Regio- and Stereoselective Addition of Grignard and Organolithium Reagents to 4-Hydroxy-2-cyclopentenones

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4-Hydroxy-2-cyclopentenones and their *O*-silyl derivatives **1** constitute valuable synthetic intermediates. In particular, their regio- and stereocontrolled transformation into the 4,5-disubstituted 3-hydroxycyclopentanones **2** is a cornerstone in the synthetic approach to prostaglandins and related bioactive compounds.[1,2] In this way, it is well-known that the additions of dialkylcuprates or Grignard reagents in the presence of copper(I) salts to compounds **1** proceed in a 1,4-anti fashion with respect to the bulky *O*-silyl substituent (Scheme 1).

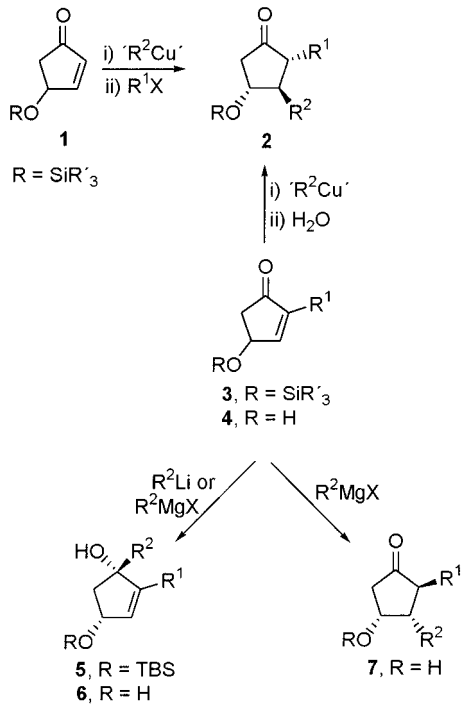
Electrophilic capture of the intermediate enolates affords cyclopentanones **2** with a 3,4-anti-4,5-anti stereochemistry in a three-component coupling. Similar findings have been reported for the reaction of silyl-protected 2-substituted 4-hydroxy-2-cyclopentenones **3** with organocopper reagents. However, to increase the synthetic potential of compounds **1** and **3**, other stereochemical arrangements in the hydroxycyclopentanones **2** would be desirable. In this way, the concept of *ligand-assisted nucleophilic addition* first developed by Liotta et al.[3] in the reaction of quinones with nucleophilic reagents can be an appealing possibility.

On the basis of this idea, in this paper we wish to account for the regio- and stereocontrolled transformation of cyclopentenones **3** and **4** into the 2,3-disubstituted 3,5-*syn*-dihydroxycyclopentenes **5** and **6** and into the 3,4-*syn*-4,5-*anti*-3-hydroxycyclopentanones **7** using organolithium or Grignard reagents (Scheme 1).

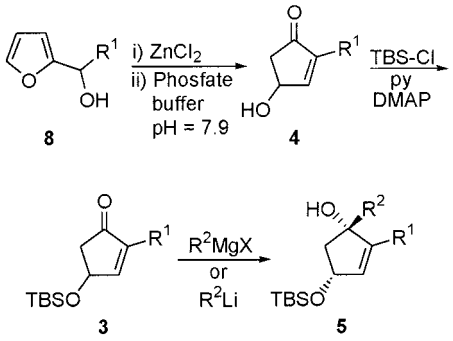
Ring opening[4] of (2-furyl)carbinols **8** followed by O-silylation of the resulting 4-hydroxy-2-cyclopentenones **4** with TBS−Cl afforded the 2-akyl- and 2-aryl-4-(ᵗbutylsilyl)-2-cyclopentenones **3** (Scheme 2). The addition of either organolithium or Grignard reagents in THF solution and in the absence of Cu(I) salts or any added cosolvent to the *O*-TBS-cyclopentenones **3** afforded the corresponding 1,2-addition products **5** (3,5-syn) in a highly regio- and stereoselective fashion.[5] No traces of the diastereomeric 3,5-anti products were observed in the crude reaction mixture.[6] The results are gathered in Table 1.

