Pergamon

Tetrahedron 55 (1999) 7461–7470

TETRAHEDRON

Chemo- and Stereoselective Dirhodium(II)-Catalyzed C-H Insertion Reaction of 5,6-Dioxygenated 2-Diazo-3-oxohexanoates: Synthesis of An Optically Active Highly Functionalized Cyclopentane

Takayuki Yakura,* Akiharu Ueki, Tsuyoshi Kitamura, Kenji Tanaka, Masatake Nameki, and Masazumi Ikeda*

Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607-8414, Japan.

Received 15 March 1999; accepted 20 April 1999

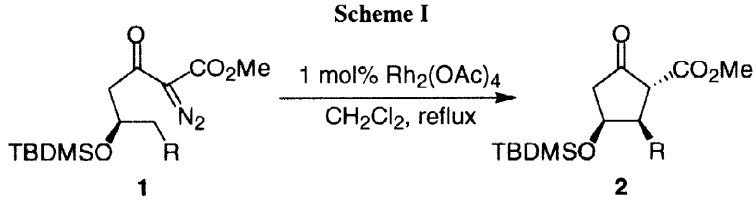
Abstract Methyl (*S*)-α-diazo-2,2-dimethyl-β-oxo-1,3-dioxolane-2-butanoate (**4**), upon treatment with dirhodium(II) tetraacetate in refluxing dichloromethane, gave methyl (1*S*,5*S*)-2,2-dimethyl-7-oxo-3,8-dioxabicyclo[3.2.1]octane-1-carboxylate (**5**) *via* oxonium ylide formation/1,2-shift. On the other hand, a similar treatment of methyl (*S*)-5,6-bis[*tert*-butyldimethylsilyl(TBDMS)oxy]-2-diazo-3-oxohexanoate (**9a**) afforded the C-H insertion product **10** which was directly reduced with lithium aluminum hydride to give stereoselectively (1*R*,2*R*,3*S*,5*R*)-2,3-bis(TBDMSoxy)-5-hydroxycyclopentanemethanol (**13**) in 52% yield from **9a**.

Keywords: Carbenes and carbenoids; Cyclopentanes; Insertion reactions; Rhodium and compounds

Introduction

A dirhodium(II)-catalyzed C-H insertion reaction of α-diazocarbonyl compounds is widely used as one of the most effective and versatile methods for the construction of functionalized five-membered carbocycles and heterocycles.[1,2] However, it is sometimes difficult to control the chemoselectivity because of the high reactivity of the rhodium carbenoid intermediates, which can react with unactivated C-H bonds, C-C multiple bonds, heteroatoms, *etc*. In previous papers,[2] we reported that 5-[*tert*-butyldimethylsilyl(TBDMS)oxy]-2-diazo-3-oxoalkanoates (**1**), upon treatment with 1 mol% of dirhodium(II) tetraacetate [$Rh_2(OAc)_4$] in dichloromethane (CH_2Cl_2) under reflux, gave 1,2-*trans*-2,3-*cis*-2-alkyl-3-(TBDMSoxy)-5-oxocyclopentanecarboxylates (**2**) with high chemo- and stereoselectivity (Scheme I).

Scheme I



Email address: yakura@mb.kyoto-phu.ac.jp

0040-4020/99/$ - see front matter
PII: S0040-4020(99)00369-5

As an extension of this chemo- and stereoselective C-H insertion reaction, we now investigated the reaction of 5,6-dioxygenated 2-diazo-3-oxohexanoates **4** and **9a** with the dirhodium(II) catalyst in order to develop a new route to 2,3-dioxygenated 5-oxocyclopentanecarboxylates, which would be useful intermediates for the synthesis of aminocyclopentitols[3] and carbocyclic nucleosides.[4] Herein, we report the contrasting behavior of these diazoketones[5] and a synthetic approach to a highly functionalized cyclopentane.

Results and Discussion

We initiated our investigation by examining the reaction of α-diazoketone **4** protected by a cyclic acetal group with the Rh(II) catalyst (Scheme II). Compound **4** was prepared by homologation of the (*S*)-2,2-dimethyl-1,3-dioxolan-4-acetaldehyde (**3**), prepared from (*S*)-malic acid,[6] with methyl diazoacetate and tin(II) chloride ($SnCl_2$),[2c,7] followed by diazotransfer reaction of the resulting β-ketoester[8] with *p*-toluenesulfonyl azide (TsN_3) and triethylamine (Et_3N).

Compound **4** thus obtained was treated with 1 mol% of $Rh_2(OAc)_4$ in CH_2Cl_2 under reflux for 5 min, and the reaction mixture was then passed through a short pad of silica gel to give methyl (1*S*,5*S*)-2,2-dimethyl-7-oxo-3,8-dioxabicyclo[3.2.1]octane-1-carboxylate (**5**) in 54% yield without any C-H insertion products.[9,10] The structure of **5** was deduced from the spectroscopic evidence. The IR spectrum showed two strong carbonyl absorptions at 1770 (a five-membered ketone) and 1745 cm^{-1} (an ester). The ^1H NMR spectrum showed the presence of the -CH_2-CH-CH_2- moiety, and the ^{13}C NMR spectrum revealed the presence of four quaternary carbons at δ 77.4 (2-C), 86.4 (1-C), 164.6 (an ester carbonyl), and 205.3 (a keto carbonyl). Final confirmation of the structure of **5** was given by its X-ray analysis (Fig. 1).

