Supplementary Material (ESI) for Chemical Communications

Asymmetric alkylation of dimethoxyphosphoryl-*N*-[1-(*S*)-α-methylbenzyl)acetamide enolates. Synthesis of both stereoisomers from the same source of chirality changing the equivalents of LDA

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Typical experimental procedure for the second alkylation of **3**. To a solution of the β-phosphonoamide **3** (1 mmol) in dry THF at -78° was added dropwise 2.0 or 2.5 equivalents of freshly preparated LDA from freshly titrated *n*-buthyllithium[15] and freshly distilled diisopropylamine in dry THF. The resulting solution was stirred for 1 h at -78°. The benzyl bromide (1.1 equiv) was added with continuous stirring, and the mixture reaction was stirred at -78° for 3-4 h and quenched with saturated aqueous NH_4Cl solution. The product was extracted with ethyl acetate, the combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuum. The crude product was analyzed by NMR ^1H at 400 MHz and NMR ^{31}P at 200 MHz. The diastereomeric mixture was cleanly separated by column chromatography (hexane:ethyl acetate 70:30) to afford (*R,S*)-**4** as colorless oil (less polar) and (*S,S*)-**5** as white solid (more polar)

(*R,S*)-**4** as a colorless oil, $[\alpha]_D$ = -100 (c = 2.2, $CHCl_3$). NMR ^1H (400 MHz, $CDCl_3$) δ 1.27 (d, J = 16.0 Hz, 3H, $CH_3C(Bn)P$), 1.50 (d, J = 7.0 Hz, 3H, CH_3CHPh), 2.88 (dd, J = 13.6, 10.0 Hz, 1H, CH_2Ph), 3.35 (dd, J = 13.6, 10.0 Hz, 1H, CH_2Ph), 3.78 (d, J = 10.8 Hz, 3H, $(CH_3O)_2P$), 3.82 (d, J = 10.8 Hz, 3H, $(CH_3O)_2P$), 5.11 (q, J = 7.0 Hz, 1H, $CH(CH_3)Ph$), 6.88-6.90 (m, 2H, H_{arom}), 7.01-7.17 (m, 3H, H_{arom}), 7.22-7.37 (m, 5H, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.8 ($CH_3C(Bn)P$), 22,0 (CH_3CHPh), 41.0 (CH_2Ph), 48.4 (d, J = 130.5, $CCH_3(Bn)P$), 49.7 ($CH(CH_3)Ph$), 53.7 (d, J = 7.6 Hz, $(CH_3O)_2P$), 53.9 (d, J = 7.6 Hz, $(CH_3O)_2P$), 126.7, 127.1, 127.6, 128.2, 128.9, 130.5, 135.4, 143.2, 168.3 C=O. ^{31}P NMR (200 MHz, $CDCl_3$) δ 33.59. Anal. calcd. for $C_{20}H_{26}NO_4P$: C, 63.99; H, 6.98; N, 3.73%; found C, 63.67; H, 7.05; N, 3.44%.

(*S,S*)-**5** as a white solid, M.p. 114-115 °C, $[\alpha]_D$ = -11 (c = 2.2, $CHCl_3$). NMR ^1H (400 MHz, $CDCl_3$) δ 1.28 (d, J = 16.0 Hz, 3H, $CH_3C(Bn)P$), 1.52 (d, J = 7.2 Hz, 3H, CH_3CHPh), 2.94 (dd, J = 13.8, 10.2 Hz, 1H, CH_2Ph), 3.45 (dd, J = 13.8, 10.2 Hz, 1H, CH_2Ph), 3.50 (d, J = 10.8 Hz, 3H,

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$(CH_3O)_2P$), 3.80 (d, J = 10.8 Hz, 3H, $(CH_3O)_2P$), 5.12 (q, J = 7.2 Hz, 1H, $CH(CH_3)Ph$), 7.15-7.17 (m, 2H, H_{arom}), 7.21-7.27 (m, 4H, H_{arom}), 7.30-7.34 (m, 4H, H_{arom}) ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.0 ($CH_3C(Bn)P$), 22,2 (CH_3CHPh), 41.0 (CH_2Ph), 48.5 (d, J = 130.6, $CCH_3(Bn)P$), 49.5 (CH_3CHPh), 53.6 (d, J = 7.6 Hz, $(CH_3O)_2P$), 53.7 (d, J = 7.6 Hz, $(CH_3O)_2P$), 126.4, 127.3, 127.4, 128.3, 128.8, 130.5, 135.4, 143.5, 168.2 C=O. ^{31}P NMR (200 MHz, $CDCl_3$) δ 33.59. Anal. calcd. for $C_{20}H_{26}NO_4P$: C, 63.99; H, 6.98; N, 3.73%; found C, 63.59; H, 6.95; N, 3.57%.

