Facile Synthesis of 11-Membered C_2 Symmetric Chiral Binaphthyl Ketone via Co(salen)-Catalyzed Macrolactonization

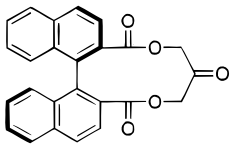
Tooru Kuroda, Ritsuo Imashiro, and Masahiko Seki*

Product & Technology Development Laboratory, Tanabe Seiyaku Co., Ltd., 3-16-89, Kashima, Yodogawa-ku, Osaka 532-8505, Japan

Received February 11, 2000

Introduction

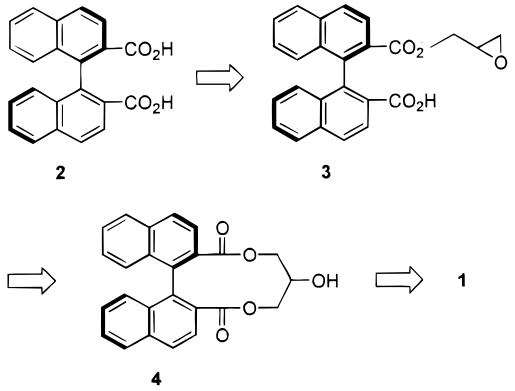
Macrocyclic lactones have received considerable attention as valuable building blocks for such compounds as drugs and natural products.[1] Development of their efficient synthetic method has thus been a subject of keen interest. Yang has developed an 11-membered C_2 symmetric chiral ketone **1**, an efficient catalyst for a dioxirane-mediated catalytic asymmetric epoxidation.[2]



1

One of the main challenges in synthesizing the chiral ketone **1** is efficiently making the 11-membered macrocyclic lactone skeleton. However, the reported procedure based on the condensation of (*R*)-1,1′-binaphthyl-2,2′-dicarboxylic acid **2** with 1, 3-dihydroxyacetone dimer requires Mukaiyama reagent and ca. 300 volume of solvent per weight of the substrate (300 v/w) to obtain only 28% yield of the cyclized product.[2a] In our previous paper[3] has been reported an intramolecular Ullmann reaction for the formation of the 11-membered ring. While the reaction provides the ring system in 67% yield, it still requires a dilution method (reaction solvent 40 v/w), and the preparation of the substrate, a diiodide, requires tedious procedures and expensive reagents.

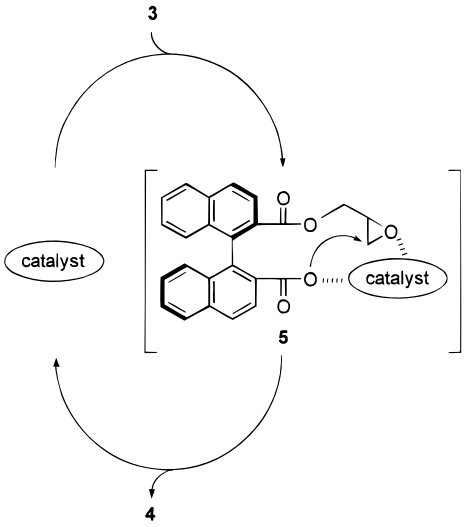
Scheme 1



2 **3** **4**

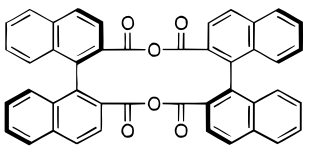
In our improved synthesis of the chiral ketone **1**, we employed a synthetic scheme outlined in Scheme 1. The most critical step in the synthesis is the use of a *catalytic process* for the formation of the 11-membered ring from (*R*)-1,1′-binaphthyl-2,2′-dicarboxylic acid monoglycidyl ester **3**. We envisaged that the macrolactonization would take place under higher concentration conditions if the cyclization could be effected only by the interaction with a catalyst, which allowed a low concentration of the reactive intermediate **5** (Scheme 2). We report herein a practical synthesis of the 11-membered chiral ketone **1** through a novel and unprecedentedly efficient Co(salen)-catalyzed macrolactonization of **3**.

