A Short Synthesis of Optically Active Corey Lactone by Means of the Dirhodium(II)-Catalyzed Intramolecular C–H Insertion Reaction of an α-Diazo Ketone

Takayuki Yakura, Seiji Yamada, Miki Azuma, Akiharu Ueki, Masazumi Ikeda*

Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607, Japan
Fax +81(75)5954763

Received 4 November 1997; revised 8 January 1998

Abstract: Optically active Corey lactone **8** has been synthesized using a dirhodium(II)-catalyzed intramolecular C–H insertion reaction of chiral α-diazo-β-oxo ester **2** as a key step.

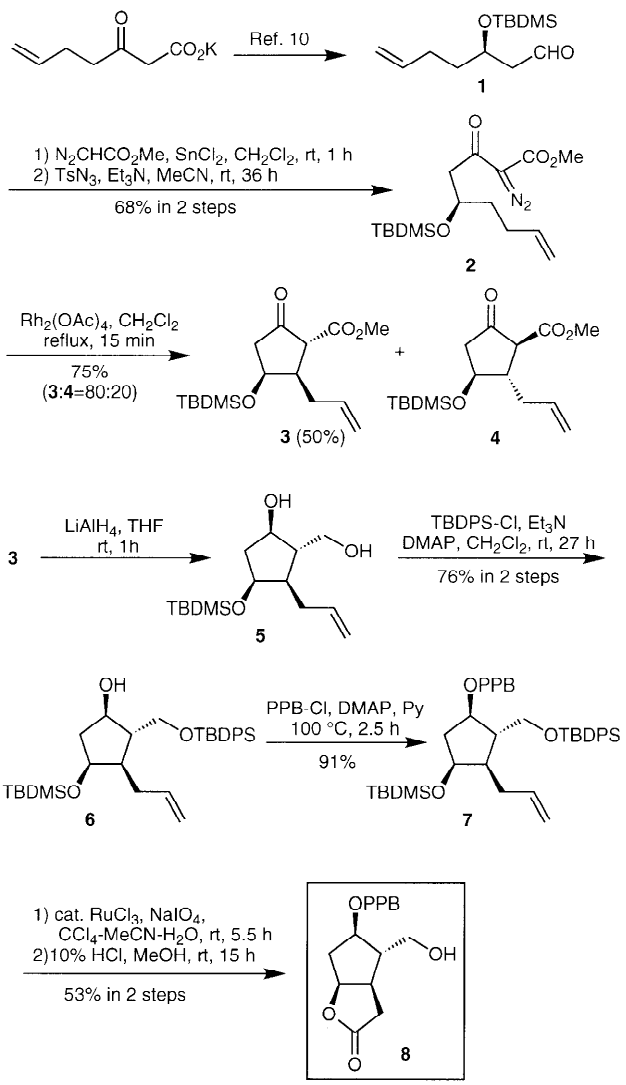
Key words: dirhodium(II)-catalyzed intramolecular C–H insertion, α-diazo ketone, 2-oxocyclopentanecarboxylate, Corey lactone, dirhodium(II) tetraacetate

Corey lactone and its derivatives are versatile intermediates for the synthesis of prostaglandins and their analogs.[1–6] Herein, we describe a short and facile synthesis of optically active Corey lactone **8** as an application of our recently developed diastereoselective dirhodium(II)-catalyzed intramolecular C–H insertion reaction of α-diazo-β-oxo esters.[7–9]

Our synthesis started from known optically active aldehyde, (–)-(*R*)-3-(*tert*-butyldimethylsilyloxy)hept-6-enal **(1)**,[10] which is readily available by enzymatic reduction of potassium 3-oxohept-6-enoate, followed by protection of the resultant secondary hydroxy group with silyl group and subsequent reduction with diisobutylaluminum hydride (DIBAL-H) in toluene. Homologation of **1** with methyl diazoacetate[11] and diazo transfer reaction produced α-diazo-β-oxo ester **2** in 68% yield. Treatment of **2** with 1 mol% of dirhodium(II) tetraacetate [$Rh_2(OAc)_4$] in dichloromethane under reflux[7] for 15 minutes afforded a 80:20 mixture of (1*R*,2*R*,3*S*)-cyclopentanecarboxylate **3** and its (1*S*,2S,3*S*)-isomer **4** in 75% yield, from which pure **3** was obtained in 50% yield after chromatographic purification.[12]

