Supporting Information

Enantioselective Michael Reaction Catalyzed by Well-Defined Chiral Ru Amido Complexes: Isolation and characterization of the catalyst intermediate, Ru malonato complex having a metal–C bond

Masahito Watanabe, Kunihiko Murata, and Takao Ikariya*

Department of Applied Chemistry, Graduate School of Science and Engineering, Tokyo

Institute of Technology and Frontier Collaborative Research Center

Ookayama, Meguro-ku, Tokyo 152-8552 Japan

CONTENTS

1) Experimental procedure for Michael reaction of 2-cyclopenten-1-one with dimethyl malonate catalyzed by Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (1f)

S3

2) Experimental procedure for Michael reaction of 2-cyclohexen-1-one with dimethyl malonate catalyzed by Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (1f)

S3

3) Experimental procedure for Michael reaction of 2-cyclohepten-1-one with dimethyl malonate catalyzed by Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (1f)

S4

4) Spectral data and analytical conditions for Michael adducts

S5

5) Preparation of Ru malonato complex Ru[CH(COOCH₃)₂][(1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine](mesitylene) (4)

S7

Oretep view of Ru[CH(COOCH₃)₂][(1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine](mesitylene) (4)

S9

1) Experimental procedure for Michael reaction of 2-cyclopenten-1-one with dimethyl malonate catalyzed by Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (1f**)**

Dimethyl malonate (228 mL, 2.0 mmol), 2-cyclopenten-1-one (168 mL, 2.0 mmol) and *t*-butyl alcohol (1.0 mL) were added to Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (**1f**) (11.0 mg, 0.02 μ mol) and the mixture was degassed by freeze-thaw cycles. The mixture was stirred at 30 °C for 72 h, then was evaporated with a vacuum pump and purified with column chromatography (silica gel, eluent: *n*-Hexane:acetone = 9:1) to give (*S*)-3-di(methoxycarbonyl)methyl-1-cyclopentanone with 98% ee in 99% isolated yield. The reaction under otherwise identical conditions except for 60 °C gave (*S*)-3-di(methoxycarbonyl)methyl-1-cyclopentanone with 97% ee in 99% isolated yield for 24 h.

¹H NMR (300 MHz, CDCl₃, ppm): δ 1.60–1.75 (m, 1H, cyclopentanone ring proton), 2.01 (ddd, *J* = 1.2, 11.2, 18.3 Hz, 1H, cyclopentanone ring proton), 2.12–2.44 (m, 3H, cyclopentanone ring protons), 2.52 (dd, *J* = 7.8, 18.6 Hz, 1H, cyclopentanone ring proton), 2.78–2.97 (m, 1H, cyclopentanone ring proton), 3.39 (d, *J* = 9.3 Hz, 1H, CH(COOCH₃)₂), 3.75, 3.78 (s, 3H x 2, CH₃ x 2).

HPLC separation conditions: column CHIRALPAK AS (4.6 mm i.d. x 250 mm); eluent Hexane/2-propanol = 80/20; flow rate 1.0 ml/min; temp 30 °C; detection UV 210 nm; retention time: (*R*), 25.1 min, (*S*), 33.0 min.

$[\alpha]_D^{21}$ –96.3 (*c* 0.54 CHCl₃) (lit. $[\alpha]_D^{23.6}$ +98.8 (*c* 0.54 CHCl₃), >99% ee (*R*), Kim, S. Y.; Matsunaga, S.; Das, J.; Sekine, A.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 6506–6507).

2) Experimental procedure for Michael reaction of 2-cyclohexen-1-one with dimethyl malonate catalyzed by Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (1f**)**

Dimethyl malonate (114 mL, 1.0 mmol), 2-cyclohexen-1-one (97 mL, 1.0 mmol) and *t*-butyl alcohol (1.0 mL) were added to Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (**1f**) (11.0 mg, 0.02 μ mol). The

reaction mixture was degassed by freeze-thaw cycles and was stirred at 30 °C for 48 h. The mixture was evaporated with a vacuum pump and purified with column chromatography (silica gel, eluent: *n*-Hexane:acetone = 9:1) to give (*S*)-3-di(methoxycarbonyl)methyl-1-cyclohexanone with 98% ee in 99% isolated yield.