Scheme 2



Results and Discussion

The monoglycidyl ester **3** was readily prepared from (*R*)-1,1′-binaphthyl-2,2′-dicarboxylic acid **2**[4] through the formation of acid anhydride(s) followed by esterification with glycidol. As shown in Table 1, the transformation was best conducted by the use of thionyl chloride ($SOCl_2$) and triethylamine (Et_3N) for the formation of the acid anhydride(s). The reaction was found to give a mixture of polymeric acid anhydrides whose major product proved to be a dimer **6** as consolidated by the X-ray crystallographic analysis.[6] Treatment of the crude mixture of the acid anhydrides with glycidol in the presence of Et_3N



6

(1) For a recent review, see: Roxburgh, C. J. *Tetrahedron* **1995**, *51*, 9767.

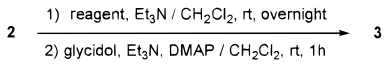
(2) (a) Yang, D.; Yip, Y.-C.; Tang, M.-W.; Wong, M.-K.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1996**, *118*, 491. (b) Yang, D.; Wang, X.-C.; Wong, M.-K.; Yip, Y.-C.; Tang, M.-W. *J. Am. Chem. Soc.* **1996**, *118*, 11311. (c) Yang, D.; Wong, M.-K.; Yip, Y.-C.; Wang, X.-C.; Tang, M.-W.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1998**, *120*, 5943.

(3) Seki, M.; Furutani, T.; Hatsuda, M.; Imashiro, R. *Tetrahedron Lett.* **2000**, *41*, 2149.

(4) The enantiopure dicarboxylic acid **2** (*R*-isomer) was prepared either by an optical resolution of the racemic dicarboxylic acid (±)-**2** using brucine[5a] or by our procedure based on an enzymatic resolution.[5b]

10.1021/jo000192g CCC: $19.00
Published on Web 06/07/2000

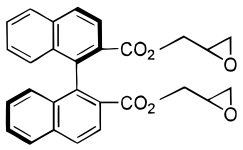
Table 1. Preparation of Monoglycidyl Ester 3 from 2[a]



		yield (%)	
entry	reagent	**3**	**7**
1	$ClP(O)(OPh)_2$	77	5
2	$POCl_3$	17	28
3	TsCl	79	8
4	$SOCl_2$	80	9

[a] The reactions were conducted using (1) **2** (1.0 mmol), reagent (1.0 mmol), Et_3N (2.2 mmol); (2) glycidol (1.3 mmol), Et_3N (1.2 mmol), DMAP (0.1 mmol).

and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) provided the desired monoglycidyl ester **3** in 80% yield along with a minor amount of a diglycidyl ester **7** (9% yield) (Table 1, entry 4).



7

The cyclization of the monoglycidyl ester **3** was first investigated by the use of quaternary ammonium hydroxide or its congeners (*n*-Bu_4NX + MOH) (Table 2). Applying the conditions for the intermolecular reaction of a glycidyl ester with a carboxylic acid[8] to the present intramolecular cyclization of **3**, the desired product **4** was obtained in 44% yield by the use of 20 v/w of solvent (Table 2, entry 2). The method is superior to the reported procedure (28% yield, reaction solvent ca. 300 v/w) to form the 11-membered ring.[2a] This result demonstrates an efficiency of the catalytic process to form the 11-membered ring of **1**.

Table 2. Macrolactonization of 3 to 4 Catalyzed by Quaternary Ammonium Hydroxide[a]

entry	catalyst	base	period (h)	yield (%)
1	*n*-Bu_4NHSO_4	NaOH	29	33
2	*n*-Bu_4NI	LiOH	7	44
3	*n*-Bu_4NOH		7	38
4	*n*-Bu_4NI	K_2CO_3	7	0

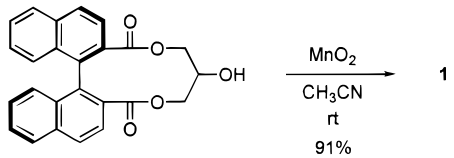
[a] The reactions were conducted in refluxing EtOH (4 mL) using **3** (0.5 mmol), catalyst (5 mol %), and base (7.5 mol %).

To further improve the yield, development of a more efficient catalyst that can properly orientate the carboxyl group in **3** toward the epoxide was needed. Jacobsen et al. reported an enantioselective ring opening of epoxides with carboxylic acids in the presence of a Co(salen) complex.[9] We envisioned a possible use of the intermolecular reaction for the present intramolecular cyclization.