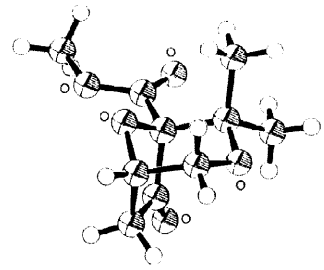
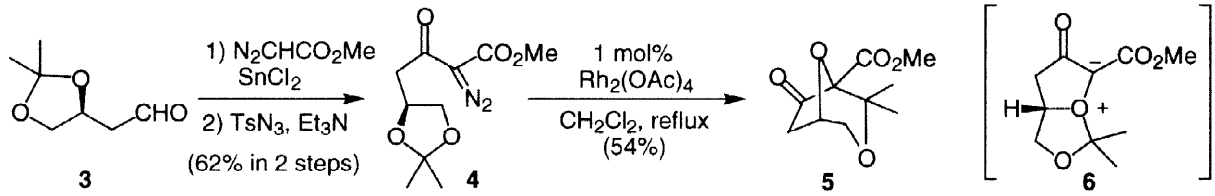


Fig. 1. ORTEP diagram of **5**

Scheme II

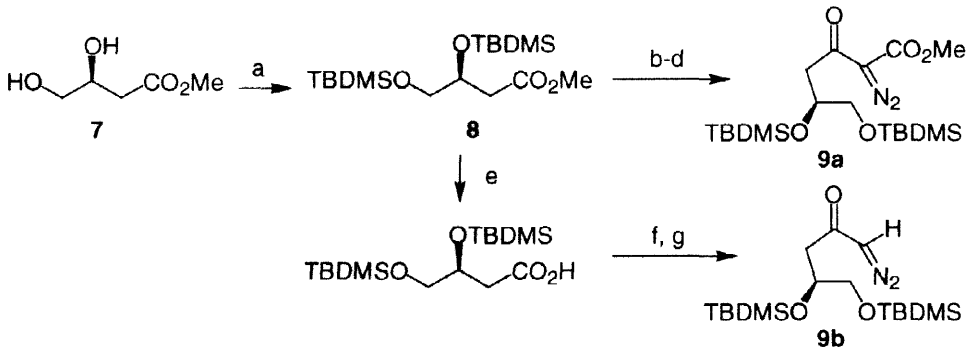


The formation of **5** can be rationalized in terms of the oxonium ylide intermediate **6** formed by the attack of the rhodium carbenoid on the ether oxygen atom, which undergoes a [1,2]-shift.[1,11]

Because the reaction of **4** with $Rh_2(OAc)_4$ did not give any C-H insertion products, we next examined the dirhodium(II)-catalyzed reaction of bis(TBDMSoxy) derivatives **9a** and **9b**. The starting α-diazoketones **9a** and **9b** were prepared from methyl (*S*)-3,4-dihydroxybutanoate (**7**)[6] (Scheme III). Treatment of **7** with TBDMS-chloride and imidazole in *N*,*N*-dimethylformamide (DMF) gave bis(TBDMSoxy)ester **8** in quantitative yield. Reduction of **8** with diisobutylaluminum hydride (DIBAL-H) followed by treatment of the resulting bis(TBDMSoxy)aldehyde with methyl diazoacetate and $SnCl_2$ gave methyl (*S*)-5,6-bis(TBDMSoxy)-3-oxohexanoate in 94% yield from **8**. Diazotransfer reaction of the β-ketoester with TsN_3 and Et_3N provided α-

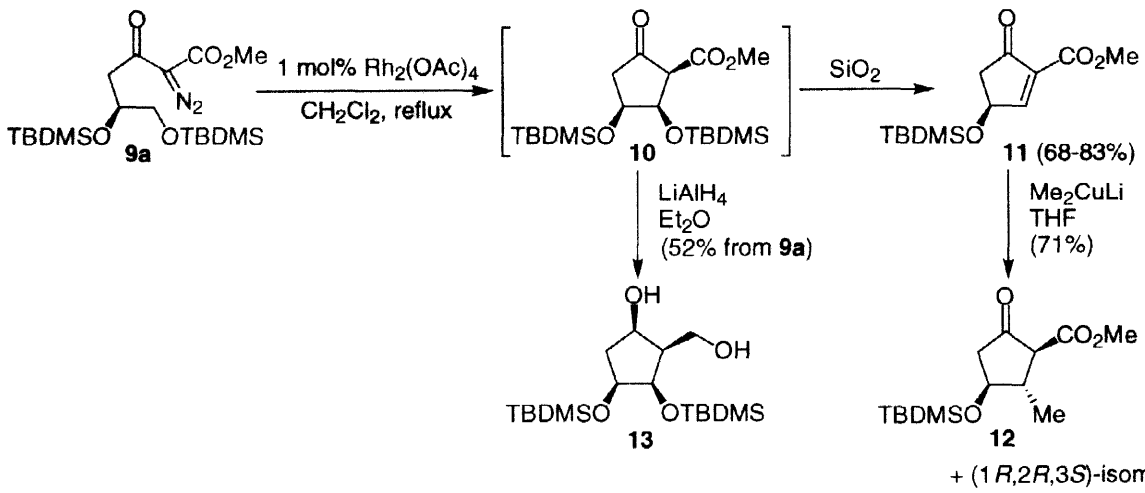
diazo-β-ketoester **9a** in 90% yield. Hydrolysis of **8**, followed by treatment of the resulting carboxylic acid with oxalyl chloride and then diazomethane, afforded diazoketone **9b**.

Scheme III [a]



[a] a) TBDMSCl, imidazole, DMF, rt, 16 h (quant.); b) DIBAL-H, CH_2Cl_2, -78 °C, 10 min (97%); c) N_2CHCO_2Me, $SnCl_2$, CH_2Cl_2, 0 °C, 10 min (97%); d) TsN_3, Et_3N, CH_3CN, rt, 15 h (90%); e) LiOH, MeOH-H_2O, rt, 45 °C, 15 h (49%); f) $(COCl)_2$, benzene, rt, 38 h; g) CH_2N_2, Et_2O, 0 °C, 30 min (66% in 2 steps)

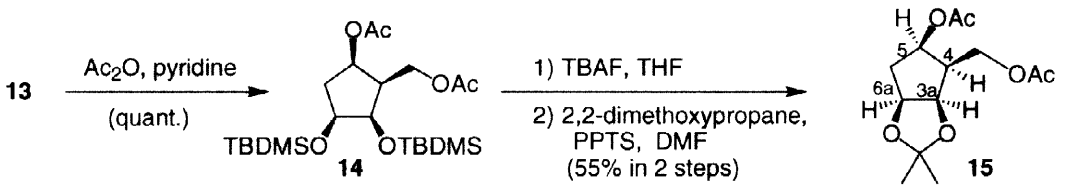
When compound **9a** was heated with $Rh_2(OAc)_4$ in CH_2Cl_2 under reflux for 5 min and the reaction mixture was then passed through a short pad of silica gel, labile methyl (*S*)-3-TBDMSoxy-5-oxo-1-cyclopentenecarboxylate (**11**) was obtained in 68-83% yield.[9,12] The structure of **11** was determined by the spectroscopic data and chemical correlations. The IR spectrum showed absorptions at 1760 and 1630 cm^{-1} (a cyclopentenone) and at 1730 cm^{-1} (an ester), and the ^1H NMR spectrum revealed a doublet at δ 8.05 (J = 2.3 Hz) due to the olefinic proton. The reaction of **11** with lithium dimethylcuprate gave an 8:1 mixture of methyl (1*S*,2*S*,3*S*)-3-TBDMSoxy-2-methyl-5-oxocyclopentanecarboxylate (**12**) and its (1*R*,2*R*,3*S*)-isomer in 71% combined yield. The spectroscopic data of **12** were identical with those of a racemic authentic sample.[2b]