¹H NMR (300 MHz, CDCl₃, ppm): δ 1.40–1.60 (m, 1H, cyclohexanone ring proton), 1.60–1.80 (m, 1H, cyclohexanone ring proton), 1.89–2.01(m, 1H, cyclohexanone ring proton), 2.02–2.15 (m, 1H, cyclohexanone ring proton), 2.19–2.35 (m, 2H, cyclohexanone ring protons), 2.35–2.65 (m, 3H, cyclohexanone ring protons), 3.35 (d, *J* = 7.8 Hz, 1H, CH(COOCH₃)₂), 3.75, 3.76 (s, 3H x 2, CH₃ x 2). HPLC separation conditions: column: CHIRALPAK AS (4.6 mm i.d. x 250 mm), eluent Hexane/2-propanol = 85/15; flow rate 0.5 ml/min; temp 30 °C, detection UV 210 nm; retention time, (*R*), 32.9 min, (*S*), 48.8 min.

$[\alpha]_D^{23}$ –3.45 (*c* 2.44 CHCl₃) (lit. $[\alpha]_D^{24}$ +3.99 (*c* 2.10 CHCl₃), >99% ee (*R*), Kim, S. Y.; Matsunaga, S.; Das, J.; Sekine, A.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, 122, 6506–6507).

3) Experimental procedure for Michael reaction of 2-cyclohepten-1-one with dimethyl malonate catalyzed by Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (**1f**)

Dimethyl malonate (114 mL, 1.0 mmol), 2-cyclohepten-1-one (114 mL, 1.0 mmol) and *t*-butyl alcohol (1.0 mL) were added to Ru[(1*R*,2*R*)-*N*-methanesulfonyl-1,2-diphenylethylenediamine](hexamethylbenzene) (**1f**) (11.0 mg, 0.02 mmol) and the mixture was degassed by freeze-thaw cycles. The mixture was stirred at 30 °C for 72 h, then was evaporated with a vacuum pump and purified with column chromatography (silica gel, eluent: *n*-Hexane:acetone = 9:1) to give (*S*)-3-di(methoxycarbonyl)methyl-1-cycloheptanone with >99% ee in 75% isolated yield.

¹H NMR (300 MHz, CDCl₃, ppm): δ 1.30–1.65 (m, 3H, cycloheptanone ring protons), 1.80–2.05 (m, 3H, cycloheptanone ring protons), 2.40–2.65 (m, 5H, cycloheptanone ring protons), 3.36 (d, *J* = 7.1 Hz, 1H, CH(COOCH₃)₂), 3.75, 3.76 (s,

3H x 2, CH₃ x 2).

The enantiomeric excess was determined by the relative intensities of diastereomeric ketals obtained by the reaction of 3-di(methoxycarbonyl)methyl-1-cycloheptanone with (2*R*,3*R*)-butanediol in the presence of *p*-TsOH in toluene.

Ketal of (*R*)-di(methoxycarbonyl)methyl-1-cycloheptane with (2*R*,3*R*)-butanediol, ¹³C NMR (75 MHz, CDCl₃, ppm): δ 16.4, 16.5, 22.3, 28.3, 33.6, 34.2, 40.3, 43.2, 52.2, 58.1, 110.7, 169.0, 169.2.

Ketal of (*S*)-3-di(methoxycarbonyl)methyl-1-cycloheptane with (2*R*,3*R*)-butanediol, ¹³C NMR (75 MHz, CDCl₃, ppm): δ 16.6, 16.8, 22.2, 26.6, 32.2, 33.5, 40.4, 42.7, 52.2, 57.6, 110.2, 169.0, 169.3.

[α]_D²⁷ −45.2 (*c* 1.76 CHCl₃) (lit. [α]_D^{21.2} +49.7 (*c* 1.76 CHCl₃), >99% ee (*R*), Kim, S. Y.; Matsunaga, S.; Das, J.; Sekine, A.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 6506–6507).

4) Spectral data and analytical conditions of Michael adducts

(*S*)-3-di(ethoxycarbonyl)methyl-1-cyclopentanone, 96% ee

¹H NMR (300 MHz, CDCl₃, ppm): δ 1.27, 1.29 (q, *J* = 7.2 Hz, 3H x 2, CH₃CH₂COO), 1.57–1.78 (m, 1H, cyclopentanone ring proton), 2.03 (ddd, *J* = 1.2, 11.2, 18.3 Hz, 1H, cyclopentanone ring proton), 2.10–2.45 (m, 3H, cyclopentanone ring protons), 2.52 (dd, *J* = 7.6, 18.3 Hz, 1H, cyclopentanone ring proton), 2.75–2.98 (m, 1H, cyclopentanone ring proton), 3.34 (d, *J* = 9.3 Hz, 1H, CH(COOC₂H₅)₂), 4.21, 4.23 (q, *J* = 7.2 Hz, 2H x 2, CH₃CH₂OCO x 2)..