However, when the reactions with Grignard reagents were carried out starting from the O-unprotected cyclopentenones **4** in THF solution, the 1,4-addition products **7** (3,4-syn-4,5-anti) were obtained with high regioselectivity with no need of added Cu(I) salts or cosolvents[7] and with 3,4-syn stereochemistry (Scheme 3). This stereoselectivity was found to be opposite[8] to that observed

Scheme 1



Scheme 2



(1) For reviews, see: (a) Noyori, R.; Suzuki, M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 847−876. (b) Perlmutter, P. In *Conjugate Addition in Organic Synthesis*; Pergamon: Oxford, 1992. (c) Collins, P. W.; Djuric, S. W. *Chem. Rev.* **1993**, *93*, 1533−1564. (d) Nicolau, K. C.; Sorensen, E. J. In *Classics in Total Synthesis*; VCH: Weinheim, Germany, 1996.

(2) For leading recent references, see: (a) Myers, A. B.; Hammond, M.; Wu, Y.; Xiang, J.-N.; Harrington, P. M.; Kuo, E. Y. *J. Am. Chem. Soc.* **1996**, *118*, 10006−10007. (b) Kawata, S.; Yoshimura, F.; Irie, J.; Ehara, H.; Hirama, M. *Synlett* **1997**, 250−252. (c) Rodríguez, A.; Nomen, M.; Spur, B. W.; Godfroid, J.-J. *Eur. J. Org. Chem.* **1999**, 2655−2662 and references cited therein.

(3) Salomon, M.; Jamison, M. L.; McCormick, M.; Liotta, D.; Cherry, D. A.; Mills, J. E.; Shah, R. D.; Rodgers, J. D.; Maryanoff, C. A. *J. Am. Chem. Soc.* **1988**, *110*, 3702−3704. See also: Beak, P.; Meyers, A. I. *Acc. Chem. Res.* **1986**, *19*, 356.

(4) Piancatelli, G.; D'Auria, M.; D'Onofrio, F. *Synthesis* **1994**, 867−889 and references cited therein. See also: D'Auria, M. *Heterocycles* **2000**, *52*, 185−194.

(5) The 3,5-syn stereochemistry of compounds **5** has been assigned by NOE measurements. Thus, an increase of the H-5 signal (δ 4.64−4.56, m) of **7a** (R^1 = Ph, R^2 = Me) was observed upon irradiation of the CH_3 (δ 1.31, s).

(6) Determined on the ^{1}H NMR spectra ($CDCl_3$, 300 MHz) of the crude reaction mixtures.

(7) Compare with the procedure described in ref 3.

(8) 3,4-Syn addition has been recently reported for the reaction of trialkylaluminum reagents to cyclopentenones **6** (R^1 = SO_2Ph or CO_2-Me). See: (a) Yakura, T.; Tanaka, K.; Iwamoto, M.; Nameki, M.; Ikeda, M. *Synlett* **1999**, 1313−1315. (b) Yakura, T.; Tanaka, K.; Kitano, T.; Uenishi, J.; Ikeda, M. *Tetrahedron* **2000**, *56*, 7715−7721.

