Organocatalytic Peroxy-Asymmetric Allylic Alkylation

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Supplementary Information

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1. General methods

NMR data were obtained for $^1$H at 400 MHz and for $^{13}$C at 50 or 100 MHz. Chemical shifts were given in parts per million ($\delta$) from tetramethylsilane with the solvent resonance as the internal standard in CDCl$_3$ solution. ESI HRMS was recorded on a Bruker Apex-2. In each case, enantiomeric ratio was determined by HPLC analysis on chiral column in comparison with authentic racemates, using a Daicel Chiralpak IC Column (250 x 4.6 mm), Chiralpak OD Column (250 x 4.6 mm) or Chiralpak AD Column (250 x 4.6 mm). UV detection was monitored at 220 nm or 254 nm. Optical rotation data were examined in CHCl$_3$ or MeOH solution at 20 °C. Column chromatography was performed on silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates. UV light and I$_2$ were used to visualize products. All chemicals were used without purification as commercially available unless otherwise noted. THF, ethyl acetate, petroleum ether, methylene chloride (CH$_2$Cl$_2$) and carbon tetrachloride (CCl$_4$) were distilled before use.

2 Synthesis of hydroperoxyalkane 1b

To a mixture of Mg (3.4 g, 142 mmol) in 20 mL dry THF was added dropwise bromobenzene (15 mL, 142 mmol) in dry THF (60 mL) under argon atmosphere. The mixture was heated at 50 °C for 3 h. Then a solution of 3-pentanone (5 mL, 47 mmol) in dry THF (30 mL) was added dropwise at 0 °C. After 30 min the mixture was warmed to rt and stirred overnight. The solution was quenched with aq NH$_4$Cl and extracted three times with ethyl acetate. The organic layers were combined and washed with brine, dried (Na$_2$SO$_4$), filtered and concentrated. Flash chromatography on silica gel (ethyl acetate/petroleum ether) gave the 3-phenylpentan-3-ol as colorless oil (4.7 g, 61% yield).

A solution of 3-phenylpentan-3-ol (328 mg, 2 mmol) was added dropwise to the stirred mixture of 30% hydrogen peroxide (150 mL) and 2.5% (w/v) sulfuric acid (15 mL). After stirring for 4 h at room temperature, the reaction mixture was extracted with DCM (3 x 50 mL), washed with water,
dried over sodium sulfate, filtered, and concentrated. Flash chromatography on silica gel (ethyl acetate/petroleum ether) gave the product 1b as yellow oil (300 mg, 83% yield). $^1$H NMR (400 MHz, CDCl$_3$): \( \delta \) (ppm) 7.48-7.42 (m, 4H), 7.37-7.32 (m, 1H), 2.04-1.90 (m, 4H), 0.88 (t, \( J = 7.2 \) Hz, 6H).

3. General procedure for the peroxy-AAA reaction

Hydroperoxyalkane 1b (22 mg, 0.12 mmol), MBH carbonate 2 (0.1 mmol), catalyst (DHQD)$_2$PHAL (7.8 mg, 0.01 mmol) in CCl$_4$ (0.4 mL) were stirred at 35 °C. After completion the solvent was removed and flash chromatography on silica gel (EtOAc/petroleum ether) gave the peroxide 3.

4. General procedure for the reduction of compound 3

Compound 3 (0.1 mmol) and zinc powder (260 mg, 4 mmol) were stirred in a mixture solvents of AcOH/H$_2$O (1:1) at 25 °C for 3 h under argon atmosphere. Then the solid was filtered and the filtrate was extracted with DCM three times. The organic layers were combined and washed with brine, dried over Na$_2$SO$_4$, filtered. Concentration and flash chromatography on silica gel (ethyl acetate/petroleum ether) gave \( \alpha \)-methylene-\( \beta \)-hydroxy ester 4.