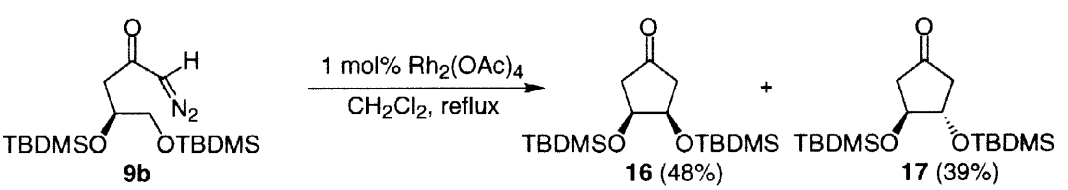
It seems likely that cyclopentenone **11** could be formed *via* β-elimination of the initially formed C-H insertion product **10** during passing through the silica gel pad. Indeed, the ^1H NMR spectrum of the crude

reaction products of **9a** before treatment with silica gel revealed new signals at δ 3.47 (d, J = 9.0 Hz), 4.32 (q, J = 3.5 Hz), and 4.55 (dd, J = 9.0, 3.5 Hz) due to the H-1, H-3, and H-2 protons of **10**, respectively, in addition to the signals of **11** in a ratio of 4:1. Interestingly, compound **10** was produced as a single diastereoisomer. After **9a** was completely consumed in the reaction with $Rh_2(OAc)_4$, the reaction mixture was added to a suspension of lithium aluminum hydride (LAH) in diethyl ether at 0 °C, and the entire mixture was stirred at room temperature for 30 min to give (1*R*,2*R*,3*S*,5*R*)-2,3-bis(TBDMSoxy)-5-hydroxycyclopentanemethanol (**13**) in 52% yield from **9a** as a sole diastereoisomer. Other reducing agents such as sodium borohydride and DIBAL-H were not suitable for this reduction; complex mixtures were obtained. The stereochemistry of **13** was confirmed by chemical correlations and differential nuclear Overhauser effect (NOE) experiments of bicyclic compound **15** (Scheme IV). Thus, **13** was allowed to react with acetic anhydride in pyridine to give diacetate **14** in quantitative yield. Desilylation of **14** by tetrabutylammonium fluoride (TBAF), followed by treatment of the resulting diol with 2,2-dimethoxypropane in the presence of pyridinium *p*-toluenesulfonate (PPTS) in DMF afforded acetonide **15** in 55% yield from **14**. This result showed the *cis* relationship between two TBDMSO groups at the C-2 and C-3 positions in **13**. The positive NOEs were observed between H-3a and H-6a (5.7 and 6.9% enhancement, respectively), H-3a and H-4 (2.7 and 3.1% enhancement, respectively), and H-4 and H-5 (both 4.0% enhancements) protons of **15**.

Scheme IV



A similar treatment of **9b** with $Rh_2(OAc)_4$ in refluxing CH_2Cl_2 proceeded with chemoselectivity but without stereoselectivity to provide 3,4-*cis*- and 3,4-*trans*-3,4-bis(TBDMSoxy)cyclopentanones (**16** and **17**) in 48 and 39% yields, respectively. The IR spectra of both diastereoisomers showed an absorption due to the cyclopentanone group (1750 cm^{-1}). The stereochemistry of both compounds was determined by a comparison of the specific rotations. Thus, the $[\alpha]_D$ value of the major isomer was zero, so that it should be a *meso* compound, *i.e.*, *cis*-isomer **16**. The minor isomer had $[\alpha]_D^{26}$ -48.6, indicating it to be *trans*-isomer **17**.



The bulky TBDMS group restricts the oxonium ylide formation and makes the C-H insertion reaction at the C-6 position favorable. One possible explanation for the stereoselectivity in this C-H insertion reaction is based on the cyclic transition states **IA** and **IB** (Fig. 2).[13] In both the transition states, the TBDMSoxy group at the C-5 position could occupy a pseudoaxial position predominantly[2b,14] and the bulky dirhodium complex a

pseudoequatorial position; these conformations might be further stabilized by a favorable electronic interaction between the ether oxygen atom at the C-5 position and the ester carbonyl group.[2b] In the transition state **IB**, severe steric repulsion between the C-6 pseudoaxial TBDMSoxy group and the dirhodium complex becomes evident, although both TBDMSoxy groups occupy more preferred pseudoaxial positions. We assumed, therefore, that the C-H insertion would proceed *via* the sterically favored transition state **IA** to form cyclopentanone **10**. The reduction of **10** with LAH would proceed stereoselectively as a result of the attack of the hydride ion on the less-hindered *Si*-face of the ketonic carbonyl group to give diol **13**. On the other hand, treatment of **10** with silica gel would result in the β-elimination[15] of a silanol due to the high acidity of the proton at the C-1 position to yield cyclopentenone **11**.

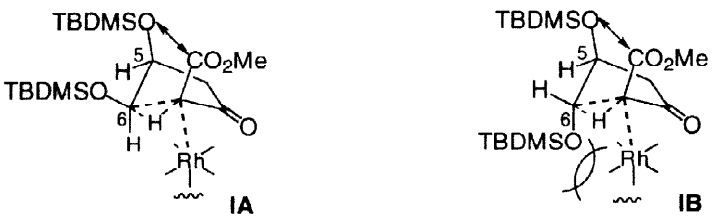


Fig. 2.

