Supporting Information

A Silicon Tether Approach for Addition of Functionalized Radicals to Chiral α-Hydroxyhydrazones: Diastereoselective Additions of Hydroxymethyl and Vinyl Synthons

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Table of Contents

Materials and Methods	S2
Experimental Procedures and Characterization Data	S2
^{1}H NMR Spectra of *trans*-**6**, **7**, *syn*-**13c**, **14d**, **21**, **23d**, **32**	S9

Materials and Methods. Reactions employed oven- or flame-dried glassware under nitrogen unless otherwise noted. THF and toluene were distilled from sodium/benzophenone ketyl under argon. CH_2Cl_2 was distilled from CaH_2 under argon or nitrogen. Nitrogen was passed successively through columns of anhydrous $CaSO_4$ and R3-11 catalyst for removal of water and oxygen, respectively. All other materials were used as received or purified by standard procedures. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator. Flash chromatography columns were packed with 230-400 mesh silica gel as a slurry in the initial elution solvent. Gradient flash chromatography was conducted by adsorption of product mixtures on silica gel, packing over a short pad of clean silica gel as a slurry in hexane, and eluting with a continuous gradient from hexane to the indicated solvent. Radial chromatography refers to centrifugally accelerated thin-layer chromatography performed with a Chromatotron using commercially supplied rotors. Melting points are uncorrected. Nuclear magnetic resonance (NMR) data were obtained at operating frequencies of 500 MHz (^{1}H) and 125 MHz (^{13}C). Infrared spectra were recorded using a single beam FT-IR spectrophotometer by standard transmission methods or by use of an attenuated total reflectance (ATR) probe. Optical rotations were determined using a digital polarimeter operating at ambient temperature. Low resolution mass spectra were obtained using sample introduction by dip, liquid chromatography or gas chromatography.

Preparation of α-Hydroxyhydrazones

General Procedure A: α-(*tert*-Butyldimethylsilyl)oxyhydrazones 9. A solution of an α-silyloxyester (e.g., **8a**–**8d**) in dry hexane (ca. 1 M) was cooled to –78 °C and a solution of diisobutylaluminum hydride (1.5 M in toluene, 1.2 equiv) was added dropwise over 30 min. After 1 h at –78 °C, saturated aqueous potassium sodium tartrate (ca. 2 mL/mmol ester) was added. Following dilution with ether/CH_2Cl_2 (1:1, ca. 4 mL/mmol ester) and vigorous stirring, the aqueous phase was extracted with ether (2 x 10 mL). The organic phase was dried (Na_2SO_4) and concentrated. The resulting solution of aldehyde in toluene was diluted with pyridine (ca. 1 mL/mmol ester) and *N*,*N*-diphenylhydrazine hydrochloride (1 mmol/mmol ester) was added at room temperature. The mixture was concentrated and partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. The organic phase was washed with 1 N aqueous HCl, dried (Na_2SO_4) and concentrated. Gradient flash chromatography (**9b**–**9d**, hexane → 10:1 hexane/EtOAc) or recrystallization from 90% EtOH (**9a**) afforded α-silyloxy hydrazones. Analytical samples of **9b**–**9d** were obtained by radial chromatography (10:1 hexane/EtOAc).

(*S*)-(–)-2-(*tert*-Butyldimethylsilyloxy)propanal *N*,*N*-Diphenylhydrazone (9a, R = Me). From ester **8a** (0.79 g, 3.6 mmol) via General Procedure A was obtained **9a** (0.755 g, 59% yield) as colorless needles: mp 70–71 °C; $[\alpha]_D^{25}$ –1.7° (*c* 1.45, $CHCl_3$); IR (film) 2955, 2929, 2856, 1593, 1496, 1086, 1058 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.36 (m, 4H), 7.16-7.12 (m, 2H), 7.11-7.08 (m, 4H), 6.39 (d, *J* = 5.9 Hz, 1H), 4.54 (m, apparent quintet, *J* = 6.2 Hz, 1H), 1.28 (d, *J* = 6.4 Hz, 3H), 0.87 (s, 9H), 0.09 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 141.6, 129.7, 124.1, 122.4, 69.5, 25.9, 22.6, 18.2, -4.4, -4.6; MS *m*/*z* (relative intensity) 355 ($[M+H]^+$, 30%), 354 (M^+, 50%), 223 (100%), 168 (55%); Anal. Calcd for $C_{21}H_{30}N_2OSi$: C, 71.14; H, 8.53; N, 7.90. Found: C, 71.22; H, 8.54; N, 7.95.