\( 3a \), 76% yield; [\( \alpha \)]$_D^{20} = +31.0$ (c = 0.40 in CHCl$_3$); 91% ee, determined by HPLC analysis [Daicel chiralpak OD, n-hexane/i-PrOH = 99/1, 1.0 mL/min, \( \lambda = 254 \) nm, t (major) = 5.69 min, t (minor) = 6.60 min]; $^1$H NMR (400 MHz, CDCl$_3$): \( \delta \) (ppm) 7.46-7.44 (m, 2H), 7.35-7.31 (m, 2H), 7.28-7.24 (m, 4H), 7.18-7.15 (m, 2H), 6.47 (t, \( J = 0.8 \) Hz, 1H), 6.02 (t, \( J = 1.2 \) Hz, 1H), 5.84 (s, 1H), 3.67 (s, 3H), 1.59-1.57 (m, 6H); $^{13}$C NMR (50 MHz, CDCl$_3$): \( \delta \) (ppm) 166.1, 145.3, 138.6, 137.2, 128.3, 128.2, 127.9, 127.0, 126.8, 125.6, 83.3, 51.8, 26.7, 26.5; ESI-HRMS: calcd. for C$_{22}$H$_{26}$O$_4$+Na 349.1416, found 349.1386.
3b, 79% yield; [$\alpha$]$_D^{20}$ = +64.8 ($c$ = 0.25 in CHCl$_3$); 93% ee, determined by HPLC analysis [Daicel chiralpak OD, n-hexane/i-PrOH = 98/2, 1.0 mL/min, $\lambda$ = 254 nm, t (major) = 4.78 min, t (minor) = 6.80 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 7.31-7.28 (m, 4H), 7.26-7.22 (m, 3H), 7.20-7.17 (m, 3H), 6.50 (t, $J$ = 0.8 Hz, 1H), 6.04 (t, $J$ = 1.2 Hz, 1H), 5.91 (s, 1H), 3.69 (s, 3H), 2.01-1.91 (m, 3H), 1.89-1.82 (m, 1H), 0.77 (t, $J$ = 7.2 Hz, 3H), 0.72 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ (ppm) 166.2, 142.9, 138.8, 137.3, 128.3, 128.2, 128.2, 127.7, 126.9, 126.6, 126.2, 88.3, 82.9, 51.8, 28.5, 28.1, 7.9; ESI-HRMS: calcd. for C$_{22}$H$_{26}$O$_4$+Na 377.1729, found 377.1729.

3c, 69% yield; [$\alpha$]$_D^{20}$ = +33.2 ($c$ = 0.75 in MeOH); 90% ee, determined by HPLC analysis after converted to the corresponding $\alpha$-methylene-$\beta$-hydroxy ester [Daicel chiralpak OD, n-hexane/i-PrOH = 98/2, 1.0 mL/min, $\lambda$ = 254 nm, t (major) = 30.65 min, t (minor) = 27.27 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 7.33-7.30 (m, 4H), 7.25-7.22 (m, 1H), 7.14-7.10 (m, 2H), 6.95 (t, $J$ = 8.4 Hz, 2H), 6.49 (s, 1H), 6.03 (s, 1H), 5.85 (s, 1H), 3.68 (s, 3H), 1.97-1.81 (m, 4H), 0.76 (t, $J$ = 7.2 Hz, 3H), 0.71 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ (ppm) 166.0, 165.1, 160.2, 142.9, 138.6, 133.2, 130.0, 129.8, 127.7, 126.7, 126.6, 126.1, 115.3, 114.9, 88.4, 82.2, 51.8, 28.4, 27.8, 7.8, 7.7; ESI-HRMS: calcd. for C$_{22}$H$_{25}$FO$_4$+Na 395.1635, found 395.1624.