Screening of the catalyst is described in Table 3. The reactions were conducted in 20 v/w of an appropriate solvent in the presence of the catalyst (5 mol %) and *N*,*N*-diisopropylethylamine (*i*-Pr_2NEt) (1.1 equiv) at ambient temperature in air atmosphere.[10] Naturally occurring Co(salen) complex, salcomine **8**, provided **4** in 43% yield (Table 3, entry 1). The use of conformationally more rigid Co(salen) complexes **9** and **10** derived from cyclic diamines gave better yields (49% and 68%, respectively) (Table 3, entries 2 and 3). The yield was remarkably elevated by employing tetrahydrofuran (THF) as the solvent in place of dichloromethane (CH_2Cl_2) (80% yield with **9** used as the catalyst) (Table 3, entry 4). Furthermore, a Co(salen) complex **11** prepared from racemic *trans*-1,2-diaminocyclohexane and 3,5-di-*tert*-butylsalicylaldehyde was found to provide **4** in 95% yield (Table 3, entry 5). The diamine ligands of the Co(salen) complexes have a crucial role for the catalytic cyclization: cobalt(II) chloride or other metal salts such as Ti(O*i*-Pr)$_4$, $FeCl_3$ and $ZnCl_2$ alone gave much poorer yields of **4** (Table 3, entries 6−9).

The 11-membered cyclic alcohol **4** thus obtained was readily oxidized with manganese(IV) oxide[3] to provide the desired chiral ketone **1** in 91% yield (Scheme 3). Com-

Scheme 3



4

parison of the product **1** with an authentic sample revealed identity with respect to IR, ^1H NMR, and mass spectra and specific rotation. The optical integrity of the product **1** obtained by this method was confirmed by chiral HPLC analysis.

In conclusion, a practical synthesis of the 11-membered chiral ketone **1** was accomplished. The chiral ketone **1** was synthesized in 69% overall yield in three steps from (*R*)-1,1′-binaphthyl-2,2′-dicarboxylic acid **2** through the Co(salen) complex **11**-catalyzed macrolactonization. The present synthesis is efficient in terms of simple operations, ready availability of the reagents, and a high yield of the cyclization step without the need for high-dilution methods. This would permit the accessibility of chiral ketone **1** by a practical large-scale preparation.

Experimental Section

General Methods. Melting points are uncorrected. ^1H NMR spectra were recorded with Me_4Si as an internal standard. Optical rotations were measured at the indicated temperature with a sodium lamp (D line, 589 nm). Silica gel column chromatography was performed using Kieselgel 60 (E. Merck). Thin-layer chromatography (TLC) was carried out on E. Merck 0.25 mm precoated glass-backed plates (60 F_{254}). Development was accomplished using 5% phosphomolybdic acid in ethanol/heat or visualized by UV light where feasible. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from P_2O_5. Other solvents and reagents were used as received. Co(salen) complexes **9**, **10**, and

(5) (a) Kanoh, S.; Hongoh, Y.; Motoi, M.; Suda, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1032. (b) Furutani, T.; Hatsuda, M.; Imashiro, R.; Seki, M. *Tetrahedron Asymmetry* **1999**, *10*, 4763.

(6) X-ray data for compound **6** have been deposited with the Cambridge Crystallographic Data Centre. Miyano et al. reported the polymeric acid anhydrides were formed in the reaction of **2** with dicyclohexylcarbodiimide.[7]

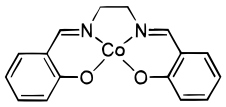
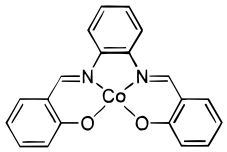
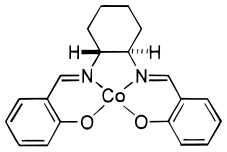
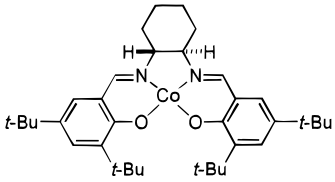
(7) Oi, S.; Matsuzaka, Y.; Yamashita, J.; Miyano, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 956.

(8) Ikeda, I.; Gu, X.-P.; Miyamoto, I.; Okahara, M. *J. Am. Oil Chem. Soc.* **1989**, *66*, 822.

(9) Jacobsen, E. N.; Kakiuchi, F.; Konsler, R. G.; Larrow, J. F.; Tokunaga, N. *Tetrahedron Lett.* **1997**, *38*, 773.