(*S*)-(+)-2-(*tert*-Butyldimethylsilyloxy)-4-methylpentanal *N*,*N*-Diphenylhydrazone (9b, R = ^{i}Bu). From ester **8b** (0.52 g, 2.0 mmol) via General Procedure A was obtained **9b** (0.636 g, 80% yield) as a colorless oil: $[\alpha]_D^{27}$ +3.4° (*c* 0.83, $CHCl_3$); IR (film) 2956, 2928, 1595, 1498, 1213, 1077, 1053 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.36 (m, 4H), 7.16-7.08 (m, 6H), 6.34 (d, *J* = 6.4 Hz, 1H), 3.96-3.92 (m, 1H), 1.75-1.68 (m, 1H), 1.48 (ddd, *J* = 13.7, 8.1, 6.1 Hz, 1H), 1.31 (ddd, *J* = 13.7, 7.8, 5.9 Hz, 1H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.11 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 141.3, 129.7, 124.1, 122.4, 71.8, 45.6, 25.9, 24.1, 23.2, 22.3, 18.2, -4.0, -

4.7; MS *m*/*z* (relative intensity) 397 ([M+H]$^+$, 65%), 396 (M$^+$, 85%), 339 (30%), 265 (100%), 168 (35%). Anal. Calcd for $C_{24}H_{36}N_2OSi$: C, 72.68; H, 9.15; N, 7.06. Found: C, 72.86; H, 9.11; N, 7.05.

(*S*)-(+)-2-(*tert*-Butyldimethylsilyloxy)-3-methylbutanal *N*,*N*-Diphenylhydrazone (9c, R = ^{i}Pr). From ester **8c** (0.626 g, 2.39 mmol) via General Procedure A was obtained **9c** (0.756 g, 83% yield) as a colorless oil: $[\alpha]_D^{27}$ +26° (*c* 1.74, $CHCl_3$); IR (film) 2957, 2930, 2857, 1592, 1496, 1213, 1072, 1049 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.38 (m, 4H), 7.17-7.13 (m, 2H), 7.12-7.09 (m, 4H), 6.35 (d, *J* = 6.9 Hz, 1H), 4.06 (t, 6.8 Hz, 1H), 1.73 (m, apparent octet, *J* = 6.7 Hz, 1H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.11 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 140.8, 129.7, 124.1, 122.4, 78.4, 34.0, 25.9, 18.5, 18.2 (2C), -4.0, -4.8; MS *m*/*z* (relative intensity) 383 ([M+H]$^+$, 50%), 382 (M$^+$, 40%), 325 (30%), 251 (100%), 168 (25%). Anal. Calcd for $C_{23}H_{34}N_2OSi$: C, 72.20; H, 8.96; N, 7.32. Found: C, 72.23; H, 8.93; N, 7.11.

(*S*)-(–)-2-(*tert*-Butyldimethylsilyloxy)-2-phenylacetaldehyde *N*,*N*-Diphenylhydrazone and Racemate (9d, R = Ph). From racemic ester **8d** (2.61 g, 9.31 mmol) was obtained via General Procedure A, using half of the aldehyde intermediate in the second step, **9d** (1.63 g, 84% yield) as a colorless oil: IR (film) 2956, 2929, 2856, 1592, 1496, 1299, 1256, 1214, 1089, 1057 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.35 (m, 6H), 7.33-7.29 (m, 2H), 7.24-7.21 (m, 1H), 7.15-7.11 (m, 2H), 7.10-7.08 (m, 4H), 6.38 (d, *J* = 6.8 Hz, 1H), 5.51 (d, *J* = 6.8 Hz, 1H), 0.92 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 142.2, 140.1, 129.7, 128.2, 127.0, 125.8, 124.3, 122.4, 75.1, 25.9, 18.3, -4.2, -4.7; MS *m*/*z* (relative intensity) 417 ([M+H]+, 40%), 285 (100%), 273 (40%), 221 (30%, 168 (45%). From (*S*)-ester **8d** (98% ee, 2.68 g, 9.57 mmol) was obtained, using one-fifth of the aldehyde intermediate in the second step, (*S*)-**9d** (0.636 g, 76% yield) as a colorless oil, spectroscopically identical to racemic **9d**; $[\alpha]_D^{26}$ –93° (*c* 0.34, $CHCl_3$); Anal. Calcd for $C_{26}H_{32}N_2OSi$: C, 74.95; H, 7.74; N, 6.72. Found: C, 75.05; H, 7.76; N, 6.70.

General Procedure B: α-Hydroxyhydrazones 10. To a solution of α-silyloxyhydrazone (e.g., **9a**–**9d**) in THF (ca. 0.1 M) was added TBAF (1 M in THF, 1.1 equiv) at room temperature. After 0.5–3 h (TLC monitoring), the mixture was concentrated and filtered through silica gel (step gradient elution, 10:1 → 1:1 hexane/EtOAc) to afford α-hydroxyhydrazones **10**.