3d, 71% yield; [$\alpha$]$_D^{20}$ = +25.4 ($c$ = 1.00 in MeOH); 89% ee, determined by HPLC analysis after converted to the corresponding $\alpha$-methylene-$\beta$-hydroxy ester [Daicel chiralpak OD, n-hexane/i-PrOH = 98/2, 1.0 mL/min, $\lambda$ = 254 nm, t (major) = 30.41 min, t (minor) = 27.05 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 7.33-7.27 (m, 4H), 7.25-7.21 (m, 1H), 7.14-7.10 (m, 2H), 6.95 (t, $J$ = 8.4 Hz, 2H), 6.47 (s, 1H), 6.00 (s, 1H), 5.83 (s, 1H), 5.83 (s, 3H), 3.68 (s, 3H), 1.96-1.80 (m, 4H), 0.76 (t, $J$ = 7.6 Hz, 3H), 0.71 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ (ppm) 166.0, 165.1, 160.2, 142.8, 138.5, 134.1, 129.5, 128.4, 127.8, 127.0, 126.7, 126.6, 126.1, 115.3, 114.9, 88.5, 82.2, 51.9, 28.3, 27.8, 7.9, 7.8; ESI-HRMS: calcd. for C$_{22}$H$_{25}$ClO$_4$+Na 411.1339, found 411.1387.

3e, 71% yield; [$\alpha$]$_D^{20}$ = +26.9 ($c$ = 0.70 in MeOH); 83% ee, determined by HPLC analysis after converted to the corresponding $\alpha$-methylene-$\beta$-hydroxy ester [Daicel chiralcel OD, n-hexane/i-PrOH = 90/10, 1.0 mL/min, $\lambda$ = 254 nm, t (major) = 9.62 min, t (minor) = 8.92 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 7.34-7.29 (m, 4H), 7.26-7.20 (m, 3H), 7.13 (s, 1H), 7.07 (d, $J$ = 6.8 Hz, 1H), 6.49
(s, 1H), 5.98 (s, 1H), 5.85 (s, 1H), 3.71 (s, 3H), 1.95 (q, J = 7.6 Hz, 2H), 1.86 (q, J = 7.2 Hz, 2H), 0.77 (t, J = 7.6 Hz, 3H), 0.71 (t, J = 7.6 Hz, 3H); 13C NMR (50 MHz, CDCl3): δ (ppm) 165.9, 142.8, 139.6, 138.2, 134.1, 129.4, 128.4, 128.1, 127.8, 127.4, 126.7, 126.3, 126.1, 88.5, 82.1, 51.9, 28.3, 27.7, 7.8, 7.7; ESI-HRMS: calcd. for C22H25ClO4+Na 411.1339, found 411.1312.

3f, 73% yield; [α]D20 = +32.4 (c = 0.90 in MeOH)1; 88% ee, determined by HPLC analysis after converted to the corresponding α-methylene-β-hydroxy ester [Daicel chiralpak IC, n-hexane/i-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t (major) = 11.84 min, t (minor) = 16.80 min]; 1H NMR (400 MHz, CDCl3): δ (ppm) 7.36-7.26 (m, 6H), 7.20 (d, J = 2.0 Hz, 1H), 7.00 (dd, J = 2.0 Hz, 8.4 Hz, 1H), 6.48 (s, 1H), 5.97 (t, J = 1.2 Hz, 1H), 5.79 (s, 1H), 3.71 (s, 3H), 1.96 (q, J = 7.2 Hz, 2H), 1.87 (q, J = 6.8 Hz, 2H), 0.78 (t, J = 7.2 Hz, 3H), 0.70 (t, J = 7.6 Hz, 3H); 13C NMR (50 MHz, CDCl3): δ (ppm) 165.7, 142.7, 137.9, 132.3, 130.2, 129.9, 127.8, 127.4, 127.3, 126.8, 126.1, 88.6, 81.6, 52.0, 28.2, 27.4, 7.8, 7.7; ESI-HRMS: calcd. for C22H24Cl2O4+Na 445.0949, found 445.0922.

3g, 65% yield; [α]D20 = +18.3 (c = 0.40 in MeOH)1; 86% ee, determined by HPLC analysis after converted to the corresponding α-methylene-β-hydroxy ester [Daicel chiralpak AD, n-hexane/i-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t (major) = 19.65 min, t (minor) = 20.87 min]; 1H NMR (400 MHz, CDCl3): δ (ppm) 7.31-7.29 (m, 4H), 7.25-7.22 (m, 1H), 7.09-7.04 (m, 4H), 6.50 (s, 1H), 6.07 (s, 1H), 5.87 (s, 1H), 3.68 (s, 3H), 2.30 (s, 3H), 1.99-1.89 (m, 3H), 1.89-1.81 (m, 1H), 0.77 (t, J = 7.2 Hz, 3H), 0.72 (t, J = 7.2 Hz, 3H); 13C NMR (50 MHz, CDCl3): δ (ppm) 166.3, 142.9, 138.8, 138.1, 134.2, 128.9, 128.2, 127.7, 126.5, 126.2, 88.3, 82.8, 51.8, 28.5, 28.0, 21.2, 7.9; ESI-HRMS: calcd. for C23H28O4+Na 391.1885, found 391.1894.