In summary, this study revealed that the chemoselectivity of the dirhodium(II)-catalyzed reaction of 5,6-dioxygenated 2-diazo-3-oxohexanoates **4** and **9a** can be controlled by selecting the protecting groups of the diol: the acetonide derivative **4** gave 3,8-dioxabicyclo[3.2.1]octane **5** *via* oxonium ylide formation/1,2-shift, whereas the bis-TBDMSoxy derivative **9a** gave the C-H insertion product **10**, which was reduced with LAH to afford cyclopentanemethanol **13** as a single stereoisomer. The latter stereoselective C-H insertion-reduction process leads to a new method for constructing four continuous stereocenters of a highly functionalized cyclopentane.

Experimental

All melting points are uncorrected. The IR spectra were recorded using a JASCO IR-1 spectrophotometer. The ^{1}H NMR spectra were determined with a JEOL JNM-MY-60 (60 MHz) or Varian XL-300 (300 MHz) spectrometer using $CDCl_3$ as a solvent and tetramethylsilane as an internal standard. The ^{13}C NMR spectra were recorded on a Varian XL-300 (75 MHz) spectrometer using $CDCl_3$ as a solvent and are reported in ppm using the solvent resonance as an internal standard (77.0 for $CDCl_3$). All ^{13}C NMR spectra were determined with complete proton decoupling. Specific rotations were recorded on a JASCO DIP-360 polarimeter. High-resolution mass spectra (HRMS) were obtained with a JEOL JMS-SX 102A QQ instrument. Column chromatography was carried out on Silica gel 60 PF_{254} (Nacalai Tesque, Inc.) under pressure. The known aldehyde **3** and ester **7** were prepared according to the reported procedures.[6]

Methyl (*S*)-α-Diazo-2,2-dimethyl-β-oxo-1,3-dioxolane-4-butanoate (4). According to the procedure of Holmquist and Roskamp,[7] a solution of **3** (1.26 g, 8.73 mmol) was added to a suspension of methyl diazoacetate (961 mg, 9.60 mmol) and $SnCl_2$ (166 mg, 0.87 mmol) in CH_2Cl_2 (20 mL) at room temperature under a nitrogen atmosphere. The mixture was stirred for 10 min and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 10:1) to give methyl (*S*)-2,2-dimethyl-β-oxo-1,3-dioxolane-4-butanoate (1.20 g, 63%) as a colorless oil, whose spectroscopic data were identical with the reported values.[8] A

solution of thus obtained ketoester (850 mg, 3.93 mmol), TsN_3 (1.16 g, 5.90 mmol), and Et_3N (794 mg, 7.86 mmol) in MeCN (40 mL) was stirred at room temperature for 15 h and then diluted with Et_2O (50 mL). The mixture was washed with H_2O (20 mL) and brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 15:1) to give **4** (937 mg, 98%) as a pale yellow oil: $[\alpha]_D^{26}$ +17.2 (*c* 1.02, $CHCl_3$); IR (CCl_4) ν 2140, 1730, 1660 cm^{-1}; ^1H NMR (300 MHz) δ 1.36, 1.42 (both 3H, s, CMe), 2.98, 3.38 (1H each, d of ABq, J = 6.5, 17.1 Hz, γ-H_2), 3.63 (1H, dd, J = 8.3, 6.5 Hz, one of 5-H_2), 3.85 (3H, s, OMe), 4.19 (1H, dd, J = 8.3, 6.1 Hz, one of 5-H_2), 4.57 (1H, quintet, J = 6.3 Hz, 4-H). HRMS (FAB) Calcd for $C_{10}H_{15}N_2O_5$ [$(M+H)^+$]: 243.0981. Found: 243.0978.

Dirhodium(II)-Catalyzed Reaction of 4. General Procedure. A solution of **4** (155 mg, 0.64 mmol) in CH_2Cl_2 (6 mL) was added to a boiling solution of $Rh_2(OAc)_4$ (3 mg, 0.006 mmol) in CH_2Cl_2 (32 mL), and the mixture was refluxed for 5 min. After evaporation of the solvent, the crude material was chromatographed on silica gel (hexane/EtOAc, 8:1) to give methyl (1*S*,5*S*)-2,2-dimethyl-7-oxo-3,8-dioxabicyclo[3.2.1]octane-1-carboxylate (**5**) (74 mg, 54%) as colorless needles: mp 93-94 °C (hexane-EtOAc); $[\alpha]_D^{25}$ -37.0 (*c* 1.01, $CHCl_3$); IR (CCl_4) ν 1770, 1745 cm^{-1}; ^1H NMR (300 MHz) δ 1.42, 1.43 (both 3H, s, CMe), 2.48 (1H, dd, J = 17.7, 1.0 Hz, one of 6-H_2), 2.77 (1H, dd, J = 17.7, 7.7 Hz, one of 6-H_2), 3.47 (1H, dd, J = 12.0, 1.0 Hz, one of 4-H_2), 3.78 (3H, s, OMe), 4.25 (1H, dd, J = 12.0, 2.0 Hz, one of 4-H_2), 4.76 (1H, ddt, J = 7.7, 2.0, 1.0 Hz, 5-H); ^{13}C NMR (75 MHz) δ 18.8 (CH_3), 23.6 (CH_3), 39.0 (6-C), 52.8 (OCH_3), 64.3 (4-C), 73.9 (5-C), 77.4 (2-C), 86.4 (1-C), 164.6 (COO), 205.3 (C-7). *Anal.* Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.73; H, 6.45.

X-ray Crystallographic Analysis of 5.[16] A single crystal of **5** was obtained by recrystallization from hexane-EtOAc. Crystal data of **5**: $C_{10}H_{14}O_5$, M = 214.22, orthorhombic (space group $P2_12_12_1$), a = 9.137(2) Å, b = 15.3035(9) Å, c = 7.7459(9) Å, V = 1083.2(2) $Å^3$, Z = 4, D_{calc} = 1.314 g/cm^3, μ(CuKα) = 9.00 cm^{-1}. The R (R_W) value of **5** was 0.049 (0.082). The data were collected on a Rigaku AFC7R diffractometer at 23±1 °C using graphite monochromated CuKα (λ = 1.54178 Å) radiation. The structure was solved by direct methods (SAPI91).[17] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. Neutral atom-scattering factors were taken from Cromer and Weber.[18] All calculations were performed using the teXsan[19] crystallographic software package of Molecular Structure Corporation.

