Ti(IV)-Catalysed Enantioselective Sulfenylation of β -Ketoesters

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Supporting Information

General

Reactions with air- or moisture-sensitive materials were carried out under an argon atmosphere using Schlenk techniques. All solvents were distilled prior to use. Complex $[\text{TiCl}_2((R,R)\text{-1-Np-TADDOLato})(\text{MeCN})_2]$ (**1**, bis(acetonitrile)dichloro [(4*R*,5*R*)-2,2-dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetra(naphthalene-1-yl)-1,3-dioxolane-4,5-dimethanolato(2-)- $\kappa\text{O},\kappa\text{O}'$]titanium)¹ and phenylsulphenyl chloride² were prepared following published procedures. ¹H and ¹³C NMR spectra were recorded on Bruker AVANCE spectrometers AC 200, DPX 250, and DPX 300. ¹H and ¹³C spectra were recorded in CDCl₃, chemical shifts are reported in ppm relative to the residual chloroform peak (7.26 ppm) for ¹H NMR and to the central line of CDCl₃ (77.0 ppm) for ¹³C NMR. IR spectra were recorded on a Perkin Elmer FT-IR Paragon 1000. Optical rotations were measured by using a Perkin Elmer 341 polarimeter with a 1-dm cell. Column chromatography was carried using Fluka silica gel 60 (230-400 mesh). Elemental analyses were carried out by the Laboratory of Microelemental Analysis (Eidgenössische Technische Hochschule, Zürich). HRMS measurements were performed by the MS-service of the Laboratorium für Organische Chemie der ETHZ. Enantiomeric excesses were determined by HPLC with Agilent (Palo Alto, CA) HPLC 1100 or HPLC 1050 Series systems (retention time of major enantiomer in italics).

General Procedure for the Enantioselective Catalytic Sulfenylation of β -Ketoesters

2a-2f:

β -Ketoester **2a** (29 mg, 0.2 mmol) and catalyst **1** (1.9 mg, 0.0024 mmol to 7.6 mg, 0.01 mmol) were placed in a heat-gun dried Schlenk tube containing 2 ml of freshly distilled toluene. After 10 minutes of stirring, 0.25 ml (0.25 mmol) of phenylsulfenyl chloride solution in toluene was added via syringe. After stirring for 12-14 h at room temperature, the reaction mixture was diluted with dichloromethane and filtered over a pad of alumina. The solvent was evaporated and the product was purified by column chromatography (SiO₂, hexane/Bu'OMe mixtures).

Representative spectroscopic data of new products:

2-Methyl-3-oxo-2-phenylsulfanyl-butyric acid-*tert*-butyl ester (**3b**)

¹H NMR (300 MHz): δ 1.45 (s, 3H), 1.49 (s, 9H), 2.38 (s, 3H), 7.27-7.44 (m, 5H); ¹³C NMR (75.5 MHz): δ 20.6, 25.9, 27.7, 66.4, 83.5, 128.9, 129.6, 129.7, 136.8, 168.8, 199.3; IR: 1712, 1370, 1256, 1162, 1124, 850, 750, 693 cm⁻¹; Elemental analysis calc. for C₁₅H₂₀SO₃: C 64.26, H 7.19, found C 64.24, H 7.32; [α]_D = -50.8 @ 88% ee (c = 0.535 CH₂Cl₂); HPLC conditions: *Daicel Chiracel* ODH column (250 x 4.6 mm); hexane/*i*-PrOH (99/1); 0.5 ml/min; detector 210.8 nm; retention times: 11.7 and 12.8 min.

2-Methyl-3-oxo-2-phenylsulfanyl-butyric acid-*tert*-amyl ester (**3c**)

¹H NMR (250 MHz): δ 0.90 (t, *J* = 7.5 Hz, 3H), 1.45 (s, 3H), 1.46 (s, 3H), 1.48 (s, 3H), 1.79 (m, 2H), 2.39 (s, 3H), 7.27-7.44 (m, 5H); ¹³C NMR (62.9 MHz): δ 8.2, 20.7, 25.0, 25.1, 26.0, 33.7, 66.5, 86.1, 128.9, 129.6, 129.7, 136.8, 168.8, 199.3; IR: 1712, 1261, 1123, 749, 692 cm⁻¹; Elemental analysis calc. for C₁₆H₂₂SO₃: C 65.27, H 7.53, found C 65.47, H 7.63; [α]_D = -49.6 @ 86% ee (c = 0.48 CH₂Cl₂); HPLC conditions: *Daicel Chiracel* OJ column (250 x 4.6 mm); hexane/*i*-PrOH (99/1); 0.8 ml/min; detector 210.8 nm; retention times: 16.1 and 20.0 min.