3h, 67% yield; [α]D20 = +16.0 (c = 0.25 in CHCl3); 92% ee, determined by HPLC analysis [Daicel chiralcel OD, n-hexane/i-PrOH = 99/1, 1.0 mL/min, λ = 254 nm, t (major) = 4.99 min, t (minor) = 5.79 min]; 1H NMR (400 MHz, CDCl3): δ (ppm) 7.31-7.29 (m, 4H), 7.25-7.22 (m, 1H), 7.16 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 7.6 Hz, 1H), 6.97 (d, J = 7.6 Hz, 1H), 6.91 (s, 1H), 6.50 (s, 1H), 6.05 (s, 1H), 5.86 (s, 1H), 3.69 (s, 3H), 2.28 (s, 3H), 1.99-1.90 (m, 3H), 1.88-1.81 (m, 1H), 0.77 (t, J = 7.2 Hz, 3H), 0.71 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3): δ (ppm) 166.3, 143.0, 138.8, 137.8, 137.1, 129.1, 128.9, 128.1, 127.7, 126.8, 126.6, 126.2, 125.3, 88.3, 83.0, 51.8, 28.5, 27.9, 21.4, 7.9, 7.8; ESI-HRMS: calcd. for C23H28O4+Na 391.1885, found 391.1894.
3i, 73% yield; $[\alpha]_{D}^{20} = +25.8$ (c = 0.40 in CHCl$_3$); 93% ee, determined by HPLC analysis [Daicel chiralpak IC, n-hexane/i-PrOH = 99/1, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 7.28 min, t (minor) = 6.77 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 7.32-7.31 (m, 4H), 7.25-7.24 (m, 1H), 7.08 (d, $J = 6.8$ Hz, 2H), 6.80 (d, $J = 6.4$ Hz, 2H), 6.50 (s, 1H), 6.09 (t, $J = 1.2$ Hz, 1H), 5.84 (s, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 1.99-1.90 (m, 3H), 1.88-1.81 (m, 1H), 0.78 (t, $J = 7.2$ Hz, 3H), 0.72 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ (ppm) 166.3, 159.7, 143.0, 138.9, 129.6, 127.7, 126.6, 126.2, 125.5, 113.6, 88.2, 82.6, 55.2, 51.8, 28.5, 27.9, 7.9, 7.8; ESI-HRMS: calcd. for C$_{23}$H$_{28}$O$_5$+Na 407.1834, found 407.1835.

3j, 50% yield; $[\alpha]_{D}^{20} = +13$ (c = 0.90 in CHCl$_3$); 89% ee, determined by HPLC analysis [Daicel chiralpak IC, n-hexane/i-PrOH = 99/1, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 8.90 min, t (minor) = 7.79 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 7.39-7.37 (m, 1H), 7.31-7.30 (m, 4H), 7.27-7.23 (m, 1H), 6.71 (d, $J = 8.0$ Hz, 1H), 6.65 (dd, $J = 8.0$ Hz, 1.6 Hz, 1H), 6.60 (d, $J = 1.6$ Hz, 1H), 6.49 (s, 1H), 6.07 (t, $J = 1.2$ Hz, 1H), 5.92 (s, 2H), 5.79 (s, 1H), 3.70 (s, 3H), 1.99-1.98 (m, 4H), 1.99-1.98 (m, 4H), 0.78 (t, $J = 7.2$ Hz, 3H), 0.72 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ (ppm) 166.2, 147.5, 142.9, 138.7, 130.9, 128.3, 127.7, 126.6, 126.4, 126.2, 122.1, 108.7, 108.0, 101.1, 88.3, 82.7, 51.8, 28.4, 27.8, 7.9, 7.8; ESI-HRMS: calcd. for C$_{23}$H$_{26}$O$_6$+Na 421.1627, found 421.1632.