(*S*)-(+)-2-Hydroxypropanal *N*,*N*-Diphenylhydrazone (10a, R = Me). From α-silyloxyhydrazone **9a** (323 mg, 0.909 mmol) via General Procedure B was obtained **10a** (220 mg, 100% yield) as a colorless viscous oil: $[\alpha]_D^{25}$ +38° (*c* 2.1, $CHCl_3$); IR (film) 3380 (br), 1591, 1496, 1214 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.37 (m, 4H), 7.20-7.15 (m, 2H), 7.14-7.09 (m, 4H), 6.54 (d, *J* = 3.4 Hz, 1H), 4.50-4.44 (m, 1H), 3.05-3.02 (br s, 1H), 1.30 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 139.8, 129.8, 124.4, 122.3, 67.4, 21.6; MS *m*/*z* (relative intensity) 241 ([M+H]$^+$, 100%), 223 ([M-OH]$^+$, 65%), 168 (25%); Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.68; H, 6.80; N, 11.54.

(*S*)-(+)-2-Hydroxy-4-methylpentanal *N*,*N*-Diphenylhydrazone (10b, R = ^{i}Bu). From α-silyloxy hydrazone **9b** (156 mg, 0.393 mmol) via General Procedure B was obtained **10b** (92 mg, 83% yield) as a colorless viscous oil: $[\alpha]_D^{28}$ +27° (*c* 4.6, $CHCl_3$); IR (film) 3400 (br, s), 2955, 1596, 1496, 1213 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.38 (m, 4H), 7.19-7.15 (m, 2H), 7.12-7.09 (m, 4H), 6.52 (d, *J* = 3.7 Hz, 1H), 4.39 (dddd, *J* = 8.4, 4.9, 3.7, 3.7 Hz, 1H), 2.90 (d, *J* = 3.7 Hz, 1H), 1.88-1.78 (m, 1H), 1.46 (ddd, *J* =13.9, 8.6, 5.8 Hz, 1H), 1.35 (ddd, *J* = 13.6, 8.1, 4.9 Hz, 1H), 0.943 (d, *J* = 6.7 Hz, 3H), 0.939 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 139.7, 129.8, 124.4, 122.3, 69.7, 44.9, 24.4, 23.3, 22.2; MS *m*/*z* (relative intensity) 283 ([M+H]$^+$, 100%), 282 (M$^+$, 45%), 265 ([M-OH]$^+$, 40%), 168 (15%). Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.56; H, 7.94; N, 9.76.

(*S*)-(+)-2-Hydroxy-3-methylbutanal *N*,*N*-Diphenylhydrazone (10c, R = ^{i}Pr). From α-silyloxy hydrazone **9c** (0. 285 g, 0.745 mmol) via General Procedure B was obtained **10c** (0.176 g, 88% yield) as

a colorless viscous oil: $[\alpha]_D^{27}$ +34° (*c* 3.8, $CHCl_3$); IR (film) 3435 (br, s), 2960, 1591, 1496, 1299, 1214, 1020 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43-7.39 (m, 4H), 7.20-7.16 (m, 2H), 7.15-7.12 (m, 4H), 6.59 (d, *J* = 3.4 Hz, 1H), 4.17-4.13 (m, 1H), 3.27 (br s, 1H), 1.87-1.78 (m, 1H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 138.7, 129.7, 124.4, 122.2, 75.5, 33.2, 18.2, 17.2; MS *m*/*z* (relative intensity) 269 ($[M+H]^+$, 90%), 268 (M+, 70%), 251 ($[M-OH]^+$, 100%), 168 (90%). Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.16; H, 7.56; N, 10.34.

(*S*)-(+)-2-Hydroxy-2-phenylacetaldehyde *N*,*N*-Diphenylhydrazone (10d, R = Ph). From α-silyloxy hydrazone **9d** (0.264 g, 0.634 mmol) via General Procedure B was obtained **10d** (0.165 g, 86% yield) as a pale tan viscous oil: $[\alpha]_D^{24}$ +97° (*c* 0.50, $CHCl_3$); IR (film) 3406 (br), 1591, 1495, 1214 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.34 (m, 8H), 7.32-7.26 (m, 1H), 7.18-7.15 (m, 2H), 7.14-7.10 (m, 4H), 6.63 (d, *J* = 3.4 Hz, 1H), 5.37 (t, *J* = 3.6 Hz, 1H), 3.81 (d, *J* = 3.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 141.0, 137.8, 129.8, 128.6, 127.8, 126.6, 124.6, 122.3, 73.7; MS *m*/*z* (relative intensity) 303 ($[M+H]^+$, 80%), 285 ($[M-OH]^+$, 45%), 170 (80%), 133 (100%), 107 (80%). Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.38; H, 6.06; N, 9.18.

