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PREPARATION OF OPTICALLY PURE DINUCLEAR COBALT(III) COMPLEX WITH Λ-CONFIGURATION AS A DIANIONIC CHIRAL CATALYST

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This manuscript is dedicated to Professor Dr. Yasuyuki Kita on the occasion of his 77th birthday.

Abstract – The disodium salt of enantiomerically pure dimeric Λ-cobalt(III) complex **1** was prepared in one-pot from sodium triscarbonatocobaltate(III) and Schiff base ligand (R_a,*S*,*S*)-**2** formed by the condensation of (*R*)-3,3′-diformyl-2,2′-dihydroxy-1,1′-binaphthyl **3** with (*S*)-*tert*-leucine **4**. Preliminary screening of **1** as a chiral catalyst was conducted for the bromocyclization of a tryptamine derivative.

Enzymes often show high chemo-, regio-, and stereoselectivities that are difficult to achieve even with the latest organic synthetic methods.[1] In an enzyme-catalyzed process, two or more reaction-promoting units in the active site increase the reaction rate by their synergistic cooperation, leading to efficient product formation.[2] Inspired by the enzymatic activation of substrates, many researchers have attempted the development of catalysts mimicking their characteristic functionalities, toward the preparation of optically enriched chemicals.[3] Chiral hetero- and homo-bimetallic catalysts such as lanthanum-lithium-tris(binaphthoxide) (LLB),[4] aluminum-lithium-bis(binaphthoxide) (ALB),[4] and dinuclear vanadium complexes[5] are representative examples in this regard. In 1977, Belokon first introduced a series of chiral octahedral cobalt(III) complexes with a rigid framework and a unique chiral environment (Λ and Δ configurations of a metal center).[6] These anionic cobalt complexes are easily prepared through the self-assembly of sodium triscarbonatocobaltate(III) and Schiff base ligands derived

from the condensation of salicylaldehydes and chiral amino acids. However, the potential of anionic cobalt(III) complexes in asymmetric catalysis has been much less recognized because of their saturation in coordination as well as the difficulty in the highly stereocontrolled complexation of the Λ or Δ stereoisomer.[7] As part of our continuous effort to develop optically pure bimetallic complexes as chiral catalysts,[4,8] we herein report the stereoselective preparation of disodium salt of the dimeric Λ-cobalt(III) complex **1** and its application as a chiral dianionic catalyst for the enantioselective bromocyclization of a tryptamine derivative.

For designing the dinuclear cobalt(III) complex, a multidentate ligand (L) of (R_a,*S*,*S*)-**2**[9] obtained from the condensation of (*R*)-3,3′-diformyl-2,2′-dihydroxy-1,1′-binaphthyl (**3**) and (*S*)-*tert*-leucine (**4**) *in situ* was selected for the one-pot complexation with sodium triscarbonatocobaltate(III) (Figure 1). We assumed that the dinuclear cobalt(III) complex **1**, which is composed of the ligand and metal in the 2:2 ratio, would be generated to form a stable 18-electron Co complex. If the 2:1 complex **5** could work as an efficient template for the next intramolecular complexation, the sterically favored dinuclear cobalt complex $Na_2[LCo]_2$ **1** could be isolated as a single diastereomer.[10]

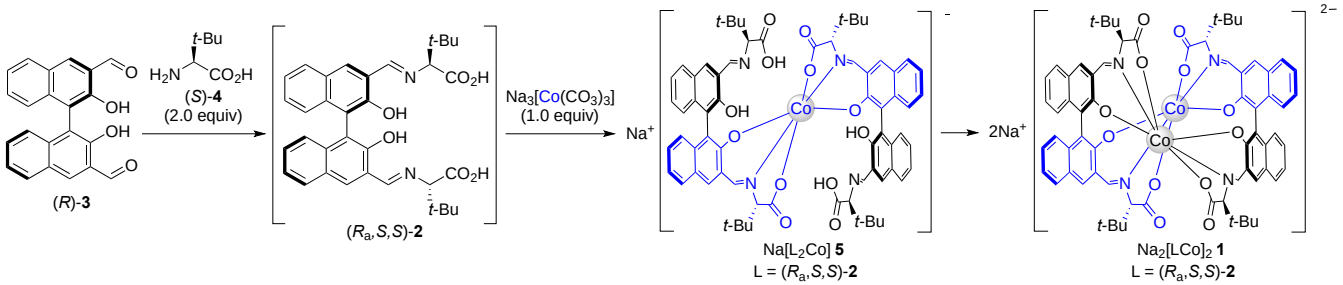


Figure 1. Expected complexation of disodium salt of the dianionic dinuclear cobalt(III) complex **1**