Methyl (*S*)-3,4-Bis(*tert*-butyldimethylsilyloxy)butanoate (8). A mixture of **7** (1.00 g, 7.52 mmol), *tert*-butyldimethylsilyl chloride (3.40 g, 22.6 mmol), and imidazole (2.56 g, 37.6 mmol) in DMF (30 mL) was stirred at room temperature for 16 h, poured into H_2O (30 mL), and extracted with Et_2O. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 50:1) to give **8** (2.81 g, quant.) as an oil: IR (CCl_4) ν 1720 cm^{-1}; ^1H NMR (60 MHz) δ 0.02 (3H, s, SiMe), 0.06 (9H, s, 3 x SiMe), 0.85, 0.89 (both 9H, s, *tert*-Bu), 2.35-2.65 (2H, m, 2-H_2), 3.32-3.79 (2H, m, 4-H_2), 3.65 (3H, s, OMe), 3.92-4.32 (1H, m, 3-H). HRMS (FAB) Calcd for $C_{17}H_{39}O_4Si_2$ [$(M+H)^+$]: 363.2387. Found: 363.2382.

Methyl (*S*)-5,6-Bis(*tert*-butyldimethylsilyloxy)-3-oxohexanoate. A solution of DIBAL-H in hexane (0.95 mol/L, 6.38 mL, 6.06 mmol) was added to a solution of **8** (2.00 g, 5.51 mmol) in CH_2Cl_2 (50 mL) at -78 °C under a nitrogen atmosphere. After the mixture was stirred at the same temperature for 10 min, MeOH (2 mL) and sat. aq. NH_4Cl (1 mL) were added to it. The entire mixture was allowed to warm to room temperature; it was then diluted with Et_2O, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 50:1) to give (*S*)-3,4-bis(*tert*-butyldimethylsilyloxy)butanal (1.77 g, 97%), which was used directly in the next step. According to a procedure similar to that described for the preparation of methyl (*S*)-2,2-dimethyl-β-oxo-1,3-dioxolane-4-butanoate, the thus obtained aldehyde (4.40 g, 13.2 mmol) was treated

with methyl diazoacetate (1.46 g, 14.6 mmol) and $SnCl_2$ (250 mg, 1.32 mmol) to give the titled compound (5.17 g, 97%) as a 3.5:1 oily mixture of keto and enol forms: IR (CCl_4) ν 1760, 1725, 1660, 1615 cm^{-1}; ^1H NMR (300 MHz) for the keto form δ 0.035 (3H, s, SiMe), 0.043 (6H, s, 2 x SiMe), 0.07 (3H, s, SiMe), 0.85, 0.88 (both 9H, s, *tert*-Bu), 2.63 (1H, d of ABq, J = 7.2, 15.6 Hz, one of 4-H_2), 2.79 (1H, d of ABq, J = 4.7, 15.7 Hz, one of 4-H_2), 3.38 (1H, dd, J = 10.0, 7.0 Hz, one of 6-H_2), 3.49 (2H, s, 2-H_2), 3.57 (1H, dd, J = 10.0, 4.9 Hz, one of 6-H_2), 3.72 (3H, s, OMe), 4.16 (1H, tt, J = 7.1, 4.9 Hz, 5-H). HRMS (FAB) Calcd for $C_{19}H_{41}O_5Si_2$ [(M+H)$^+$]: 405.2493. Found: 405.2501.

Methyl (*S*)-5,6-Bis(*tert*-butyldimethylsilyloxy)-2-diazo-3-oxohexanoate (9a). According to a procedure similar to that described for the preparation of **4**, treatment of methyl (*S*)-5,6-bis(*tert*-butyldimethylsilyloxy)-3-oxohexanoate (445 mg, 1.10 mmol) with TsN_3 (325 mg, 1.65 mmol) and Et_3N (278 mg, 2.75 mmol) gave **9a** (427 mg, 90%) as a pale yellow oil: $[\alpha]_D^{24}$ -35.0 (*c* 0.95, $CHCl_3$); IR (CCl_4) ν 2130, 1720, 1655 cm^{-1}; ^1H NMR (300 MHz) δ 0.03, 0.045, 0.050, 0.07 (all 3H, s, SiMe), 0.84, 0.88 (both 9H, s, *tert*-Bu), 3.04 (1H, d of ABq, J = 5.0, 15.6 Hz, one of 4-H_2), 3.11 (1H, d of ABq, J = 7.3, 15.5 Hz, one of 4-H_2), 3.45 (1H, dd, J = 10.0, 6.8 Hz, one of 6-H_2), 3.59 (1H, dd, J = 9.9, 5.3 Hz, one of 6-H_2), 3.83 (3H, s, OMe), 4.25 (1H, tt, J = 7.0, 5.2 Hz, 5-H). HRMS (FAB) Calcd for $C_{19}H_{39}N_2O_5Si_2$ [(M+H)$^+$]: 431.2397. Found: 431.2402.

(*S*)-4,5-Bis(*tert*-butyldimethylsilyloxy)-1-diazopentan-2-one (9b). A mixture of **8** (100 mg, 0.28 mmol) and LiOH·H_2O (12 mg, 0.28 mmol) in MeOH (1 mL) and H_2O (0.6 mL) was stirred at 45 °C for 23 h. The mixture was cooled to 0 °C, then acidified with 10% HCl, and extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated to give crude (*S*)-3,4-bis(*tert*-butyldimethylsilyloxy)-butanoic acid (44 mg, 49%). Pyridine (23 mg, 0.29 mmol) and oxalyl chloride (109 mg, 0.86 mmol) were added to a solution of the carboxylic acid (100 mg, 0.29 mmol) in benzene (3 mL) at 0 °C. The mixture was stirred at room temperature for 38 h, and the precipitate was filtered off. The filtrate was concentrated to afford crude acid chloride (89 mg). The acid chloride in Et_2O (2 mL) was treated with a solution of a large excess of diazomethane in Et_2O at 0 °C. After the mixture was stirred for 30 min, excess diazomethane was decomposed by the addition of acetic acid. The resulting mixture was diluted with Et_2O and washed with sat. aq. $NaHCO_3$ and H_2O, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 10:1) to give **9b** [70 mg, 66% from (*S*)-3,4-bis(*tert*-butyldimethylsilyloxy)butanoic acid] as a yellow oil: $[\alpha]_D^{21}$ -53.9 (*c* 0.49, $CHCl_3$); IR (CCl_4) ν 2110, 1650 cm^{-1}; ^1H NMR (300 MHz) δ 0.05 (9H, br s, 3 x SiMe), 0.07 (3H, s, SiMe), 0.87, 0.89 (both 9H, s, *tert*-Bu), 2.27-2.45 (1H, m, one of 3-H_2), 2.59 (1H, dd, J = 13.9, 4.1 Hz, one of 3-H_2), 3.42 (1H, dd, J = 10.1, 6.6 Hz, one of 5-H_2), 3.58 (1H, dd, J = 10.0, 5.1 Hz, one of 5-H_2), 4.10-4.21 (1H, m, 4-H), 5.30 (1H, br s, 1-H). HRMS (FAB) Calcd for $C_{17}H_{37}N_2O_3Si_2$ [(M+H)$^+$]: 373.2343. Found: 373.2346.