Glycolaldehyde *N*,*N*-Diphenylhydrazone (15). A solution of glycolaldehyde (dimeric form, 304 mg, 2.53 mmol) in toluene (ca. 50 mL) at room temperature was treated with *N*,*N*-diphenylhydrazine (931 mg, 5.06 mmol) and Na_2SO_4 (15 g). After 24 h, filtration, concentration, and flash chromatography (5:1 → 1:1 hexane/EtOAc) furnished **15** (894 mg, 78% yield) as a colorless oil: IR (film) 3400 (br, s), 1591, 1496 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 7.16-7.10 (m, 2H), 7.11-7.09 (m, 4H), 6.63 (t, *J* = 3.3 Hz, 1H), 4.32 (d, *J* = 3.3 Hz, 2H), 2.7 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 135.8, 129.7, 124.4, 122.3, 62.5; MS (CI) *m*/*z* (relative intensity) 227 ($[M+H]^+$, 100%), 168 (25%); Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.23; N, 12.38. Found: C, 74.50; H, 6.36; N, 12.27.

D-Glyceraldehyde *N*,*N*-Diphenylhydrazone. A solution of D-glyceraldehyde (70% aqueous solution, 34 mg, 0.26 mmol) in toluene (ca. 7.60 mL) was treated with *N*,*N*-diphenylhydrazine hydrochloride (57 mg, 0.26 mmol) and Na_2SO_4 (2.4 g) at room temperature. After 2 d, filtration, concentration, and flash chromatography (10:1 hexane/EtOAc) afforded the title compound (29 mg, 43% yield) as a yellow oil: $[\alpha]_D^{28}$ –3.3° (*c* 3.23, $CHCl_3$); IR (film) 3391 (br, s), 1590, 1495, 1297, 1213, 1053, 749, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 7.18-7.17 (m, 2H), 7.10-7.08 (m, 4H), 6.54 (d, *J* = 3.2 Hz, 1H), 4.40 (ddd, *J* = 5.5, 3.3, 3.3 Hz, 1H), 3.79 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.65 (dd, *J* = 11.5, 5.6 Hz, 1H), 3.40 (br s, 1H), 2.50 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3, 135.6, 129.8, 124.6, 122.2, 71.6, 65.0; MS (CI) *m*/*z* (relative intensity) 257 ($[M+H]^+$, 81%), 168 (100%); Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.22; H, 6.23; N, 10.74.

Crotonaldehyde *N*,*N*-Diphenylhydrazone (29). A mixture of *E*-crotonaldehyde (1.5 mL, 18 mmol) and *N*,*N*-diphenylhydrazine hydrochloride (3.99 g, 18.1 mmol) in pyridine (18 mL) was stirred for 3 d at ambient temperature. After concentration, the residue was partitioned between CH_2Cl_2 and aqueous $NaHCO_3$ and the organic fraction was dried (Na_2SO_4) and concentrated. Flash chromatography (5:1 hexane/EtOAc) afforded **29** (2.88 g, 67% yield, *E*/*Z* = 9:1) as a colorless oil. Major isomer: ^1H NMR (500 MHz, $CDCl_3$) δ 7.45-7.41 (m, 4H), 7.22-7.16 (m, 6H), 6.96 (d, J = 9.0 Hz, 1H), 6.46 (ddd, J = 14.0, 9.0, 1.6 Hz, 1H), 5.78 (dq, J = 13.7, 6.8 Hz, 1H), 1.87 (dd, J = 6.8, 1.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 138.8, 132.4, 129.9, 129.6, 124.2, 122.5, 18.3. *E*/*Z* mixture: IR (film) 3029, 2910, 1589, 1495, 1291, 1214, 1056 cm^{-1}; MS (CI) *m*/*z* (relative intensity) 237 ($[M+H]^+$, 46%), 168 (44%); Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85. Found: C, 81.29; H, 6.78; N, 11.80.