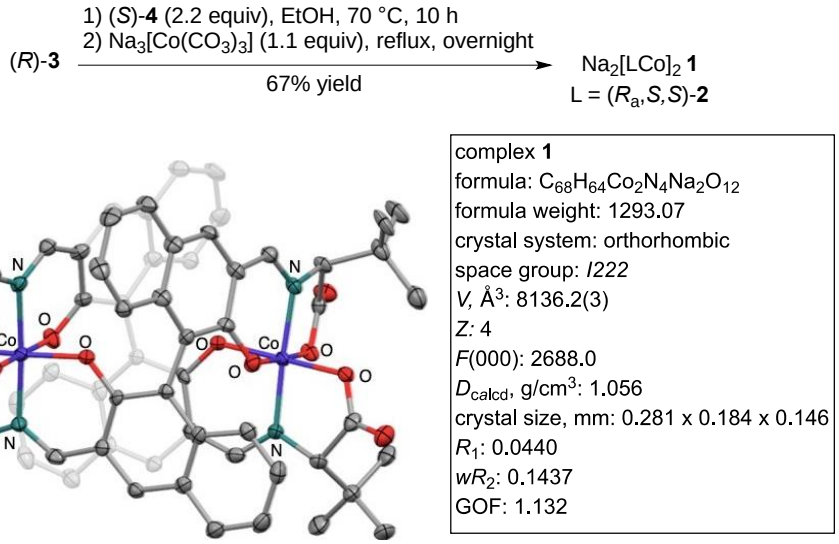
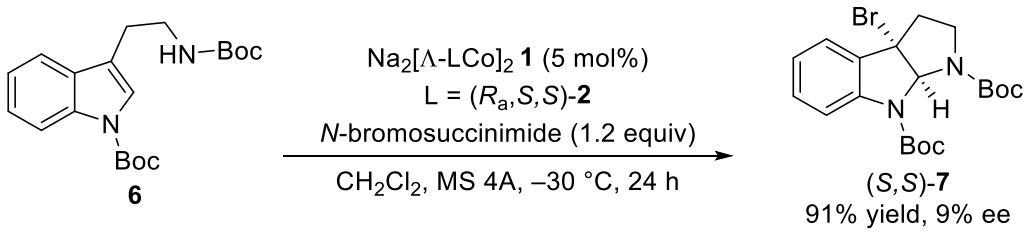


Figure 2. ORTEP drawing of the dimeric Λ-cobalt(III) complex **1** showing 50% probability thermal ellipsoids. Na^+ ions and hydrogen atoms are omitted for clarity

As expected, the dimeric complex **1** was isolated in 67% yield (Figure 2).[11] An immeasurable amount of oligomeric complexes was formed when using diastereomeric ligand (S_a,*S*,*S*)-**2**, indicating that (R_a,*S*,*S*)-**2** constitutes the matched pair and (S_a,*S*,*S*)-**2** would be the mismatched pair for this complexation. The characteristic optical rotation of optically pure **1** showed the value $[\alpha]_D^{23}$ −7274 (*c* 0.021, MeOH). The cobalt(III) centers in **1** adopt Λ- or Δ-helical mutual orientations of their tridentate ligands relative to the C_2 symmetry axis. The absolute configuration of the cobalt metal centers is determined to be Λ based on the starting materials (*R*)-**3**, (*S*)-**4**, and the Flack parameter [0.015(5)][12] obtained via the X-ray crystallographic analysis (Figure 2).[13]

Recently, chiral cobalt(III) complexes have been recognized as highly enantioselective anionic catalysts[14] for Michael reaction,[15,16] halocyclization,[7,17] Mannich reaction,[18] and Povarov reaction.[19,20] We also carried out preliminary screening for the catalytic activity of the dimeric Λ-cobalt(III) complex **1** in the enantioselective bromocyclization of tryptamine derivative **6**.[21] Although the complex **1** afforded tricyclic product (*S*,*S*)-**7** in excellent chemical yield (91%), the enantioselectivity (9% ee) is still challenging at this stage (Scheme 1).



Scheme 1. Enantioselective bromocyclization of tryptamine derivative **6** catalyzed by the chiral dinuclear cobalt(III) complex **1**

In summary, we prepared the chiral dinuclear Λ-cobalt(III) complex **1** for the first time and conducted preliminary screening of its chiral catalytic activity. Further studies aimed to improve the catalytic activity and enantioselectivity of this cobalt complex are in progress.