Dirhodium(II)-Catalyzed Reaction of 9a. Following the general procedure, **9a** (500 mg, 1.16 mmol) was treated with $Rh_2(OAc)_4$ (5 mg, 0.012 mmol), and the crude material was chromatographed on silica gel (hexane/EtOAc, 7:1) to give labile methyl (*S*)-3-(*tert*-butyldimethylsilyloxy)-5-oxo-1-cyclopentenecarboxylate (**11**) (212-259 mg, 68-83%) as a colorless oil: IR (CCl_4) ν 1760, 1730, 1630 cm^{-1}; ^1H NMR (300 MHz) δ 0.14, 0.15 (both 3H, s, SiMe), 0.91 (9H, s, *tert*-Bu), 2.44 (1H, dd, J = 18.3, 2.6 Hz, one of 4-H_2), 2.89 (1H, dd, J = 18.3, 6.2 Hz, one of 4-H_2), 3.85 (3H, s, OMe), 4.98 (1H, dt, J = 6.2, 2.4 Hz, 3-H), 8.05 (1H, d, J = 2.3 Hz, 2-H). HRMS (FAB) Calcd for $C_{13}H_{23}O_4Si$ [(M+H)$^+$]: 271.1365. Found: 271.1374.

Methyl (1*S*,2*S*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-2-methyl-5-oxocyclopentanecarboxylate (12) and Its (1*R*,2*R*,3*S*)-Isomer. A solution of methyllithium in Et_2O (1.14 M, 2.74 mL, 3.12 mmol) was added to a solution of copper(I) iodide (297 mg, 1.56 mmol) in Et_2O (6 mL) at -78 °C under a nitrogen atmosphere, and the mixture was stirred at the same temperature for 2 h. A solution of **11** (210 mg, 0.78 mmol)

in Et_2O (3 mL) was added to this mixture, and the whole was stirred for a further 15 min; aq. NH_4Cl was then added. The organic layer was separated, and the aqueous layer was extracted with Et_2O; 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 a mixture of **12** and its (1*R*,2*R*,3*S*)-isomer (total 158 mg, 71%) as a colorless oil. The ratio of **12** and its (1*R*,2*R*,3*S*)-isomer was estimated to be 8:1 by an integrated intensity of the peak heights of the signals due to the methine proton at the C-1 position appearing at δ 3.13 (d) and 2.82 (d), respectively. The mixture was rechromatographed on silica gel (hexane/EtOAc, 50:1) to give pure **12** as colorless needles: mp < 30 °C (hexane), whose spectroscopic data were identical with those of a racemic authentic sample,[2b] $[\alpha]_D^{20}$ +29.7 (*c* 1.80, $CHCl_3$).

Dirhodium(II)-Catalyzed Reaction/LAH Reduction of 9a. A solution of **9a** (300 mg, 0.70 mmol) in CH_2Cl_2 (2 mL) was added to a boiling solution of $Rh_2(OAc)_4$ (3 mg, 0.01 mmol) in CH_2Cl_2 (7 mL), and the mixture was refluxed for 5 min. After the mixture was cooled to room temperature, it was added to a suspension of LAH (106 mg, 2.79 mmol) in Et_2O (9 mL) at 0 °C. The reaction mixture was stirred at room temperature for 30 min, quenched with 5% HCl (1 mL), and extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The crude material was chromatographed on silica gel (hexane/EtOAc, 3:1) to give (1*R*,2*R*,3*S*,5*R*)-2,3-bis(*tert*-butyldimethylsilyloxy)-5-hydroxycyclopentanemethanol (**13**) (137 mg, 52%) as colorless needles: mp 86-88 °C (hexane); $[\alpha]_D^{24}$ +9.3 (*c* 1.18, $CHCl_3$); IR (CCl_4) ν 3700-3100 cm^{-1}; ^1H NMR (300 MHz) δ 0.068, 0.073 (both 3H, s, SiMe), 0.10 (6H, s, 2 x SiMe), 0.908, 0.910 (both 9H, s, *tert*-Bu), 1.73 (1H, dtd, *J* = 14.4, 2.2, 1.1 Hz, one of 4-H_2), 1.76-1.89 (1H, br, OH), 1.93 (1H, ddd, *J* = 14.4, 7.1, 3.9 Hz, one of 4-H_2), 2.12-2.22 (1H, m, 1-H), 2.49-2.77 (1H, br, OH), 3.63 (1H, dd, *J* = 10.5, 6.4 Hz, one of CH_2O), 3.70 (1H, dd, *J* = 8.2, 3.5 Hz, 2-H), 3.90 (1H, dd, *J* = 10.4, 4.5 Hz, one of CH_2O), 3.94-4.02 (1H, br, 5-H), 4.02 (1H, q, *J* = 3.2 Hz, 3-H). *Anal.* Calcd for $C_{18}H_{40}O_4Si_2$: C, 57.40; H, 10.70. Found: C, 56.98; H, 10.54.