(2*S*,3*S*)-Dihydroxybutyraldehyde *N*,*N*-diphenylhydrazone (30). To a mixture of AD-mix-α (1.4 g) and methanesulfonamide (95 mg, 1.0 mmol) in *t*-BuOH/H_2O (1:1, 10 mL) was added hydrazone **29** (236 mg, 1.00 mmol) as a solution in *t*-BuOH (1 mL) at 0 °C. After 7 h, the reaction was quenched at 0 °C by addition of sodium sulfite (1.5 g) and warmed to ambient temperature. The mixture was partitioned between EtOAc and water, and the organic layer was washed with 2 N KOH, dried (Na_2SO_4),

and concentrated. Flash chromatography (5:1 → 1:1 hexane/EtOAc) afforded diol **30** (206 mg, 76% yield) as a colorless oil containing a mixture of *syn* and *anti* diastereomers. The enantiomeric excess of the major diastereomer was found to be 76% via analysis of the bis-Mosher ester. Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 7.19-7.16 (m, 2H), 7.10-7.08 (m, 4H), 6.55 (d, J = 3.6 Hz, 1H), 4.10-4.07 (m, 1H), 3.81-3.77 (m, 1H), 3.55-3.20 (br s, 1H), 2.90-2.45 br s, 1H), 1.21 (d, J = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 136.2, 129.8, 124.6, 122.2, 75.2, 69.6, 18.6. Diastereomeric mixture: IR (film) 3400 (br, s), 1591, 1496, 1299, 1214, 1037 cm^{-1}; MS (CI) *m*/*z* (relative intensity) 271 ([M+H]$^+$, 90%), 168 (100%); Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.69; H, 6.71; N, 10.25.

General Procedure D: Acetonides 14. A solution of the hydrazino-1,3-diol (e.g., **13a**–**13d**) in $CHCl_3$ (ca. 0.2 M) was treated with 2,2-dimethoxypropane (ca. 1 mL/mmol diol) and PPTS (1 equiv). After 1 d at room temperature, the reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Radial chromatography (hexane/EtOAc) furnished diastereomerically pure *anti* acetonides **14**.

Acetonide 14a (R = Me). From **13a** (29 mg, 0.107 mmol) via General Procedure D was obtained **14a** (21 mg, 63% yield) as a colorless viscous oil; $[\alpha]_D^{27}$ –28° (*c* 0.43, $CHCl_3$); IR (film) 3289 (br, w), 3179 (br, w), 1589, 1497, 1269, 1200, 1180 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.27 (m, 4H), 7.14-7.11 (m, 4H), 7.04-7.00 (m, 2H), 3.94-3.88 (m, 1H), 3.92 (dd, *J* = 11.5, 5.0 Hz, 1H), 3.85 (br s, 1H), 3.73 (dd, *J* = 11.5, 9.5 Hz, 1H), 2.90 (ddd, apparent td, *J* = 9.3, 9.2, 5.0 Hz, 1H), 1.49 (s, 3H), 1.37 (s, 3H), 1.22 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 129.2, 122.7, 120.4, 98.4, 68.2, 62.8, 57.3, 28.9, 19.6, 19.2; MS *m*/*z* (relative intensity) 313 ([M+H]$^+$, 30%), 312 (M$^+$, 25%), 184 (35%), 170 (40%), 168 (100%). Anal. Calcd for $C_{19}H_{24}N_2O_2$: C, 73.05; H, 7.74; N, 8.97. Found: C, 73.33; H, 7.90; N, 8.97.

Acetonide 14b (R = ^{i}Bu). From **13b** (47 mg, 0.15 mmol) via General Procedure D was obtained **14b** (38 mg, 72% yield) as a colorless viscous oil which crystallized on standing; mp 59–61 °C; $[\alpha]_D^{27}$ –69° (*c* 1.3, $CHCl_3$); IR (film) 3289 (br), 3183 (br, w), 2956, 1589, 1499, 1273, 1200 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.28 (m, 4H), 7.15-7.12 (m, 4H), 7.04-7.00 (m, 2H), 3.94 (dd, *J* = 11.6, 4.9 Hz, 1H), 3.87 (br s, 1H), 3.81 (ddd, apparent td, *J* = 9.2, 9.2, 2.4 Hz, 1H), 3.75 (dd, *J* = 11.6, 8.5 Hz, 1H), 2.93 (ddd, apparent td, *J* = 8.7, 8.7, 4.9 Hz, 1H), 1.88-1.80 (m, 1H), 1.50 (s, 3H), 1.42-1.30 (m, 2H), 1.36 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 129.2, 122.6, 120.4, 98.5, 69.7, 62.8, 56.4, 41.8, 28.4, 23.8, 23.7, 21.4, 19.9; MS *m*/*z* (relative intensity) 355 ([M+H]$^+$, 97%), 354 (M$^+$, 100%), 297 (25%), 209 (20%), 168 (25%). Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.45; H, 8.46; N, 7.81.