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Scheme 3

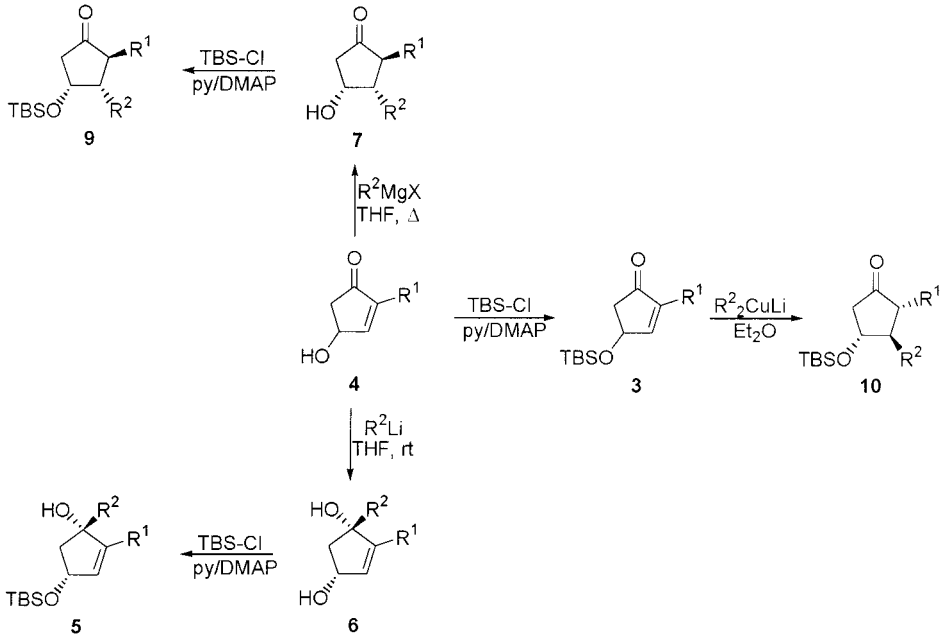


Table 1. Reaction of Cyclopentenones 3 with Organolithium or Grignard Reagents

no.	3	R^1	R^2M[a]	5 (%)[b]
1	**3a**	Ph	MeLi	**5a** (70)
2	**3a**	Ph	MeMgI	**5a** (90)
3	**3a**	Ph	PhLi	**5b** (90)
4	**3b**	Me	PhLi	**5c** (50)
5	**3b**	Me	PhMgBr	**5c** (75)

[a] THF was used as a solvent. Reactions with R^2Li (1.1 equiv) were carried out from −78 °C to room temperature, and reactions with R^2MgX (1.1 equiv) were carried out at reflux temperature. [b] Isolated yields after silica gel chromatography (2:1 Hx−EtOAc).

Table 2. Reaction of Cyclopentenones 4 with Organolithium or Grignard Reagents

no.	4	R^1	R^2M[a]	7:6[b] (%)[c]
1	**4a**	Ph	MeMgI	**7a**:**6a** = 90:10 (**7a**, 60)
2	**4a**	Ph	EtMgBr	**7b**:**6b** = 95:05 (**7b**, 65)
3	**4a**	Ph	PhMgBr	**7c**:**6c** = 95:05 (**7c**, 70)
4	**4a**	Ph	*p*-F−C_6H_5−MgBr	**7d**:**6d** = 95:05 (**7d**, 65)
5	**4b**	Me	MeMgI	**7e**:**6e** = 90:10 (**7e**, 65)
6	**4a**	Ph	MeLi	**7a**:**6a** = 0:100 (**6a**, 65)
7	**4b**	Me	MeLi	**7e**:**6e** = 0:100 (**6b**, 70)

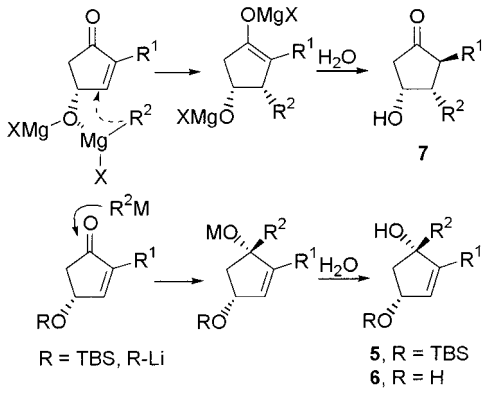
[a] THF was used as a solvent. Reactions with R^2Li (2.2 equiv) were carried out from −78 °C to room temperature, and reactions with R^2MgX (2.2 equiv) were carried out at reflux temperature. [b] Determined by integration of the ^1H NMR spectra ($CDCl_3$, 300 MHz) of the crude reaction mixtures. [c] Isolated yields after silica gel chromatography (2:1 Hx−EtOAc).

in the addition of cuprate reagents to cyclopentenones **3**, as evidenced by the comparison of the spectroscopic data of compounds **9a** and **10a** (R^1 = Ph, R^2 = Me).

On the other hand, the reaction of organolithium reagents with cyclopentenones **4** took place in a 1,2-fashion to afford compounds **6** (3,5-syn), with the same stereoselectivity previously observed for the addition of organolithium and organomagnesium reagents to the TBS derivatives **3**, as produced by the conversion of compounds **6** into the related *O*-TBS derivatives **5** (Scheme 3). The results are given in Table 2.