Reduction of **3** with lithium aluminum hydride in THF at room temperature proceeded in a stereoselective manner to give diol **5**, as a result of attack of hydride ion on the less hindered *Si*-face of the ketonic carbonyl group. When DIBAL-H was used as a reducing agent, the stereoselectivity was reduced to 3:1. The selective protection of the primary hydroxy group in **5** with *tert*-butyldiphenylsilyl group followed by acylation of the secondary hydroxy group of the resulting **6** with *p*-phenylbenzoyl chloride (PPB-Cl) and pyridine in the presence of 4-(dimethylamino)pyridine gave PPB-ester **7**. Oxidation–lactonization of **7** was accomplished by treatment with a catalytic amount of ruthenium(III) chloride and sodium periodate in carbon tetrachloride/acetonitrile/water (1:1:1)[13] at room temperature, followed by desilylation with 10% HCl to give Corey lactone **8** in 53% yield, whose spectroscopic data and specific rotation were identical with those of an authentic sample.[4]

In summary, we succeeded in the synthesis of Corey lactone **8** in 18% overall yield and in 6 steps from **2**.



Mps were determined using a Yanaco micro melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO IR-1 spectrophotometer for solutions in CCl_4. ^1H NMR spectra (300 MHz) were determined with a Varian XL-300 spectrometer for solutions in $CDCl_3$. δ-Values quoted are relative to TMS. Specific rotations were recorded on a JASCO DIP-360 polarimeter in $CHCl_3$. Column chromatography was performed on silica gel 60 PF_{254} (Nacalai Tesque, Inc.) under pressure.

(–)-Methyl (*R*)-5-(*tert*-Butyldimethylsilyloxy)-2-diazo-3-oxonon-8-enoate (2):

According to the procedure of Holmquist and Roskamp,[11] a solution of **1**[10] {$[\alpha]_D^{26}$ +0.85 (*c* = 1.05), lit.[10] $[\alpha]_D^{25}$ +0.84 (*c* = 1.43, $CHCl_3$), 1.38 g, 6.44 mmol} was added to a suspension of methyl diazoacetate (709 mg, 7.08 mmol) and $SnCl_2$ (121 mg, 0.64 mmol) in CH_2Cl_2 (35 mL) at r.t. The mixture was stirred for 1 h and concentrated. The

residue was chromatographed on silica gel (hexane/EtOAc 80:1) to give (–)-methyl (*R*)-5-(*tert*-butyldimethylsilyloxy)-3-oxonon-8-enoate[14] as a colorless oil; yield: 1.48 g (73%); $[\alpha]_D^{26}$ –17.9 (*c* = 1.01).
A solution of the thus obtained oxo ester (1.29 g, 4.09 mmol), Et_3N (826 mg, 8.18 mmol), and *p*-toluenesulfonyl azide (968 mg, 4.91 mmol) in MeCN (40 mL) was stirred at r.t. for 36 h and then diluted with Et_2O (50 mL). The mixture was washed with 9% aq KOH (20 mL) and brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc 50:1) to give **2**[14] as a pale yellow oil; yield: 1.29 g (93%); $[\alpha]_D^{27}$ –26.3 (*c* = 1.23).

(–)-Methyl (1*R*,2*R*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-5-oxo-2-(prop-2-enyl)cyclopentanecarboxylate (3):
A solution of **2** (848 mg, 2.49 mmol) in CH_2Cl_2 (10 mL) was added to a boiling solution of $Rh_2(OAc)_4$ (9 mg, 0.02 mmol) in CH_2Cl_2 (90 mL) and the mixture was refluxed for 15 min. After evaporation of the solvent, the crude material was chromatographed on silica gel (hexane/EtOAc 10:1) to give a 80:20 mixture of **3** and its (1*S*,2*S*,3*S*)-isomer **4** as a colorless oil; yield: 584 mg (75%). The mixture was rechromatographed on silica gel (hexane/EtOAc 80:1) to give pure **3**[14] as a colorless oil; yield: 389 mg (50%); $[\alpha]_D^{25}$ –28.3 (*c* = 0.93).