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REFERENCES AND NOTES

1. K. Drauz, H. Gröger, and O. May, Eds. "Enzyme Catalysis in Organic Synthesis, Third Edition" Wiley‐VCH Verlag GmbH & Co. KGaA, Weinheim, 2012.
2. (a) S. Takizawa, H. Gröger, and H. Sasai, *Chem. Eur. J.*, 2015, **21**, 8992; (b) G. A. I. Moustafa, Y. Oki, and S. Akai, *Angew. Chem. Int. Ed.*, 2018, **57**, 10278; (c) K. Sugiyama, S. Kawanishi, Y. Oki, M. Kamiya, R. Hanada, M. Egi, and S. Akai, *Bioorg. Med. Chem.*, 2018, 26, 1378; (d) S. Kawanishi, S. Oki, D. Kundu, and S. Akai, *Org. Lett.*, 2019, 21, 2978; (e) G. A. I. Moustafa, K. Kasama, K. Higashio, and S. Akai, *RSC Adv.*, 2019, 9, 1165; (f) K. Higashio, S. Katsuragi, D. Kundu, N. Adebar, C. Plass, F. Kühn, H. Gröger, and S. Akai, *Eur. J. Org. Chem.*, 2020, 1961; (g) F. Kühn, S. Katsuragi, Y. Oki, C. Scholz, S. Akai, and H. Gröger, *Chem. Comuun.*, 2020, 56, 2885; (h) K. Kasama, H. Aoyama, and S. Akai, *Eur. J. Org. Chem.*, 2020, 654.
3. R. Peters "Cooperative Catalysis: Designing Efficient Catalysts for Synthesis" Wiley‐VCH Verlag GmbH & Co. KGaA, Weinheim, 2015.
4. M. Shibasaki, H. Sasai, and T. Arai, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1236.
5. S. Takizawa, T. Katayama, and H. Sasai, *Chem. Commun.*, 2008, 4113.
6. Y. N. Belokon, V. M. Belikov, S. V. Vitt, T. F. Savel'eva, V. M. Burbelo, V. I. Bakhmutov, G. G. Aleksandrov, and Y. T. Struchkov, *Tetrahedron*, 1977, **33**, 2551.
7. H.-J. Jiang, K. Liu, J. Yu, L. Zhang, and L.-Z. Gong, *Angew. Chem. Int. Ed.*, 2017, **56**, 11931.
8. (a) S. Takizawa, *Chem. Pharm. Bull.*, 2009, **57**, 1179; (b) M. Sako, S. Takizawa, and H. Sasai, *J. Synth. Org. Chem. Jpn.*, 2018, **76**, 874; (c) M. Sako, S. Takizawa, and H. Sasai, *Tetrahedron*, 2020, **76**, 131645.
9. (a) H. Somei, Y. Asano, T. Yoshida, S. Takizawa, H. Yamataka, and H. Sasai, *Tetrahedron Lett.*, 2004, **45**, 1841; (b) S. Takizawa, D. Rajesh, T. Katayama, and H. Sasai, *Synlett*, 2009, 1667; (c) M. Sako, K. Ichinose, S. Takizawa, and H. Sasai, *Chem. Asian J.*, 2017, **12**, 1305.
10. Y. N. Belokon, D. A. Chusov, T. V. Skrupskaya, D. A. Bor'kin, L. V. Yashkina, K. A. Lyssenko, M. M. Il'in, T. V. Strelkova, G. I. Timofeeva, A. S. Peregudov, and M. North, *Russ. Chem. Bull.*, 2008, **57**, 1981.
11. In a 50 mL round-bottom flask were placed (*R*)-3,3′-diformyl-2,2′-dihydroxy-1,1′-binaphthyl (**3**) (5.0 mmol, 1.71 g) and (*S*)-*tert*-leucine (**4**) (11 mmol, 1.44 g) in EtOH (25 mL) under N_2 atmosphere. The reaction mixture was heated at 70 °C for 10 h to afford ligand (R_a,*S*,*S*)-**2** *in situ*. Then, freshly prepared $Na_3[Co(CO_3)_3]$[22] (5.5 mmol, 1.69 g) was added and the mixture was refluxed overnight.