The stereochemical outcome of the addition reactions with organomagnesium reagents may be understood on the basis of an intramolecular chelation-directed delivery

Scheme 4



of the Grignard species to the *β*-vinyl carbon of the starting 4-hydroxycyclopentenones **4** (Scheme 4), which should take place in a syn fashion.[3,9] Conversely, coordination of the organomagnesium species to the oxygen at carbon C-4 would not be possible in the presence of the bulky TBS group in compounds **3**, and thus intermolecular addition would take place in a 1,2-fashion from the less encumbered diastereotopic face of the carbonyl group, with anti diastereoselectivity. On the other hand, organolithiums, which are harder nucleophiles than organomagnesium reagents, would always give 1,2-addition irrespective of the substitution at C-4 of the starting cyclopentenone. This addition takes place opposite to the bulky substituent at C-4 (TBSO or RLi−O complex), affording cyclopentenones **5** or **6** (3,5-syn).

In conclusion, a highly regio- and stereoselective method for the 1,2- or 1,4-addition reactions to 4-hydroxy-2-cyclopentenones has been devised, which makes use of readily available organolithium and Grignard reagents. This procedure allows for stereochemistry complementary to that observed in the 1,4-addition of organocuprates and makes possible the attachment of aromatic groups to carbons C-2 and C-3 of cyclopentenones **5** or **6**

(9) For related models, see: Felkin, H.; Swierczewski, G.; Tambuté, A. *Tetrahedron Lett.* **1969**, *9*, 707−710.

and carbons C-4 and C-5 of cyclopentanones **7**, which are of interest for further elaboration into biologically active targets.[10]

Experimental Section

Silica gel 60 F_{254} was used for TLC, and the spots were detected with UV and vainilline solution. Flash column chromatography was carried out on silica gel 60. IR spectra have been recorded as $CHCl_3$ solutions. ^1H and ^{13}C NMR spectra were recorded at 200 or 300 MHz and 50.5 or 75.5 MHz, respectively. MS was carried out at 70 eV. The 4-hydroxy-2-cyclopentenones **4** were prepared from furans **8** as previously reported.[3]

Synthesis of Cyclopentenones 3: General Procedure. To a solution of **4** (2.48 mmol) in pyridine (12.4 mL) were added TBS−Cl (748 mg, 4.96 mmol) and DMAP (60 mg, 0.49 mmol). The mixture was stirred for 24 h at room temperature. Filtration of the reaction mixture, rinsing with CH_2Cl_2 (2 × 5 mL), and evaporation of the solvent afforded an oil that was purified by chromatography (2:1 hexane−ethyl acetate).

4-(ᵗButyldimethylsilyloxy)-2-phenylcyclopent-2-enone (3a): 90%, white solid, mp 58−59 °C (MeOH); IR ($CHCl_3$) ν 1700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68−7.65 (2H, m), 7.51 (1H, d, ^3J = 2.3 Hz), 7.38−7.33 (3H, m), 4.98 (1H, m), 2.91 (1H, B part of ABX system, ^3J = 5.7 Hz, ^3J = 18.0 Hz), 2.47 (1H, A part of ABX system, ^3J = 2.4 Hz, ^3J = 18.0 Hz), 0.91 (9H, s), 0.15 (3H, s), 0.13 (3H, s); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 204.0, 157.3, 143.5, 130.6, 128.9, 128.4, 127.5, 68.3, 46.6, 25.7, 18.1. Anal. Calcd for $C_{17}H_{24}O_2Si$: C, 70.78; H, 8.39. Found: C, 70.99; H, 8.42.

4-(ᵗButyldimethylsilyloxy)-2-methylcyclopent-2-enone (3b): 90%, colorless oil; IR ($CHCl_3$) ν 1715 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.98−6.94 (1H, m), 4.78−4.72 (1H, m), 2.59 (1H, B part of ABX system, ^3J = 5.9 Hz, ^3J = 18.3 Hz), 2.13 (1H, A part of ABX system, ^3J = 2.1 Hz, ^3J = 18.3 Hz), 1.16 (3H, d, ^4J = 2.9 Hz), 0.78 (9H, s), 0.01 (3H, s), 0.00 (3H, s); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 206.3, 157.4, 142.7, 68.8, 45.0, 25.6, 18.0, 9.7. Anal. Calcd for $C_{12}H_{22}O_2Si$: C, 63.67; H, 9.80. Found: C, 63.77; H, 9.70.