X-ray crystal data of (*S,S*)-**5** were collected at 298 K using a Bruker APEX CCD instrument (Mo Kα radiation, λ = 0.71073 Å). The SHELXTL v. 6.1 program package was used for structure solution and refinement. The structure was solved by direct methods and refined by full-matrix least squares procedures. All non-hydrogen atoms were refined anisotropically. (*S,S*)-**5**: $C_{20}H_{34}NO_4P$, M = 375.39, monoclinic space group P3(1)c, a = 11.172(4), b = 11.172(4), c = 13.401(7) Å, $\beta = 90^o$, V = 1448.4(10) $Å^3$, $Z = 3$, $D_c = 1.291$ g cm^{-1}, 5242 reflections measured, 3277 unique (R_{int} = 0.1165) which were used in all calculations, final R values were 0.0761 [$F > 4\sigma(F)$] and 0.0772 (all data).

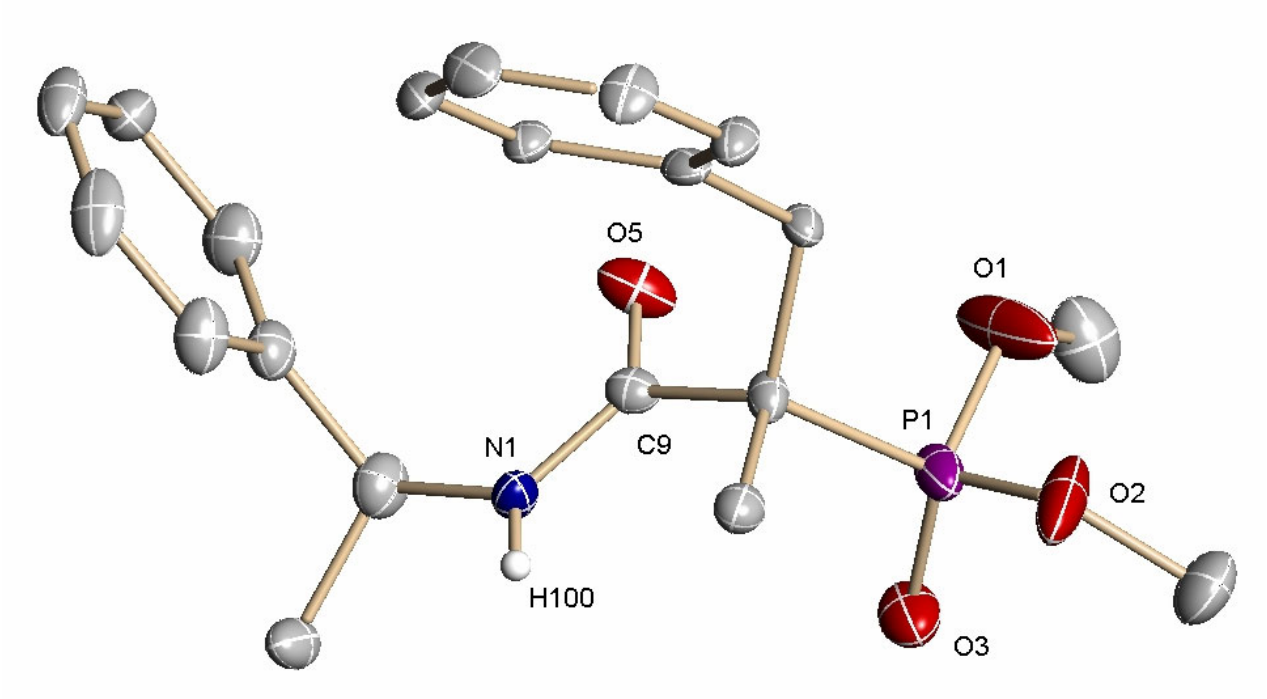

Figure 1. X-Ray crystal structure of (*S,S*)-**5**.

15. E. Juaristi, A. Martínez-Richa, A. García-Rivera, and J. S. Cruz-Sánchez, *J. Org. Chem.* **1983**, *48*, 2603.