI_2 (0.1 M in THF, 3.3 mL, 0.33 mmol) gave **9** (18 mg, 72%) as a colorless oil, whose spectroscopic data were identical with those of an authentic sample.[10]

Conjugate addition of triethylaluminum to 2. Following the general procedure, **2** (83 mg, 0.24 mmol) was treated with Et_3Al (1.0 M in hexane, 0.52 mL, 0.52 mmol) in toluene (6 mL) to give (2*R*,3*S*,4*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-3-ethylcyclopentanone (**6b**) (58 mg, 65%) as colorless crystals: mp 102–107°C (hexane); $[\alpha]_D^{23}=-60.1$ (*c* 1.14, $CHCl_3$); IR (CCl_4) ν 1760, 1320, 1140 cm^{-1}; ^1H NMR δ: 0.03, 0.07 (both 3H, s), 0.81 (9H, s), 1.01 (3H, t, *J*=7.4 Hz), 1.70–1.93 (2H, m), 2.34 (1H, br d, *J*=16.6 Hz), 2.55 (1H, dd, *J*=16.6, 3.9 Hz),

2.76 (1H, tt, J=10.0, 4.0 Hz), 3.48 (1H, br d, J=9.6 Hz), 4.50 (1H, t, J=3.6 Hz), 7.54–7.62 (2H, m), 7.65–7.72 (1H, m), 7.85–7.90 (2H, m). Anal. Calcd for $C_{19}H_{30}O_4SSi$: C, 59.65; H, 7.90. Found: C, 59.37; H, 7.90.

Conjugate addition of triisobutylaluminum to 2. Following the general procedure, **2** (100 mg, 0.28 mmol) was treated with iBu$_3$Al (15% in hexane, 0.86 mL, 0.62 mmol) in toluene (6 mL) to give (2*R*,3*S*,4*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-3-(2-methylpropyl)cyclopentanone (**6c**) (38 mg, 32%) as colorless crystals: mp 102–107°C (hexane); IR (CCl_4) ν 1760, 1310, 1140 cm^{-1}; ^{1}H NMR δ: 0.01, 0.06 (both 3H, s), 0.81 (9H, s), 0.93 (3H, d, J=6.5 Hz), 0.98 (3H, d, J=6.4 Hz), 1.36–1.49 (1H, m), 1.60–1.86 (2H, m), 2.34 (1H, d, J=16.6 Hz), 2.55 (1H, dd, J=16.6, 3.7 Hz), 2.92 (1H, tt, J=10.2, 3.9 Hz), 3.46 (1H, d, J=9.8 Hz), 4.43 (1H, t, J=3.5 Hz), 7.54–7.62 (2H, m), 7.65–7.72 (1H, m), 7.85–7.90 (2H, m). HRMS (FAB) Calcd for $C_{21}H_{35}O_4SSi$ [(M+H)$^+$]: 411.2025. Found: 411.2017.

Conjugate addition of alkynylaluminum to 2. According to the procedure reported by Carreño et al.,[17] a solution of butyllithium (1.6 M in hexane, 0.44 mL, 0.71 mmol) was added to a solution of (trimethylsilyl)acetylene (70 mg, 0.71 mmol) in toluene (5 mL) at 0°C, and the mixture was stirred at room temperature for 30 min. A solution of diethylaluminum chloride (1 M in hexane, 0.71 mL, 0.71 mmol) was added at 0°C and then stirred for 30 min at the same temperature to give a solution of diethyl[(trimethylsilyl)ethynyl]aluminum in toluene-hexane. Following the general procedure from here, **2** (100 mg, 0.28 mmol) was treated with the above prepared aluminun reagent in toluene–hexane to give a 51:31:18 inseparable mixture of (2*S*,3*R*,4*S*)-2-benzenesulfonyl-4-(*tert*-butyldimethylsilyloxy)-3-[(trimethylsilyl)ethynyl]cyclopentanone (**4e**), its (2*R*,3*S*,4*S*)-isomer **6d**, and **6b** (total 124 mg, quant.) as colorless crystals; IR (CCl_4) ν 1760, 1320, 1150 cm^{-1}; ^{1}H NMR for **4e** δ: 0.04 (9H, s), 0.09, 0.13 (both 3H, s), 0.90 (9H, s), 2.50–2.75 (2H, m), 3.48 (1H, dd, J=9.8, 8.0 Hz), 3.84 (1H, d, J=9.7 Hz), 4.23 (1H, ddd, J=10.1, 7.9, 6.8 Hz), 7.75–7.62 (2H, m), 7.66–7.73 (1H, m), 7.85–7.97 (2H, m). Selected signals for **6d** δ: 0.84 (9H, s), 2.43 (1H, dt, J=16.8, 1.3 Hz), 3.64 (1H, dd, J=9.4, 3.8 Hz), 3.95 (1H, d, J=9.3 Hz). HRMS (FAB) for **4e** and **6d** Calcd for $C_{22}H_{35}O_4SSi_2$ [(M+H)$^+$]: 451.1796. Found: 451.1791. The ratio of **4e**, **6d** and **6b** was estimated to be 51:31:18 by an integrated intensity of the peak heights of the signals due to the protons of the *tert*-butyl group appeared at δ 0.90, 0.84 and 0.81, respectively.