Reaction of Cyclopentenones 3 and 4 with Grignard Reagents: General Procedure. To a solution of **3** or **4** (2.56 mmol) in THF (3.0 mL) at 0 °C was added dropwise a 1 M solution of R^2MgX in THF (3.0 mL for compounds **3**, 6.0 mL for compounds **4**). The mixture was stirred at reflux temperature for 2 h, cooled to room temperature, and hydrolyzed with saturated NH_4Cl solution (3.0 mL). The organic layer was decanted and the aqueous layer extracted with Et_2O (3 × 10 mL). The combined organic layers were dried on $MgSO_4$. Filtration and elimination of the solvent under reduced pressure afforded an oil that was purified by chromatography (10:1 hexane−Et_2O).

Reaction of Cyclopentenones 3 and 4 with Organolithium Reagents: General Procedure. To a solution of **3** (2.56 mmol) in THF (3.0 mL) at 0 °C was added dropwise a 1 M solution of MeLi in Et_2O (3.0 mL for compounds **3**, 6.0 mL for compounds **4**) or a 1.8 M solution of PhLi in cyclohexanes−Et_2O (1.67 mL for compounds **3**, 3.34 mL for compounds **4**). After the mixture was stirred for 2 h at room temperature, all operations were followed as above.

(1*S,4*R**)-4-(ᵗButyldimethylsilyloxy)-1-methyl-2-phenylcyclopent-2-enol (5a):** white solid, mp 55−56 °C (hexane − ethyl acetate); IR ($CHCl_3$) ν 3400 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.55−7.49 (2H, m), 7.27−7.13 (3H, m), 5.87 (1H, d, ^3J = 2.3 Hz), 4.60 (1H, m), 2.33 (1H, B part of ABX system, ^3J = 6.3 Hz, ^3J = 13.5 Hz), 1.89 (1H, A part of ABX system, ^3J = 3.2 Hz, ^3J = 13.5 Hz), 1.31 (3H, s), 0.79 (9H, s), 0.01 (3H, s), 0.00 (3H, s); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 150.6, 134.8, 131.2, 128.2, 127.7, 127.5, 82.1, 73.1, 52.8, 25.9, 25.7, 18.1. Anal. Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.27. Found: C, 71.16; H, 9.32.

(1*S,4*R**)-4-(ᵗButyldimethylsilyloxy)-1,2-diphenylcyclopent-2-enol (5b):** white solid, mp 76−78 °C (hexane−ethyl acetate); IR ($CHCl_3$) ν 3415 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31−7.02 (10H, m), 6.26 (1H, d, ^3J = 2.3 Hz), 4.77 (1H, m), 2.53 (1H, B part of ABX system, ^3J = 6.3 Hz, ^3J = 13.5 Hz), 2.12 (1H, A part of ABX system, ^3J = 3.7 Hz, ^3J = 13.5 Hz), 0.80 (9H, s), 0.01 (6H, s); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 149.3, 145.3, 133.9, 132.9, 128.5, 128.3, 127.9, 127.7, 126.8, 125.0, 86.2, 73.6, 56.1, 26.1, 18.4 Anal. Calcd for $C_{23}H_{30}O_2Si$: C, 75.36; H, 8.25. Found: C, 75.48; H, 8.44.

(1*S,4*R**)-4-(ᵗButyldimethylsilyloxy)-2-methyl-1-phenylcyclopent-2-enol (5c):** colorless oil; IR ($CHCl_3$) ν 3425 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.29−7.15 (5H, m), 5.59 (1H, m), 4.69 (1H, m), 2.59 (1H, B part of ABX system, ^3J = 6.6 Hz, ^3J = 13.9 Hz), 1.99 (1H, A part of ABX system, ^3J = 3.6 Hz, ^3J = 13.9 Hz), 1.47 (3H, s), 0.83 (9H, s), 0.00 (6H, s); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 147.8, 144.6, 131.2, 128.2, 126.6, 127.8, 85.8, 74.0, 54.1, 25.9, 18.1, 11.9. Anal. Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.27. Found: C, 71.25; H, 9.51.