Acetonide 14c (R = ^{i}Pr). From *anti*-**13c** (35 mg, 0.117 mmol) via General Procedure D was obtained **14c** (23 mg, 58% yield) as a colorless viscous oil; $[\alpha]_D^{20}$ –44° (*c* 1.15, $CHCl_3$); IR (film) 3289 (br, w), 3179 (br, w), 2963, 2876, 1590, 1498, 1265, 1228, 1201, 1076 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.29 (m, 4H), 7.26-7.23 (m, 4H), 7.04-7.00 (m, 2H), 3.90 (dd, *J* = 11.5, 4.7 Hz, 1H), 3.87 (br s, 1H), 3.75 (dd, *J* = 11.5, 7.3 Hz, 1H), 3.56 (ddd, *J* = 8.7, 7.3, 4.7 Hz, 1H), 3.06 (ddd, *J* = 8.7, 7.3, 4.7 Hz, 1H), 1.82 (m, apparent septet of d, *J* = 6 x 6.8, 3.2 Hz, 1H), 1.47 (s, 3H), 1.35 (s, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.2, 129.2, 122.7, 120.5, 98.7, 75.1, 62.3, 53.5, 29.0, 27.9, 20.4, 19.2, 15.4; MS *m*/*z* (relative intensity) 341 ([M+H]$^+$, 20%), 340 (M$^+$, 20%), 174 (35%), 170 (100%), 168 (55%). Anal. Calcd for $C_{21}H_{28}N_2O_2$: C, 74.08; H, 8.29; N, 8.23. Found: C, 74.20; H, 8.27; N, 8.11.

Acetonide 14d (R = Ph). From **13d** (15 mg, 0.045 mmol) via General Procedure D was obtained **14d** (12 mg, 71% yield) as a colorless viscous oil; IR (film) 3281 (br, w), 3176 (br, w), 1590, 1498, 1265, 1223, 1198, 1164, 1086 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.38 (m, 5H), 7.20-7.16 (m, 4H), 6.97-6.93 (m, 2H), 6.85-6.82 (m, 4H), 4.69 (d, *J* = 9.7 Hz, 1H), 4.15 (dd, *J* = 11.4, 4.9 Hz, 1H),

4.02 (dd, *J* = 11.3, 10.1 Hz, 1H), 3.90 (br s, 1H), 3.15 (ddd, *J* = 9.8, 9.8, 4.9 Hz, 1H), 1.64 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 129.0, 128.8, 127.6, 122.4, 120.4, 99.3, 74.8, 64.0, 56.0, 29.3, 19.3; MS *m*/*z* (relative intensity) 375 ([M+H]+, 45%), 374 (M+, 40%), 209 (35%), 183 (90%), 168 (100%). Anal. Calcd for $C_{24}H_{26}N_2O_2$: C, 76.98; H, 7.00; N, 7.48. Found: C, 75.78; H, 6.88; N, 7.13.

Tin-Mediated Vinyl Addition

(2,4-Dihydroxy-3-(*N*,*N*-diphenylhydrazino)-1-butyl)tributylstannane (20). A solution of silyl ether **17** (464 mg, 1.5 mmol) and tributyltin hydride (0.60 mL, 2.25 mmol) in benzene (7.5 mL) was deoxygenated (nitrogen via needle) for 5 min, then AIBN (15 mg, 0.09 mmol) was added and the mixture was heated at reflux. At 2 h and 14 h, additional aliquots of AIBN (2 x 15 mg) were added. After 17 h, TLC showed complete consumption of reactant. The mixture was concentrated in vacuo, leaving a residual oil (0.96 g). To a portion of the residual oil (0.24 g) in THF (3 mL) and methanol (3 mL) was added KF (44 mg, 0.76 mmol), $KHCO_3$ (75 mg, 0.75 mmol), and H_2O_2 (30%, 0.23 mL, 2.0 mmol), and the mixture was heated at reflux. After 2 h, the mixture was cooled, diluted with ether, and filtered. The filtrate was washed with brine, dried (Na_2SO_4), and concentrated. Flash chromatography (10:1 → 5:1 hexanes/EtOAc) afforded diol **20** (124 mg, 60% yield, dr 1.9:1) as a pale yellow waxy solid. Major diasteromer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.29 (m, 4H), 7.20-7.17 (m, 4H), 7.05-7.01 (m, 2H), 4.62 (br s, 1H), 4.05 (ddd, *J* = 10.2, 6.2, 4.4 Hz, 1H), 3.92 (dd, *J* = 11.5, 3.3 Hz, 1H), 3.67 (dd, *J* = 11.3, 3.6 Hz, 1H), 2.89 (ddd, *J* = 6.8, 3.6, 3.6 Hz, 1H), 2.19 (br s, 1H), 2.10 (br s, 1H), 1.52-1.42 (m, 6H), 1.34-1.27 (m, 6H), 1.20 (dd, *J* = 13.1, 4.2 Hz, 1H), 1.07 (dd, *J* = 13.1, 9.9 Hz, 1H), 0.92-0.79 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 129.3, 122.9, 120.7, 71.5, 65.1, 61.7, 29.2, 27.3, 16.2, 13.7, 9.7; Minor diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.13 (ddd, *J* = 9.6, 6.5, 3.4 Hz, 1H), 3.91-3.88 (m, 2H), 3.01-2.97 (m, 1H), 2.72 (br s, 1H), 1.14 (dd, *J* = 12.8, 9.7 Hz, 1H), 0.97 (dd, *J* = 12.9, 6.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 122.8, 120.5, 70.5, 63.8, 60.6, 13.9, 9.5; some resonances were not resolved from those of the major isomer. Diastereomer mixture: IR (film) 3390 (br, s), 3066, 3036, 2925 (s), 1559, 1500 (s), 1276, 1051 cm^{-1}; MS (CI) *m*/*z* (relative intensity) 562.9 ([M+H]$^+$, ^{120}Sn, 1.9%), 561.2 ([M+H]$^+$, ^{118}Sn, 1.5%), 291 (Bu_3Sn^+, ^{120}Sn, 23%), 289 (Bu_3Sn^+, ^{120}Sn, 15%), 227 (100%), 170 (97%); Anal. Calcd for $C_{28}H_{46}N_2O_2Sn$: C, 59.91; H, 8.26; N, 4.99. Found: C, 60.14; H, 8.28; N, 5.00.