3k, 53% yield; $[\alpha]_{D}^{20} = +35.8$ (c = 0.50 in MeOH)$^1$; 92% ee, determined by HPLC analysis after converted to the corresponding $\alpha$-methylene-$\beta$-hydroxy ester [Daicel chiralpak IC, n-hexane/i-PrOH = 95/5, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 22.18 min, t (minor) = 32.73 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 7.35-7.30 (m, 4H), 7.27-7.23 (m, 2H), 6.92 (dd, $J = 3.6$ Hz, 4.8 Hz, 1H), 6.86 (d, $J = 3.2$ Hz, 1H), 6.54 (s, 1H), 6.17 (s, 1H), 6.10 (s, 1H), 3.74 (s, 3H), 2.01-1.85 (m, 4H), 0.80-0.73 (m, 6H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ (ppm) 166.0, 142.8, 140.1, 138.8, 127.8, 127.1, 126.8, 126.4, 126.2, 122.1, 108.7, 108.0, 101.1, 88.5, 77.8, 51.9, 28.4, 28.1, 7.8; ESI-HRMS: calcd. for C$_{20}$H$_{24}$O$_4$S+Na 383.1293, found 383.1310.

3l, 62% yield; $[\alpha]_{D}^{20} = +29.3$ (c = 0.30 in CHCl$_3$); 91% ee, determined by HPLC analysis [Daicel chiralpak IC, n-hexane/i-PrOH = 98/2, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 7.28 min, t (minor) = 9.09 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$
(ppm) 7.38-7.37 (m, 1H), 7.31-7.28 (m, 4H), 7.26-7.21 (m, 1H), 6.53 (s, 1H), 6.30 (dd, \( J = 2.0 \) Hz, 3.2 Hz, 1H), 6.22 (d, \( J = 3.6 \) Hz, 1H), 6.15 (t, \( J = 2.8 \) Hz, 1H), 6.00 (s, 1H), 3.74 (s, 3H), 1.96 (q, \( J = 7.2 \) Hz, 2H), 1.90 (q, \( J = 7.2 \) Hz, 2H), 0.78-0.72 (m, 6H); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)): \( \delta \) (ppm) 165.9, 150.5, 143.1, 142.7, 136.6, 127.7, 127.5, 126.5, 126.0, 110.4, 110.1, 88.6, 76.0, 51.9, 28.7, 28.4, 7.8; ESI-HRMS: calcd. for C\(_{20}\)H\(_{24}\)O\(_5\)+Na 367.1521, found 367.1539.

\[ \text{4b, 93\% yield; } [\alpha]^D_{20} = +82.9 \text{ (c = 0.6 in MeOH)} \] \{lit.: \(^2\) [\( \alpha \)]\(_D^{22} \) = +85.5 (c = 1.11 in MeOH, 84\% ee); 93\% ee, determined by HPLC analysis [Daicel chiralpak IC, \( n \)-hexane/i-PrOH = 95/5, 1.0 mL/min, \( \lambda = 220 \) nm, t (major) = 19.96 min, t (minor) = 35.15 min]; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) (ppm) 7.38-7.32 (m, 4H), 7.29-7.25 (m, 1H), 6.33 (s, 1H), 5.82 (s, 1H), 5.56 (d, \( J = 5.2 \) Hz, 1H), 3.71 (s, 3H), 3.03 (d, \( J = 5.6 \) Hz, 1H); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)): \( \delta \) (ppm) 166.8, 142.0, 141.3, 128.4, 127.8, 126.6, 126.1, 73.2, 51.9.

Notes and references

(1) The optical rotation was related to the corresponding \( \alpha \)-methylene-\( \beta \)-hydroxy ester.

5. NMR and HPLC spectra

![NMR spectra of compound 3b](image)

![HPLC spectrum of compound 3b](image)
3I

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