(1*S,3*R**)-1-Methyl-5-phenyl-cyclopent-4-ene-1,3-diol (6a):** colorless oil; IR ($CHCl_3$) ν 3280 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.56−7.49 (2H, m), 7.27−7.19 (3H, m), 5.94 (1H, d, ^3J = 2.3 Hz), 4.61 (1H, m), 2.44 (1H, B part of ABX system, ^3J = 6.9 Hz, ^3J = 14.2 Hz), 1.94 (1H, A part of ABX system, ^3J = 2.9 Hz, ^3J = 14.2 Hz), 1.32 (3H, s); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 151.2, 134.4, 130.5, 128.2, 127.8, 127.5, 82.1, 72.7, 52.0, 26.5. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.92; H, 7.61.

(1*S,3*R**)-1,5-Dimethylcyclopent-4-ene-1,3-diol (6b):** colorless oil; IR ($CHCl_3$) ν 3390 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.44 (1H, m), 4.48 (1H, m), 2.34 (1H, B part of ABX system, ^3J = 6.9 Hz, ^3J = 14.3 Hz), 1.78 (1H, A part of ABX system, ^3J = 3.0 Hz, ^3J = 14.3 Hz), 1.69 (3H, s), 1.21 (3H, s); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 149.1, 128.9, 81.4, 73.0, 50.7, 25.6, 11.3. Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.75; H, 9.61.

(2*R,3*S**,4*R**)-4-Hydroxy-3-methyl-2-phenylcyclopentanone (7a):** colorless oil; IR ($CHCl_3$) ν 3450, 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.30−7.13 (3H, m), 7.02−6.98 (2H, m), 4.33 (1H, m), 3.20 (1H, d, ^3J = 12.6 Hz), 2.48−2.46 (2H, m), 2.37−2.13 (1H, m), 1.04 (3H, d, ^3J = 6.7 Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 216.7, 137.2, 128.5, 126.9, 70.0, 58.4, 48.3, 42.6, 12.9. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.91; H, 7.66.

(2*R,3*S**,4*R**)-4-Hydroxy-3-ethyl-2-phenylcyclopentanone (7b):** colorless oil; IR ($CHCl_3$) ν 3450, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31−7.14 (3H, m), 7.03−6.97 (2H, m), 4.53 (1H, m), 3.26 (1H, d, ^3J = 12.5 Hz), 2.49−2.47 (2H, m), 2.18−2.02 (1H, m), 1.69−1.39 (2H, m), 0.86 (3H, t, ^3J = 7.4 Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 216.9, 138.0, 128.9, 128.8, 127.2, 67.8, 58.1, 51.8, 48.6, 21.0, 11.8. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.61; H, 8.03.

(2*R,3*R**,4*R**)-4-Hydroxy-2,3-diphenylcyclopentanone (7c):** white solid, mp 102−103 °C (hexanes−ethyl acetate); IR ($CHCl_3$) ν 3460, 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31−7.04 (10H, m), 4.50 (1H, m), 4.02 (1H, d, ^3J = 13.1 Hz), 3.68 (1H, dd, ^3J = 3.5 Hz, ^3J = 13.1 Hz), 2.61 (2H, m); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 214.5, 136.6, 136.2, 128.9, 128.5, 128.4, 128.3, 127.5, 127.0, 70.5, 54.6, 54.3, 46.9. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 81.11; H, 6.50.

***(2R*,3R*,4R*)*-3-(4-Fluorophenyl)-4-hydroxy-2-phenylcyclopentanone (7d):** white solid, mp 106−107 °C (hexane−ethyl acetate); IR ($CHCl_3$) ν 3460, 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.35−7.21 (5H, m), 7.18−7.01 (4H, m), 4.54 (1H, m), 3.98 (1H, d, ^3J = 13.2 Hz), 3.67 (1H, dd, ^3J = 3.4 Hz, ^3J = 13.1 Hz), 2.65 (2H, m); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 214.2, 162.1 (d, $^1J_{CF}$ = 245 Hz), 138.0, 132.4 (d, $^4J_{CF}$ = 3 Hz), 129.9 (d, $^3J_{CF}$ = 3 Hz), 128.6, 128.4, 127.1, 115.9 (d, $^2J_{CF}$ = 21 Hz), 70.5, 54.7, 53.9, 46.9. Anal. Calcd for $C_{17}H_{15}FO_2$: C, 75.54; H, 5.59. Found: C, 75.70; H, 5.71.