1-(2-Methoxy-2-propyl)oxy-2-(*N*,*N*-diphenylhydrazino)-3-butene (21) and *N*-(Diphenylamino)vinylglycinol (19). A solution of diol **20** (35.5 mg, 0.063 mmol), PPTS (16 mg, 0.063 mmol) and 2,2-dimethoxypropane (0.12 mL) in $CHCl_3$ (0.6 mL) was stirred at ambient temperature for 14 h. Concentration and gradient flash chromatography afforded **21** (12.3 mg, 60% yield) and **19** (4.6 mg, 29% yield). The latter was identical to **19** formed through tandem thiyl addition–cyclization (See Experimental Section). **21**: pale yellow oil; IR (film) 3290 (br, w), 3070, 2998 (s), 2934 (s), 1592 (s), 1498 (s), 1381, 1273, 1217 (s), 1150, 1075 (s), 1046 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.18 (m, 8H), 6.99-6.95 (m, 2H), 5.80 (ddd, *J* = 17.3, 10.4, 7.9 Hz, 1H), 5.17-5.11 (m, 2H), 4.61 (s, 1H), 3.66 (m, apparent q, *J* = 7.1 Hz, 1H), 3.47 (ABq (Δν = 15.4 Hz, *J* = 14.5 Hz, 2H), 3.17 (s, 3H), 1.34 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 136.7, 128.9, 121.9, 120.3, 118.4, 100.1, 62.3, 60.3, 48.6, 24.32, 24.28; MS (CI) *m*/*z* (relative intensity) 327 ([M+H]$^+$, 100%), 295 ([M–OCH_3]$^+$, 70%).

General Procedure G: Preparation of 2,2-Dimethyloxazolidines (25, 26a–26c). A solution of hydrazino alcohol (e.g., **19**, **23a**–**23c**) in $CHCl_3$ (ca. 0.2M) was treated with 2,2-dimethoxypropane (ca. 1 mL/mmol of hydrazino alcohol) and PPTS (1 equiv). After 1 d at room temperature, the reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Radial or flash chromatography (10:1 hexane/EtOAc) furnished the major *cis* diastereomer. Only from **23a** was the minor diastereomer *trans*-**26a** obtained in pure form.

Oxazolidine 25 (R = H). From **19** (12 mg, 0.047 mmol), 2,2-dimethoxypropane (0.2 mL), and PPTS (12 mg, 0.047 mmol) by General Procedure G was obtained oxazolidine **25** (7.1 mg, 51% yield)

as a colorless solid: mp 89-91 °C; IR (film) 3061 (w), 2981, 2867, 1588 (s), 1490 (s), 1298, 1268, 1193, 1029 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29-7.20 (m, 8H), 7.00-6.90 (m, 2H), 5.98 (ddd, *J* = 17.4, 10.1, 8.0 Hz, 1H), 5.11 (d, *J* = 10.1 Hz, 1H), 5.05 (d, *J* = 17.4 Hz, 1H), 4.15 (dd, apparent t, *J* = 8.4, 1H), 4.05 (ddd, apparent q, *J* = 8.1 Hz, 1H), 3.71 (dd, apparent t, *J* = 8.2 Hz, 1H), 1.37 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.1, 128.8 (broad peak, unresolved resonances), 117.8, 97.6, 67.9, 60.4, 27.5, 23.4; MS (CI) *m*/*z* (relative intensity) 294 (M^+, 44%), 183 (50%), 168 (Ph_2N^+, 100%); Anal. Calcd for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.49; H, 7.59; N, 9.60.