2-*tert*-Butoxycarbonyl-2-phenylsulfanylcyclopentanone (**3d**)

¹H NMR (250 MHz): δ 1.42 (s, 9H), 1.87-2.18 (m, 3H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.48-2.59 (m, 1H), 7.30-7.35 (m, 3H), 7.55-7.59 (m, 2H); ¹³C NMR (62.9 MHz): δ 19.1, 27.8, 35.1, 36.9, 65.2, 83.0, 128.7, 129.2, 130.5, 136.0, 168.1, 208.1; IR: 1733, 1369, 1251,

1146, 751, 691 cm^{-1} ; EI-MS (m/z %) 292 (M^+ , 4), 236 (44), 192 (41), 163 (14), 136 (20), 110 (15), 109 (18), 91 (12), 77 (6), 57 (100); HRMS calc. for $\text{C}_{16}\text{H}_{20}\text{SO}_3$: 292.1128, found 292.1125; $[\alpha]_{\text{D}} = +59.5$ @ 88% ee ($c = 0.5$ CH_2Cl_2); HPLC conditions: *ReproSil Chiral-DP* column (250 x 4.6 mm); hexane/*i*-PrOH (99/1); 0.5 ml/min; detector 210.8 nm; retention times: 30.2 and 32.8 min.

2-Methyl-3-oxo-2-phenylsulfanyl-pentanoic acid-*tert*-butyl ester (3e)

^1H NMR (250 MHz): δ 1.15 (t, $J = 7.5$ Hz, 3H), 1.46 (s, 3H), 1.48 (s, 9H), 2.56 (qd, $J = 18$, $J = 7.5$ Hz, 1H), 2.93 (qd, $J = 18$, $J = 7.5$ Hz, 1H), 7.27-7.43 (m, 5H); ^{13}C NMR (75.5 MHz): δ 8.8, 20.7, 27.7, 31.4, 66.1, 83.4, 128.8, 129.6, 129.7, 136.8, 169.0, 202.6; IR: 1712, 1370, 1258, 1162, 1123, 1025, 968, 849, 750, 692 cm^{-1} ; Elemental analysis calc. for $\text{C}_{16}\text{H}_{22}\text{SO}_3$: C 65.27, H 7.53, found C 65.72, H 7.01; EI-MS (m/z %) 294 (M^+ , 5), 238 (3), 193 (17), 164 (100), 109 (15), 105 (46), 57 (65); HRMS calc. for $\text{C}_{15}\text{H}_{20}\text{SO}_3$: 294.1285, found 294.1286; $[\alpha]_{\text{D}} = -35.9$ @ 89% ee ($c = 0.51$ CH_2Cl_2); HPLC conditions: *Daicel Chiracel OJ* column (250 x 4.6 mm); hexane/*i*-PrOH (99/1); 0.8 ml/min; detector 210.8 nm; retention times: 11.3 and 13.2 min.

2-Methyl-3-oxo-2-phenylsulfanyl-pentanoic acid 2,4,6-triisopropylbenzyl ester (3f)

^1H NMR (250 MHz): δ 1.04 (t, $J = 7.5$ Hz, 3H), 1.24 (t, $J = 7.2$ Hz, 18H), 1.48 (s, 3H), 2.50 (qd, $J = 18$, $J = 7.2$ Hz, 1H), 2.89 (m, 2H), 3.15 (m, 2H), 5.33 (d, $J = 2.6$ Hz, 2H), 7.03 (s, 2H), 7.15-7.37 (m, 5H); ^{13}C NMR (75.5 MHz): δ 8.3, 20.8, 23.9, 24.3, 24.4, 29.4, 31.3, 34.3, 34.4, 61.2, 65.4, 121.2, 125.3, 128.8, 129.4, 129.7, 137.0, 149.0, 150.0, 170.4, 202.2; IR: 1715, 1460, 1224, 1117, 942, 750, 692 cm^{-1} ; Elemental analysis calc. for $\text{C}_{28}\text{H}_{38}\text{SO}_3$: C 73.97, H 8.42, found C 74.21, H 8.48; $[\alpha]_{\text{D}} = -36.0$ @ 84% ee ($c = 0.5$ CH_2Cl_2); HPLC conditions: *Daicel Chiracel ODH* column (250 x 4.6 mm); hexane/*i*-PrOH (99.6/0.4); 0.9 ml/min; detector 210.8 nm; retention times: 26.5 and 48.0 min.

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- (2) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, 43, 1208-1217.