After being cooled to room temperature, the mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography first on silica gel (MeOH/CH_2Cl_2 = 1/4), then on neutral Al_2O_3 (MeOH as eluent) to afford the disodium salt of dimeric Λ-cobalt(III) complex **1** (2.17 g) in 67% yield as a dark red crystal. ^{1}H-NMR (700 MHz, DMSO-d_6) δ 7.65 (d, J = 8.3 Hz, 4H), 7.38 (s, 4H), 7.28 (s, 4H), 6.89 (t, J = 7.0 Hz, 4H), 6.80 (t, J = 7.0 Hz, 4H), 6.58 (d, J = 8.3 Hz, 4H), 3.24 (s, 4H), 0.99 (s, 36H); ^{13}C-NMR (175 MHz, DMSO-d_6): δ 180.5, 167.5, 157.4, 138.2, 135.1, 128.5, 128.2, 125.4, 123.4, 122.3, 120.2, 119.3, 80.4, 36.2, 28.8; HRMS (ESI): calcd for $C_{68}H_{64}Co_2N_4O_{12}$ *m/z* 623.1593 $[M–2Na]^{2–}$, found 623.1560; $[\alpha]_D^{23}$ –7274 (*c* 0.021, MeOH); IR (KBr): 3434, 2956, 2873, 1643, 1616, 1481, 1398, 1350, 1178, 1080 cm^{-1}.

12. H. D. Flack, *Acta Cryst.*, 1983, **A39**, 876.
13. X-Ray crystallographic data of the dimeric Λ-cobalt(III) complex **1** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 2036038.
14. T. Cruchter and V. A. Larionov, *Coord. Chem. Rev.*, 2018, **376**, 95.
15. V. I. Maleev, M. North, V. A. Larionov, I. V. Fedyanin, T. F. Savel'yeva, M. A. Moscalenko A. F. Smolyakov, and Y. N. Belokon, *Adv. Synth. Catal.*, 2014, **356**, 1803.
16. C. Q. Kabes, W. J. Maximuck, S. K. Ghosh, A. Kumar, N. Bhuvanesh, and J. A. Gladysz, *ACS Catal.*, 2020, **10**, 3249.
17. K. Liu, H.-J. Jiang, N. Li, H. Li, J. Wang, Z.-Z. Zhang, and J. Yu, *J. Org. Chem.*, 2018, **83**, 6815.
18. H. Joshi, S. K. Ghosh, and J. A. Gladysz, *Synthesis*, 2017, **49**, 3905.
19. J. Yu, H.-J. Jiang Y. Zhou, S.-W. Luo, and L.-Z. Gong, *Angew. Chem. Int. Ed.*, 2015, **54**, 11209.
20. H.-J. Jiang, K. Liu, J. Wang, N. Lia, and J. Yu, *Org. Biomol. Chem.*, 2017, **15**, 9077.
21. A 10 mL oven-dried vial was charged with tryptamine derivative **6** (0.10 mmol, 36.0 mg), the dimeric Λ-cobalt(III) complex **1** (0.0050 mmol, 6.47 mg), activated molecular sieves 4A (microwave 600 w, 1 min x 3, 100 mg) and dry CH_2Cl_2 (1 mL) at room temperature in the absence of light. The mixture was cooled to –30 °C and stirred for 15 min. *N*-Bromosuccinimide (0.12 mmol, 21.4 mg) was added portionwise and the resulting solution was stirred vigorously under air for 24 h. The reaction was then quenched with NEt_3 (1.0 mmol, 140 μL) and saturated aqueous $Na_2S_2O_3$ (0.2 mL). The mixture was purified by flash column chromatography (silica gel, *n*-hexane/EtOAc = 6:1) to give the tricyclic product **7** (40.0 mg) in 91% yield. The ^{1}H-NMR and ^{13}C-NMR spectra of compound **7** were perfectly matched with the reported spectra.[17,23] ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.56 (brs, 1H), 7.34 (dd, J = 7.6, 1.4 Hz, 1H), 7.27 (td, J = 7.6, 1.4 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.41 (s, 1H), 3.71 (dd, J = 10.3, 7.6 Hz, 1H), 2.81-2.67 (m, 3H), 1.56 (s, 9H), 1.46 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 153.5, 152.2, 142.1, 132.8, 130.3, 124.1, 123.8, 117.4, 83.9, 82.1, 80.8, 62.2,

46.2, 41.6, 28.3, 28.2; Enantiomeric excess 9% determined by HPLC (Daicel Chiralpak IC, *n*-hexane/*i*-PrOH = 50:1, flow rate 1.0 mL/min, 315 nm, $t_{(R,R)\text{-}7}$ = 4.17 min, $t_{(S,S)\text{-}7}$ = 5.68 min).

22. Y. N. Belokon, V. I. Maleev, D. A. Kataev, T. F. Saveleva, T. V. Skrupskaya, Y. V. Nelyubina, and M. North, *Tetrahedron: Asymmetry*, 2009, **20**, 1746.
23. W. Xie, G. Jiang, H. Liu, J. Hu, X. Pan, H. Zhang, X. Wan, Y. Lai, and D. Ma, *Angew. Chem. Int. Ed.*, 2013, **52**, 12924.