(10) The reactive species of the present macrolactonization (Co(II) complex or Co(III) complex) is not clear. The reaction rate did not change either under strictly anaerobic conditions or under an oxygen atmosphere.

Table 3. Macrolactonization of 3 to 4 Catalyzed by Co(salen)[a]

Entry	Catalyst	Solvent (20 v/w)	Period (h)	Yield (%)
1	 **8**	CH_2Cl_2	88	43
2	 **9**	CH_2Cl_2	232	49
3	 **10** (racemic)	CH_2Cl_2	183	68
4	**9**	THF	183	80
5	 **11** (racemic)	THF	142	95
6	$CoCl_2$	CH_2Cl_2	135	1
7	$Ti(Oi\text{-}Pr)_4$	CH_2Cl_2	135	8
8	$FeCl_3$	CH_2Cl_2	142	19
9	$ZnCl_2$	CH_2Cl_2	142	10

[a] The reactions were conducted in 2 mL of solvent at room temperature using **3** (0.25 mmol), *i*-Pr_2NEt (0.275 mmol), and catalyst (5 mol %).

11 were prepared from the corresponding salen ligand and Co(II) acetate tetrahydrate according to the literature.[11]

(*R*)-1,1′-Binaphthyl-2,2′-dicarboxylic Acid Monoglycidyl Ester (3). To a solution of (*R*)-1,1′-binaphthyl-2,2′-dicarboxylic acid **2** (342 mg, 1.0 mmol) and Et_3N (307 mL, 2.2 mmol) in CH_2Cl_2 (5 mL) was added $SOCl_2$ (143 mg, 1.2 mmol) in CH_2Cl_2 (1 mL) at room temperature over 1 h, and the mixture was stirred overnight. After evaporation of the solvent, the residue was azeotroped with toluene, and the solution was evaporated to dryness. To the residue were successively added CH_2Cl_2 (5 mL), Et_3N (170 mL, 1.2 mmol), glycidol (101 mg, 1.3 mmol), and DMAP (12 mg, 0.1 mmol) at room temperature. After stirring for 1 h at room temperature, the reaction mixture was quenched by addition of 10% aqueous citric acid and extracted with AcOEt. The organic layer was washed with water and brine and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by silica gel column chromatography ($CHCl_3$/AcOEt = 50:1 to 30:1) to give monoglycidyl ester **3** (319 mg, 80% yield) and diglycidyl ester **7** (43 mg, 9% yield). Data for **3**: colorless powder; ^{1}H NMR ($CDCl_3$) δ 8.19−8.11 (m, 2H), 8.03−7.92 (m, 4H), 7.56−7.48 (m, 2H), 7.32−7.19 (m, 2H), 7.02 (d, J = 8.7 Hz, 2H), 4.07−3.89 (m, 1H), 3.89−3.77 (m, 1H), 2.73−2.63 (m, 1H), 2.56−2.50 (m, 1H), 2.30−2.21 (m, 1H); IR (KBr) 3435, 3070, 3003, 1723, 1621, 1598 cm^{-1}; MS *m*/*z* 398 (M^+).

(11) (a) West, B. O. *J. Chem. Soc.* **1954**, 395. (b) Leung, W.-H.; Chan, E. E. Y.; Chow, E. K. F.; Williams, I. D.; Peng, S.-M. *J. Chem. Soc., Dalton Trans.* **1996**, 1229.

(*R*)-Diglycidyl 1,1′-binaphthyl-2,2′-dicarboxylate (7): colorless powder; ^{1}H NMR ($CDCl_3$) δ 8.22 (dd, J = 4.0, 8.7 Hz, 2H), 8.03 (d, J = 8.7 Hz, 2H), 7.96 (d, J = 8.2 Hz, 2H), 7.58−7.50 (m, 2H), 7.30−7.13 (m, 2H), 7.13−7.02 (m, 2H), 4.08−3.99 (m, 2H), 3.88−3.77 (m, 2H), 2.69−2.62 (m, 2H), 2.62−2.51 (m, 2H), 2.32−2.21 (m, 2H); MS *m*/*z* 454 (M^+).