(+)-(1*R*,2*S*,3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-[(*tert*-butyldiphenylsilyloxy)methyl]-3-(prop-2-enyl)cyclopentanol (6):
A solution of **3** (377 mg, 1.21 mmol) in THF (7 mL) was added to a suspension of $LiAlH_4$ (184 mg, 4.84 mmol) in THF (18 mL) at 0 °C under N_2. After the mixture had been stirred at r.t. for 1 h, 5% aq NaOH (1 mL) was added to the mixture. The resulting mixture was dried ($MgSO_4$) and concentrated to give crude (+)-(1*S*,2*R*,3*S*,5*R*)-3-(*tert*-butyldimethylsilyloxy)-5-hydroxy-2-(prop-2-enyl)cyclopentanemethanol (**5**) (271 mg, 78%), which was used without further purification in the next step. A mixture of the crude **5** (141 mg, 0.49 mmol), TBDPS-chloride (71 mg, 0.99 mmol), Et_3N (111 mg, 1.10 mmol), and DMAP (4 mg, 0.03 mmol) in CH_2Cl_2 (10 mL) was stirred at r.t. for 27 h. The mixture was diluted with Et_2O (30 mL) and washed with sat. aq NH_4Cl (10 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc 3:1) to give **6** as a colorless oil; yield: 249 mg (76% from **3**); $[\alpha]_D^{24}$ +25.3 (*c* = 1.26).
IR: ν = 3700–3500 cm^{-1}.
^1H NMR: δ = 0.08 (s, 3H, SiMe), 0.11 (s, 3H, SiMe), 0.91 (s, 9H, *t*-Bu), 1.04 (s, 9H, *t*-Bu), 1.71–1.97 (m, 4H, 2-H, 3-H, and 5-H_2), 2.04-2.14 (m, 1H, one of CH_2CH=), 2.25–2.37 (m, 1H, one of CH_2CH=), 2.94 (d, 1H, *J* = 10.0 Hz, 1-OH), 3.53 (dd, 1H, *J* = 10.1, 5.5 Hz, one of CH_2O), 3.84 (dd, 1H, *J* = 10.1, 4.1 Hz, one of CH_2O), 4.12–4.21 (m, 1H, 1-H), 4.25–4.31 (m, 1H, 4-H), 4.87–5.04 (m, 2H, =CH_2), 5.62–5.77 (m, 1H, CH=), 7.34–7.46 (m, 6H, ArH), 7.62–7.68 (m, 4H, ArH).
Anal. Calcd for $C_{31}H_{48}O_3Si_2$: C, 70.94; H, 9.22. Found: C, 71.20; H, 9.37.

(+)-(1*R*,2*S*,3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-[(*tert*-butyldiphenylsilyloxy)methyl]-3-(prop-2-enyl)cyclopentyl 1,1'-Biphenyl-4-carboxylate (7):
A mixture of **6** (240 mg, 0.46 mmol), 4-phenylbenzoyl chloride (199 mg, 0.92 mmol), and DMAP (1 mg, 0.005 mmol) in pyridine (10 mL) was heated at 100 °C for 2.5 h. After the mixture had been cooled to r.t., MeOH (5 mL) was added. The resulting mixture was stirred for a further 10 min. The mixture was diluted with EtOAc (30 mL) and washed with 10% HCl (10 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc 50:1) to give **7** as a colorless oil; yield: 295 mg (91%); $[\alpha]_D^{25}$ +19.2 (*c* = 1.28).
IR: ν = 1710 cm^{-1}.
^1H NMR: δ = 0.02 (s, 3H, SiMe), 0.06 (s, 3H, SiMe), 0.89 (s, 9H, *t*-Bu), 1.04 (s, 9H, *t*-Bu), 1.85–2.42 (m, 6H, 2-H, 3-H, 5-H_2, and CH_2CH=), 3.69 (dd, 1H, *J* = 10.5, 4.2 Hz, one of CH_2O), 3.95 (dd, 1H, *J* = 10.5, 3.5 Hz, one of CH_2O), 4.26–4.31 (m, 1H, 4-H), 4.94–5.09 (m, 2H, =CH_2), 5.51 (ddd, 1H, *J* = 8.1, 5.4, 2.7 Hz, 1-H), 5.72–5.87 (m, 1H, CH=), 7.30–7.51 (m, 9H, ArH), 7.62–7.69 (m, 8H, ArH), 8.08–8.13 (m, 2H, ArH).
Anal. Calcd for $C_{44}H_{56}O_4Si_2$: C, 74.95; H, 8.01. Found: C, 74.98; H, 8.13.