(1*R*,2*R*,3*S*,5*R*)-5-Acetoxy-2,3-bis(*tert*-butyldimethylsilyloxy)cyclopentanemethyl Acetate (14). A mixture of **13** (15 mg, 0.04 mmol), pyridine (0.5 mL), and acetic anhydride (0.5 mL) was stirred at room temperature overnight. After the mixture was concentrated *in vacuo*, the residue was chromatographed on silica gel (hexane/EtOAc, 10:1) to give **14** (18 mg, quant.) as colorless needles: mp 57.5-58.5 °C (hexane); $[\alpha]_D^{22}$ +0.8 (*c* 0.84, $CHCl_3$); IR (CCl_4) ν 1745 cm^{-1}; ^1H NMR (300 MHz) δ 0.02 (3H, s, SiMe), 0.05 (6H, s, 2 x SiMe), 0.06 (3H, s, SiMe), 0.90, 0.91 (both 9H, s, *tert*-Bu), 1.71 (1H, dt, *J* = 14.7, 3.1 Hz, one of 4-H_2), 2.02, 2.05 (both 3H, s, COMe), 2.11 (1H, ddd, *J* = 14.7, 8.3, 4.3 Hz, one of 4-H_2), 2.46-2.55 (1H, m, 1-H), 3.70 (1H, dd, *J* = 8.5, 3.6 Hz, 2-H), 3.95 (1H, q, *J* = 3.7 Hz, 3-H), 4.10 (1H, d of ABq, *J* = 4.3, 11.4 Hz, one of CH_2O), 4.22 (1H, d of ABq, *J* = 3.8, 11.3 Hz, one of CH_2O), 4.88 (1H, ddd, *J* = 8.5, 5.7, 3.0 Hz, 5-H). *Anal.* Calcd for $C_{22}H_{44}O_6Si_2$: C, 57.35; H, 9.63. Found: C, 57.08; H, 9.67.

(3a*R*,4*R*,5*R*,6a*S*)-5-(Acetoxy)tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-methyl Acetate (15) A solution of TBAF in THF (1.0 M, 1.54 mL, 1.54 mmol) was added to a solution of **14** (284 mg, 0.62 mmol) in THF (5 mL) at room temperature, and the mixture was stirred for 1 h. After the mixture was diluted with H_2O and extracted with EtOAc, the extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (EtOAc) to give (1*R*,2*R*,3*S*,5*R*)-5-acetoxy-2,3-dihydroxy-cyclopentanemethyl acetate (91 mg, 63%), which was used directly in the next step. 2,2-Dimethoxypropane (2 mL) and PPTS (5 mg, 0.019 mmol) were added to a solution of thus obtained diol (90 mg, 0.39 mmol) in DMF (2 mL) at room temperature, and the mixture was stirred for 40 h. The reaction mixture was diluted with H_2O (10 mL) and extracted with Et_2O. The extract was washed with sat. aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc, 3:1) to give **15** (93 mg, 88%) as a colorless oil; $[\alpha]_D^{23}$ -9.6 (*c* 1.12, $CHCl_3$); IR (CCl_4) ν 1750 cm^{-1}; ^1H NMR (300 MHz) δ 1.31, 1.52 (both 3H, s, 2-Me), 2.04-2.14 (1H, m, one of 6-H_2), 2.06, 2.07 (both 3H, s, COMe), 2.24 (1H,

dt, J = 15.3, 6.2 Hz, one of 6-H_2), 2.51-2.59 (1H, m, 4-H), 4.07 (2H, br d, J = 6.0 Hz, CH_2O), 4.46 (1H, dd, J = 6.1, 2.6 Hz, 3a-H), 4.71 (1H, td, J = 6.1, 2.0 Hz, 6a-H), 4.97 (1H, dt, J = 6.1, 3.2 Hz, 5-H). HRMS (FAB) Calcd for $C_{13}H_{21}O_6$ [$(M+H)^+$]: 273.1338. Found: 273.1332.

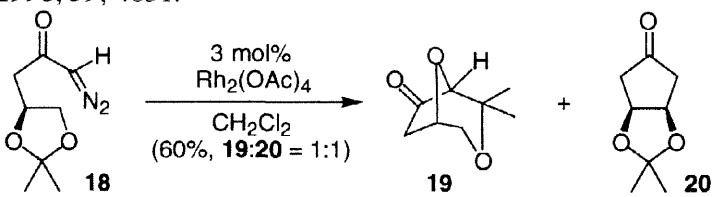
Dirhodium(II)-Catalyzed Reaction of 9b. Following the general procedure, compound **9b** (400 mg, 1.07 mmol) was treated with $Rh_2(OAc)_4$ (5 mg, 0.011 mmol), and the crude material was chromatographed on silica gel (hexane/EtOAc, 50:1). The first eluent gave (3*S*,4*S*)-3,4-bis(*tert*-butyldimethylsilyloxy)cyclopentanone (**17**) (143 mg, 39%) as colorless plates: mp 65-66 °C (hexane); $[\alpha]_D^{26}$ -48.6 (*c* 0.93, $CHCl_3$); IR (CCl_4) ν 1755 cm^{-1}; ^1H NMR (300 MHz) δ 0.07, 0.09 (both 6H, s, 2 x SiMe), 0.87 (18H, s, 2 x *tert*-Bu), 2.07 (2H, br dd, J = 16.5, 1.5 Hz, one of 2-H_2 and one of 5-H_2), 2.57 (2H, br dd, J = 16.5, 4.5 Hz, one of 2-H_2 and one of 5-H_2), 4.21 (2H, dt, J = 4.5, 1.5 Hz, 3-H and 4-H). *Anal.* Calcd for $C_{17}H_{36}O_3Si_2$: C, 59.25; H, 10.53. Found: C, 58.97; H, 10.45.

The second eluent gave *meso*-3,4-bis(*tert*-butyldimethylsilyloxy)cyclopentanone (**16**) (178 mg, 48%) as colorless needles: mp 40-41 °C (hexane); $[\alpha]_D^{25}$ 0 (*c* 1.00, $CHCl_3$); IR (CCl_4) ν 1755 cm^{-1}; ^1H NMR (300 MHz) δ 0.08, 0.09 (both 6H, s, 2 x SiMe), 0.89 (18H, s, 2 x *tert*-Bu), 2.27 (2H, br dd, J = 18.5, 5.0 Hz, one of 2-H_2 and one of 5-H_2), 2.39 (2H, dd, J = 18.4, 5.0 Hz, one of 2-H_2 and one of 5-H_2), 4.29 (2H, td, J = 5.0, 1.7 Hz, 3-H and 4-H). *Anal.* Calcd for $C_{17}H_{36}O_3Si_2$: C, 59.25; H, 10.53. Found: C, 58.90; H, 10.45.