Dimeric anhydride (6): colorless crystals; mp 227−243 °C; $[\alpha]^{22}_D$ +771 (*c* 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.95 (d, J = 8.1 Hz, 4H), 7.88 (d, J = 8.6 Hz, 4H), 7.61−7.50 (m, 8H), 7.23−7.31 (m 4H), 6.96 (d, J = 7.9 Hz, 4H); IR (KBr) 3050, 1775, 1730, 1712, 1614, 1594 cm^{-1}; SIMS *m*/*z* 648 (M^+).

(*R*)-5*H*-Dinaphtho[2,1-*g*:1′,2′-*i*][1,5]dioxacycloundecin-6-hydroxy-3,9(7*H*)-dione (4). To a stirred solution of **3** (100 mg, 0.25 mmol) in THF (2 mL) were added *i*-Pr_2NEt (35 mg, 0.275 mmol) and Co(salen) complex **11** (7.5 mg, 0.0125 mmol) at room temperature. The mixture was stirred at the same temperature for 142 h. The resulting mixture was diluted with AcOEt, washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo, and the resulting solids were purified by silica gel column chromatography (hexane/AcOEt = 2:1) to give **4** (95 mg, 95% yield) as colorless crystals: mp 256−257 °C; $[\alpha]^{25}_D$ −230 (*c* 1.01, $CHCl_3$); optical purity = 100% ee (HPLC analysis, Daicel Chiralcel OD, hexane/*i*-PrOH = 10:1, 1.0 mL/min, 18 min (*S*-enantiomer), 25 min (*R*-enantiomer)); ^{1}H NMR ($CDCl_3$) δ 8.02−7.93 (m, 4H), 7.65 (dd, J = 8.5, 11.4 Hz, 2H), 7.56−7.49 (m, 2H), 7.31 (d, J = 7.4 Hz, 2H), 7.17 (d, J = 8.6 Hz, 2H), 4.85 (dd, J = 3.2, 12.4 Hz,

1H), 4.57 (dd, J = 8.3, 10.7 Hz), 4.29 (m, 1H), 4.12 (dd, J = 6.7, 10.7 Hz, 1H), 4.03 (dd, J = 1.3, 12.4 Hz, 1H), 2.11 (d, J = 8.4 Hz, 1H); IR (KBr) 3520, 3420, 3050, 2940, 2880, 1744, 1720, 1592 cm^{-1}; MS m/z 398 (M^+). Anal. Calcd for $C_{25}H_{18}O_5$: C, 75.37; H, 4.55. Found: C, 75.37; H, 4.47.

(*R*)-5*H*-Dinaphtho[2,1-*g*:1′,2′-*i*][1,5]dioxacycloundecin-3,6,9(7*H*)-trione (1). To a suspension of **4** (200 mg, 0.5 mmol) in CH_3CN (15 mL) was added MnO_2 (1.2 g, 13.8 mmol). The mixture was stirred at room temperature for 24 h and filtered through a pad of Celite. The undissolved solid was extracted with $CHCl_3$. The extracts were combined and evaporated. The crystals formed were washed with *i*-PrOH (3 mL) to give **1** (181 mg, 91%) as colorless crystals: mp 300 °C (dec); $[\alpha]^{27}_D$ +10.9 (*c* 1.02, $CHCl_3$); optical purity = 100% ee (HPLC analysis, Daicel Chiralcel OD, hexane/*i*-PrOH = 10:1; 1.0 mL/min, 16 min (*S*-enantiomer), 26 min (*R*-enantiomer)); ^{1}H NMR ($CDCl_3$) δ 8.04 (d, J = 8.5 Hz, 2H), 7.97 (d, J = 8.2 Hz, 2H), 7.66 (d, J = 8.5 Hz, 2H), 7.56 (dd, J = 1.5, 6.6 Hz, 2H), 7.30−7.37 (m, 2H), 7.25 (d, J = 14.1 Hz, 2H), 5.56 (d, J = 15.4 Hz, 2H), 4.20 (d, J = 15.4 Hz, 2H); IR (KBr) 3550, 3430, 3050, 2970, 2925, 1755, 1730, 1593 cm^{-1}; MS m/z 396 (M^+). Anal. Calcd for $C_{25}H_{16}O_5$: C, 75.71; H, 4.07. Found: C, 75.41; H, 3.96.

Acknowledgment. We are indebted to Mr. Hajime Hiramatsu of Tanabe Seiyaku Co., Ltd., for the X-ray analysis.

JO000192G