(–)-[3a*R*-(3a*α*,4*α*,5*β*,6a*α*)]-Hexahydro-4-hydroxymethyl-2-oxo-2*H*-cyclopenta[*b*]furan-5-yl 1,1'-Biphenyl-4-carboxylate (8):
A suspension of **7** (295 mg, 0.42 mmol), $NaIO_4$ (449 mg, 2.10 mmol), and $RuCl_3 \cdot xH_2O$ (1 mg) in CCl_4/MeCN/H_2O (1:1:1, 15 mL) was stirred at r.t. for 5.5 h. The mixture was extracted with Et_2O (3 × 10 mL) and the extracts were dried ($MgSO_4$), and concentrated. The residue was dissolved in MeOH (10 mL) and 10% HCl (3 mL) was added to this mixture. The resultant mixture was stirred at r.t. for 15 h and was diluted with H_2O (20 mL) and then was extracted with EtOAc (3 × 20 mL). The extracts were washed with sat. aq $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/EtOAc 1:1) to give **8** as colorless plates; yield: 76 mg (53%); mp 130.5–132.0 °C (CH_2Cl_2/hexane); $[\alpha]_D^{26}$ –86.9 (*c* = 1.19); {lit.[4] mp 130–131 °C; $[\alpha]_D$ –87.3 (*c* = 1.0, $CHCl_3$)}.
IR: ν = 3800–3300, 1770, 1710 cm^{-1}.
^1H NMR: δ = 2.22–2.31 (m, 1H), 2.36–2.45 (m, 4H), 2.86–2.98 (m, 2H, 3-H_2), 3.62–3.79 (m, 2H, CH_2O), 5.08 (td, 1H, *J* = 6.1, 1.7 Hz, 6a-H), 5.42 (dt, 1H, *J* = 6.3, 4.3 Hz, 5-H), 7.36–7.50 (m, 3H, ArH), 7.59–7.69 (m, 4H, ArH), 8.04–8.09 (m, 2H, ArH).
Anal. Calcd for $C_{21}H_{20}O_5$: C, 71.58; H, 5.72. Found: C, 71.77; H, 5.72.

(1) Corey, E. J.; Weinshenker, N. M.; Schaaf, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675.
(2) Corey, E. J.; Schaaf, T. K.; Huber, W.; Koelliker, U.; Weinshenker, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 397.
(3) Corey, E. J.; Shirahama, H.; Yamamoto, H.; Terashima, S.; Venkateswarlu, A.; Schaaf, T. K. *J. Am. Chem. Soc.* **1971**, *93*, 1490.
(4) Corey, E. J.; Albonico, S. M.; Koelliker, U.; Schaaf, T. K.; Varma, R. K. *J. Am. Chem. Soc.* **1971**, *93*, 1491.
(5) For reviews, see: Roberts, S. M.; Scheinmann, F. *New Synthetic Routes to Prostaglandins and Thromboxanes*; Academic Press: 1982.
Collins, P. W.; Djuric, S. W. *Chem. Rev.* **1993**, *93*, 1533.
(6) A recent report on the synthesis of the optically active Corey lactone: Node, M.; Nakamura, D.; Nishide, K.; Inoue, T. *Heterocycles* **1997**, *46*, 535, and references cited therein.
(7) Yakura, T.; Yamada, S.; Kunimune, Y.; Ueki, A.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3643.
Yakura, T.; Yamada, S.; Ueki, A.; Ikeda, M. *Synlett* **1997**, 185.
(8) Taber, D. F.; Song, Y. *J. Org. Chem.* **1997**, *62*, 6603.
Taber, D. F.; You, K. K.; Rheingold, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 547, and references cited therein.
(9) For recent reviews of Rh(II)-catalyzed reactions, see: Doyle, M. P. *Aldrichimica Acta* **1996,** *29*, 3.
Hashimoto, S.; Watanabe, N.; Anada, M.; Ikegami, S. *J. Synth. Org. Chem., Jpn.* **1996**, *54*, 988.
(10) Hayakawa, K.; Nagatsugi, F.; Kanematsu, K. *J. Org. Chem.* **1988**, *53*, 860.
(11) Holmquist, C. R.; Roskamp, E. J. *J. Org. Chem.* **1989**, *54*, 3258.
(12) In practice, it is not necessary to separate the two isomers **3** and **4** at this stage. The mixture of **3** and **4** was converted into **8** in 18% overall yield from α-diazo ketone **2**. The oxidation of the (2*S*,3*S*,4*S*)-isomer of **7** derived from **4** gave the corresponding carboxylic acid which could be easily removed by washing with a weak base solution.
(13) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.
(14) The spectroscopic properties (IR and ^1H NMR) of these compounds were identical with those of the corresponding racemic samples.[7]