References and Notes

1. For reviews, see: Doyle, M. P. *Acc. Chem. Res.* **1986**, *19*, 348; Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919; Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765; Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385; Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091; Padwa, A.; Austin, D. J. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1797; Doyle, M. P. *Aldrichimica Acta* **1996**, *29*, 3; Hashimoto, S.; Watanabe, N.; Anada, M.; Ikegami, S. *J. Synth. Org. Chem., Jpn.* **1996**, *54*, 988; Zaragoza, F. *Tetrahedron* **1997**, *53*, 3425; Doyle, M. P.; McKervey, M. A. *Chem. Commun.* **1997**, 983; Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911; Sulikowski, G. A.; Cha, K. L.; Sulikowski, M. M. *Tetrahedron: Asymmetry* **1998**, *9*, 3145; Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; John Willey & Sons: New York, 1998.
2. (a) Yakura, T.; Yoshida, D.; Ueki, A.; Nakao, K.; Ikeda, M. *Chem. Pharm. Bull.* **1997**, *45*, 651. (b) Yakura, T.; Yamada, S.; Kunimune, Y.; Ueki, A.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3643. (c) Yakura, T.; Yamada, S.; Azuma, M.; Ueki, A.; Ikeda, M. *Synthesis* **1998**, 973.
3. For a review, see: Martínez-Grau, A.; Marco-Contelles, J. *Chem. Soc. Rev.* **1998**, *27*, 155. For recent syntheses of aminocyclopentitols, see: Boiron, A.; Zillig, P.; Faber, D.; Giese, B. *J. Org. Chem.* **1998**, *63*, 5877; de Gracia, I. S.; Dietrich, H.; Bobo, S.; Chiara, J. L. *J. Org. Chem.* **1998**, *63*, 5883; Ling, R.; Mariano, P. S. *J. Org. Chem.* **1998**, *63*, 6072. See also references cited therein.
4. For reviews, see: Huryn, D. M.; Okabe, M. *Chem. Rev.* **1992**, *92*, 1745; Borthwick, A. D.; Biggadike, K. *Tetrahedron* **1992**, *48*, 571; Agrofoglio, L.; Suhas, E.; Farese, A.; Condom, R.; Challand, S. R.; Earl, R. A.; Guedj, R. *Tetrahedron* **1994**, *50*, 10611; Crimmins, M. T. *Tetrahedron* **1998**, *54*, 9229.
5. A part of this work has appeared as a preliminary communication: Yakura, T.; Ueki, A.; Morioka, Y.; Kurata, T.; Tanaka, K.; Ikeda, M. *Chem. Pharm. Bull.* **1998**, *46*, 1182.
6. Saito, S.; Hasegawa, T.; Inaba, M.; Nishida, R.; Fujii, T.; Nomizu, S.; Moriwake, T. *Chem. Lett.* **1984**, 1389.
7. Holmquist, C. R.; Roskamp, E. J. *J. Org. Chem.* **1989**, *54*, 3258.
8. Sugita, Y.; Sakaki, J.; Sato, M.; Kaneko, C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2855.

9. When the reaction was carried out at room temperature, yields of **5** and **11** decreased.
10. Very recently Tester and West reported a similar reaction of α-diazoketone **18** with 3 mol% of $Rh_2(OAc)_4$ in CH_2Cl_2 at room temperature gave a 1:1 mixture of 2,2-dimethyl-3,8-dioxabicyclo[3.2.1]octan-7-one (**19**) and the C-H insertion product **20** in 60% combined yield, see: Tester, R. W.; West, F. G. *Tetrahedron Lett.* **1998**, *39*, 4631.



18 **19** **20**

11. Doyle and co-workers have recently described a similar oxonium ylide formation/1,2-shift of acetonide derivatives with chiral dirhodium reagents, see: Doyle, M. P.; Ene, D. G.; Forbes, D. C.; Tedrow, J. S. *Tetrahedron Lett.* **1997**, *38*, 4367. For a review, see: Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. For the oxonium ylide formation reactions using dirhodium catalysts, see: Brogan, J. B.; Zercher, C. K. *Tetrahedron Lett.* **1998**, *39*, 1691; Brogan, J. B.; Zercher, C. K.; Bauer, C. B.; Rogers, R. D. *J. Org. Chem.* **1997**, *62*, 3902; Brogan, J. B.; Bauer, C. B.; Rogers, R. D.; Zercher, C. K. *Tetrahedron Lett.* **1996**, *37*, 5053. See also references cited therein.
12. Similar reactions of the other diazoketones such as 5,6-bis(*tert*-butyldiphenylsilyloxy)- and 6-benzyloxy-5-TBDMSoxy-2-diazo-3-oxohexanoates with $Rh_2(OAc)_4$ under the same conditions, followed by purification by silica gel column chromatography gave the corresponding cyclopentenones in lower yields (37-40%).
13. Doyle, M. P.; Westrum, L. J.; Wolthuis, W. N. E.; See, M. M.; Boone, W. P.; Bagheri, V.; Pearson, M. M. *J. Am. Chem. Soc.* **1993**, *115*, 958; Taber, D. F.; You, K. K.; Rheingold, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 547; Taber, D. F.; Song, Y. *J. Org. Chem.* **1996**, *61*, 6706.
14. Gorthey, L. A.; Vairamani, M.; Djerassi, C. *J. Org. Chem.* **1985**, *50*, 4173; Nagao,Y.; Goto, M.; Ochiai, M.; Shiro, M. *Chem. Lett.* **1990**, 1503; Nagao, Y.; Goto, M. *Heterocycles* **1995**, *41*, 883; Eliel, E. L.; Satici, H. *J. Org. Chem.* **1994**, *59*, 688.
15. Dauben, W. G.; Lewis, T. A. *Synlett* **1995**, 857.
16. The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.
17. Fan, H.-F. (1991). Structure analysis programs with intelligent control, Rigaku Corporation, Tokyo, Japan.
18. Cromer D. T.; Waber J. T. In *International Tables for X-ray Crystallography*; The Kynoch Press: Birmingham, 1974; Vol. 4, Table 2.2 A.
19. Crystal Structure Analysis Package, Molecular Structure Corporation (1985 and 1992).