The enantiomeric excess was determined by a HPLC analysis after derived to ethylene ketal by the reaction with 2-ethyl-2-methyl-1,3-dioxolane in the presence of *p*-TsOH. HPLC separation conditions: column CHIRALCEL OD (4.6 mm i.d. x 250 mm); eluent Hexane/2-propanol = 97/3; flow rate 0.5 ml/min; temp 30 °C; detection UV 210 nm; retention time: (*R*), 17.9 min, (*S*), 19.5 min.

[α]_D²⁵ −79.3 (*c* 1.06 CHCl₃) (lit. [α]_D²⁴ −82.7 (*c* 1.00 CHCl₃), 98% ee (*S*), Nara, S.; Toshima, H.; Ichihara, A. *Tetrahedron* **1997**, *53*, 9509–9524).

Optically active 3-[1,1-di(methoxycarbonyl)ethane-1-yl]-1-cyclopentanone, 97% ee

^1H NMR (300 MHz, CDCl_3 , ppm): δ 1.46 (s, 3H, $\text{CH}_3\text{C}(\text{COOCH}_3)_2$), 1.63–1.85 (m, 1H, cyclopentanone ring proton), 2.03–2.30 (m, 3H, cyclopentanone ring protons), 2.30–2.520 (m, 2H, cyclopentanone ring protons), 2.76–2.95 (m, 1H, cyclopentanone ring proton), 3.74, 3.75 (s, 3H x 2, CH_3 x 2).

^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 17.9, 24.6, 38.4, 40.7, 41.6, 52.6, 55.5, 171.6, 171.7, 217.4.

The enantiomeric excess was determined by a HPLC analysis. HPLC separation conditions: column CHIRALPAK AS (4.6 mm i.d. x 250 mm); eluent Hexane/2-propanol = 80/20; flow rate 1.5 ml/min; temp 30 °C; detection UV 210 nm; retention time of two enantiomers: 18.9 min (minor) , 36.6 min (major).

$[\alpha]_{\text{D}}^{25} -87.2$ (c 1.00 CHCl_3).

MS (CI, 70 eV) 229 (M+1).

Optically active 3,3-dimethyl-4-di(methoxycarbonyl)methyl-1-cyclopentanone, >99% ee

^1H NMR (300 MHz, CDCl_3 , ppm): δ 1.01, 1.11 (s, 3H x 2, CH_3 x 2), 2.06–2.28 (m, 3H, cyclopentanone ring protons), 2.57 (dd, $J = 8.3, 19.1$ Hz, 1H, cyclopentanone ring proton), 2.75–2.92 (m, 1H, cyclopentanone ring proton), 3.51(d, $J = 9.5$ Hz, 1H, $\text{CH}(\text{COOCH}_3)_2$), 3.73, 3.77 (s, 3H x 2, CH_3 x 2).

^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 21.6, 27.6, 38.7, 41.3, 45.3, 52.3, 52.7, 52.8, 55.3, 168.7, 169.0, 215.5.

The enantiomeric excess was determined by a HPLC analysis after transformation to ethylene ketal by reaction with 2-ethyl-2-methyl-1,3-dioxolane in the presence of *p*-TsOH.

HPLC separation conditions: column CHIRALCEL OD (4.6 mm i.d. x 250 mm); eluent Hexane/2-propanol = 97/3; flow rate 0.5 ml/min; temp 30 °C; detection UV 210 nm; retention time of two enantiomers: 17.6 min (minor), 19.7 min (major).

$[\alpha]_{\text{D}}^{25} -101.6$ (c 1.04 CHCl_3).

MS (EI, 70 eV) 242 (M^+), 227, 182, 153, 132, 111, 95, 83, 59.

Optically active 3-[(acetyl)(methoxycarbonyl)methyl]-1-cyclopentanone, 91% ee

with a single stereogenic center at cyclopentane ring

Obtained as a 1:1 mixture of two diastereomers with a single stereogenic center at the cyclopentanone ring.

^1H NMR (300 MHz, CDCl_3 , ppm): δ 1.45–1.70 (m, 2H, cyclopentanone ring protons), 1.83 (dd, $J = 11.0, 18.3$ Hz, 1H, cyclopentanone ring proton), 1.95 (dd, $J = 11.0, 18.3$ Hz, 1H, cyclopentanone ring proton), 2.10–2.40 (m, 6H, cyclopentanone ring protons), 2.25 (s, 3H, CH_3CO), 2.28 (s, 3H, CH_3OCO), 2.88 (m, 2H, cyclopentanone ring protons), 3.44 (d, $J = 5.1$ Hz, 1H, $\text{CH}(\text{COCH}_3)$), 3.47 (d, $J = 4.9$ Hz, 1H, $\text{CH}(\text{COCH}_3)$), 3.75 (s, 3H, CH_3OCO), 3.78 (s, 3H, CH_3OCO).