(*S*)-2-Benzenesulfonyl-4-(triisopropylsilyloxy)-2-cyclopentenone (10). According to a procedure similar to that described for the preparation of **2**, alkylation of the TIPS ether of methyl (*S*)-3,4-dihydroxybutanoate, followed by diazotransfer reaction and Rh(II)-catalyzed reaction gave **10** as a colorless oil: $[\alpha]_D^{23}$=−43.3 (c 1.08, $CHCl_3$); IR (CCl_4) ν 1730, 1630, 1320, 1160 cm^{-1}; ^{1}H NMR δ: 1.04–1.09 (21H, m), 2.49 (1H, dd, J=18.5, 2.5 Hz), 2.92 (1H, dd, J=18.5, 6.1 Hz), 5.09 (1H, dt, J=6.0, 2.4 Hz), 7.54–7.59 (2H, m), 7.64–7.69 (1H, m), 8.06–8.10 (2H, m), 8.17 (1H, d, J=2.4 Hz). HRMS (FAB) Calcd for $C_{20}H_{31}O_4SSi$ [(M+H)$^+$]: 395.1712. Found: 395.1718.

Conjugate addition of trimethylaluminum to 10. Following the general procedure, **10** (25 mg, 0.063 mmol) was treated with Me_3Al (1.0 M in hexane, 0.14 mL, 0.14 mmol) in toluene (3 mL) to give unreacted **10** (6 mg, 24%) and (1*R*,2*S*,3*S*)-2-benzenesulfonyl-3-methyl-4-(triisopropylsilyloxy)cyclopentanone (**12**) (16 mg, 62%) as a colorless oil: $[\alpha]_D^{26}$=−66.4 (c 1.01, $CHCl_3$); IR (CCl_4) ν 1760, 1320, 1150 cm^{-1}; ^{1}H NMR δ: 0.99–1.05 (21H, m), 1.37 (3H, d, J=6.8 Hz), 2.43 (1H, dt, J=16.8, 1.5 Hz), 2.58 (1H, dd, J=16.8, 4.0 Hz), 3.01 (1H, dqd, J=9.5, 6.8, 4.0 Hz), 3.50 (1H, dt, J=9.5, 0.6 Hz), 4.53 (1H, td, J=4.0, 1.3 Hz), 7.56–7.61 (2H, m), 7.67–7.72 (1H, m), 7.87–7.90 (2H, m). Anal. Calcd for $C_{21}H_{34}O_4SSi$: C, 61.42; H, 8.35. Found: C, 61.00; H, 8.28.

Conjugate addition of trimethylaluminum to 3. Following the general procedure, **3** (526 mg, 0.91 mmol) was treated with Me_3Al (1.0 M in hexane, 3.64 mL, 3.64 mmol) in toluene (10 mL) to give methyl (1*R*,2*R*,3*S*)-3-(*tert*-butyldimethylsilyloxy)-2-methyl-5-oxocyclopentanecarboxylate (**7a**) (172 mg, 66%) as colorless crystals: mp 64–65°C (pentane); $[\alpha]_D^{24}$=−32.2 (c 1.06, $CHCl_3$), whose spectroscopic data were identical with a racemic authentic sample.[10]

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