***(2S*,3S*,4R*)*-4-Hydroxy-2,3-dimethylcyclopentanone (7e):** colorless oil; IR ($CHCl_3$) ν 3450, 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.30 (1H, m), 2.34 (1H, m), 211−1.95 (1H, m), 1.79−1.61 (1H, m), 1.13 (3H, d, ^3J = 7.5 Hz), 1.00 (3H, d, ^3J = 7.0 Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 219.9, 70.6, 47.6, 46.5, 44.6, 13.2, 12.4. Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.73; H, 9.61.

Synthesis of (2*R,3*S**,4*R**)-4-(ᵗButyldimethylsilyloxy)-3-methyl-2-phenyl-cyclopentanone (9a).** To a solution of **7a** (471 mg, 2.48 mmol) in pyridine (12.4 mL) were added TBS−Cl (748 mg, 4.96 mmol) and DMAP (60 mg, 0.49 mmol). The mixture was stirred for 24 h at room temperature. Filtration of

(10) For example benzoprostacyclins, see: Larock, R. C.; Lee, N. H. *J. Org. Chem.* **1991**, *56*, 6253−6254 and references cited therein.

the reaction mixture, rinsing with CH_2Cl_2 (2 × 5 mL), and evaporation of the solvent afforded an oil that was purified by chromatography (2:1 hexane−ethyl acetate): 90%, white solid, mp 56−57 °C (hexane−ethyl acetate); IR ($CHCl_3$) ν 1745 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.27−7.10 (3H, m), 7.01−6.96 (2H, m), 4.31 (1H, m), 3.13 (1H, d, ^3J = 12.5 Hz), 2.42−2.39 (2H, m), 2.30−2.17 (1H, m), 0.98 (3H, d, ^3J = 6.7 Hz), 0.80 (3H, s), 0.02 (3H, s), 0.01 (3H, s), 18.0, 13.5. Anal. Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.27. Found: C, 71.25; H, 9.39.

Synthesis of (2*R,3*S**,4*S**)-4-(ᵗButyldimethylsilyloxy)-3-methyl-2-phenyl-cyclopentanone (10a).** To a solution of CuI (145 mg, 0.76 mmol) in Et_2O (5.0 mL) at 0 °C was added dropwise a 1.6 M solution of MeLi in Et_2O (0.95 mL, 1.52 mmol). After the mixture was stirred for 10 min, a solution of **3a** (199 mg, 0.69 mmol) in Et_2O (5 mL) was added. The mixture was stirred at 0 °C for 2 h and hydrolyzed with saturated NH_4Cl solution (3.0 mL). The organic layer was decanted and the aqueous layer extracted with Et_2O (3 × 10 mL). The combined organic layers were dried on $MgSO_4$. Filtration and elimination of the solvent under reduced pressure afforded a pale yellow oil that was purified by chromatography (10:1 hexane−Et_2O): 85%, colorless oil; IR ($CHCl_3$) ν 1745 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.29−7.12 (3H, m), 7.09−6.99 (2H, m), 3.97−3.85 (1H, m), 2.81 (1H, d, ^3J = 12.7 Hz), 2.69 (1H, B part of ABX system, ^3J = 7.2 Hz, ^3J = 18.5 Hz), 2.26 (1H, A part of ABX system, ^3J = 9.0 Hz, ^3J = 18.5 Hz), 2.30−2.10 (1H, m), 1.04 (3H, d, ^3J = 6.4 Hz), 0.80 (3H, s), 0.02 (3H, s), 0.01 (3H, s); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 213.1, 136.5, 128.6, 128.5, 127.0, 62.9, 47.8, 47.5, 25.6, 17.9, 15.9. Anal. Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.27. Found: C, 71.21; H, 9.50.

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Supporting Information Available: ^1H and ^{13}C NMR of compounds **3**, **5**−**7**, **9**, and **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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