^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 27.4, 27.5, 29.3, 29.5, 35.8, 35.9, 38.0, 38.1, 42.7, 42.9, 52.6, 64.3, 64.5, 168.8, 168.9, 201.3, 201.5, 216.8, 216.9.

HPLC separation conditions: column CHIRALPAK AS (4.6 mm i.d. x 250 mm); eluent Hexane/2-propanol = 80/20; flow rate 1.0 ml/min; temp 30 °C; detection UV 210 nm; retention time of four stereoisomers: 22.8 min (major), 29.4 min (minor), 35.8 min (major), 41.8 min (minor).

$[\alpha]_{\text{D}}^{25} -83.5$ (c 1.35 CHCl_3).

MS (EI, 70 eV) 198 (M^+), 183, 155, 141, 116, 101, 96, 83.

Stereochemistry of the stereogenic center of cyclopentanone ring was determined by converting to a known diketone, (*R*)-3-(2-oxyopropyl)cyclopentanone.

$[\alpha]_{\text{D}}^{29} -79.1$ (c 0.5 benzene). (lit. $[\alpha]_{\text{D}} -70.6$ benzene, 92% ee (*R*)), Yamamoto, K.; Kanoh, M.; Yamamoto, N.; Tsuji, J. *Tetrahedron Lett.*, **1987**, 28, 6347–6350).

5) Preparation of Ru malonato complex $\text{Ru}[\text{CH}(\text{COOCH}_3)_2][(\text{1R,2R})\text{-N-(p-toluenesulfonyl)-1,2-diphenylethylenediamine}](\text{mesitylene})$

Dimethyl malonate (0.78 mL, 0.68 mmol) and acetone (4 mL) were added to $\text{Ru}[(\text{1R,2R})\text{-Tsdpen}](\text{mesitylene})$ (50 mg, 0.085 mmol) and the reaction mixture was then stirred at room temperature for 10 min. The dark orange solution was concentrated under reduced pressure to ca 1 mL giving a yellow crystalline compound. The crystalline solid was dried under reduced pressure to give 43 mg, $\text{Ru}[\text{CH}(\text{COOCH}_3)_2][(\text{1R,2R})\text{-N-(p-toluenesulfonyl)-1,2-}$

diphenylethylenediamine](mesitylene). Isolated yield, 70 %. Single crystals suitable for X-ray structural analysis was obtained by recrystallization from acetone.

^1H NMR (300 MHz, CD_2Cl_2 at -30° , ppm): δ 2.06 (s, 9H, $\text{CH}_3 \times 9$), 2.20 (s, 3H, CH_3 of Ts), 3.55–3.80 (m, 7H, $\text{CH}(\text{COOCH}_3)_2 + \text{NHH}$), 3.88 (t, $J = 11.5$ Hz, 1H, $\text{CH}-\text{NH}_2$), 4.09 (s, 1H, $\text{CH}(\text{COOCH}_3)_2$), 4.27 (d, $J = 11.5$ Hz, 1H, $\text{CH}-\text{NTs}$), 5.06 (s, 3H, mesitylene ring protons), 6.65–7.35 (m, 15H, aromatic ring protons of phenyl and Ts group + NHH).

Elemental analysis: calcd. for $\text{C}_{35}\text{H}_{40}\text{N}_2\text{O}_6\text{SRu}$: C 58.56, H 5.62, N 3.90; found: C 58.78, H 5.53, N 3.81.

Figure ORTEP view of $\text{Ru}[\text{CH}(\text{CO}_2\text{CH}_3)_2][1R,2R]\text{-}N\text{-(}p\text{-toluenesulfonyl)-1,2-diphenylethanediamine(mesitylene) (4)}$

All hydrogen atoms except for NH_2 , have been omitted for clarity. Selected bond lengths ($\text{\AA}$): Ru1-C31 , 2.22(10); Ru1-N1 , 2.13(8); Ru1-N2 , 2.18(6); C31-C32 , 1.48(13); C31-C34 , 1.49(13). Selected bond angles (deg): C31-Ru1-N1 , 85.5(3); C31-Ru1-N2 , 94.2(3); N1-Ru1-N2 , 76.8(3); Ru1-C31-C34 , 105.2(6); Ru1-C31-C32 , 118.6(7); C32-C31-C34 , 109.4(8). Priority for the assignment of absolute configuration at Ru; Mesitylene>NTs> NH_2 >CH.