Oxazolidine 26a (R = Me). From **23a** (89 mg, 0.33 mmol), 2,2-dimethoxypropane (0.33 mL, 2.68 mmol), and PPTS (83 mg, 0.33 mmol) by General Procedure G was obtained acetonide as a mixture of diastereomers (82 mg, 81% yield) as a colorless oil. Major diastereomer (*cis*-**26a**): $[\alpha]_D^{28}$ –19.5° (*c* 0.38, ether); IR (film) 2978, 1589, 1491, 1376, 1260, 1178, 1070, 925, 747 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.30-7.20 (m, 4H), 7.15-7.10 (m, 4H), 7.05-6.90 (m, 2H), 5.98 (ddd, *J* = 19.5, 10.5, 9.0 Hz, 1H), 5.21 (d, *J* = 19.0 Hz, 1H), 5.19 (d, *J* = 10.5 Hz, 1H), 4.25 (ddd, 7.7, 6.5, 6.5, 6.5), 1H), 4.08 (dd, *J* = 8.8, 7.9 Hz, 1H), 1.47 (s, 3H), 1.27 (d, *J* = 6.5 Hz, 3H), 1.05 (s, 3H) ; ^{13}C NMR (125 MHz, C_6D_6) δ 136.9, 128.8, 118.4, 94.1, 72.8, 63.6, 27.7, 23.3, 18.3; MS (CI) *m*/*z* (relative intensity) 309 ($[M+H]^+$, 47%), 170 (100%). Minor diastereomer (*trans*-**26a**): $[\alpha]_D^{25}$ +27.6° (*c* 0.51 ether); IR (film) 2979, 1589, 1491, 1376, 1260, 1070, 856, 747, 695 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.25-7.20 (m, 4H), 7.20-7.15 (m, 4H), 6.90-7.00 (m, 2H), 5.90 (ddd, *J* = 18.4, 10.0, 8.4 Hz, 1H), 5.14 (d, *J* = 10.0 Hz, 1H), 5.06 (d, *J* = 18.1 Hz, 1H), 3.99 (dddd, *J* = 8.3, 6.1, 6.1, 6.1 Hz, 1H), 3.59 (dd, *J* = 8.3, 8.3 Hz, 1H), 1.40 (s, 3H), 1.33 (s, 3H), 1.30 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 138.5, 128.7, 118.0, 96.6, 74.7, 67.5, 28.2, 24.2, 17.2; MS (CI) *m*/*z* (relative intensity) 309 ($[M+H]^+$, 73%), 168 (100%). Diastereomeric mixture: Anal. Calcd for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.95; H, 8.06; N, 8.81.

Oxazolidine 26b (R = ^{i}Bu). From **23b** (98 mg, 0.31 mmol), 2,2-dimethoxypropane (0.31 mL, 2.52 mmol), and PPTS (78 mg, 0.31 mmol) by General Procedure G was obtained **26b** as a mixture of diastereomers (73 mg, 67% yield) as a colorless oil. Major diastereomer (*cis*-**26b**): $[\alpha]_D^{28}$ –23.1° (*c* 0.88, ether); IR (film) 2955, 1589, 1491, 1376, 1259, 1176, 1028, 746 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.24-7.22 (m, 4H), 7.13-7.11 (m, 4H), 6.88-6.80 (m, 2H), 6.00 (ddd, *J* = 19.5, 10.4, 9.2 Hz, 1H), 4.93 (d, *J* = 19.1 Hz, 1H), 4.91 (d, *J* = 10.0 Hz, 1H), 4.11 (ddd, *J* = 10.9, 7.9, 3.3 Hz, 1H), 4.00 (dd, *J* = 8.9, 8.0 Hz, 1H), 2.05-1.95 (m, 1H), 1.78 (ddd, *J* = 13.5, 10.5, 4.9 Hz, 1H), 1.52 (s, 3H), 1.25 (ddd, *J* = 13.5, 8.8, 3.3 Hz, 1H), 1.10 (s, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 137.3, 128.9, 118.3, 94.2, 74.9, 63.7, 41.4, 27.9, 24.8, 23.7, 23.4, 21.5; MS (CI) *m*/*z* (relative intensity) 351 ($[M+H]^+$, 80%), 170 (100%). Diastereomeric mixture: Anal. Calcd for $C_{23}H_{30}N_2O$: C, 78.82; H, 8.63; N, 7.99. Found: C, 78.81; H, 8.68; N, 7.98.

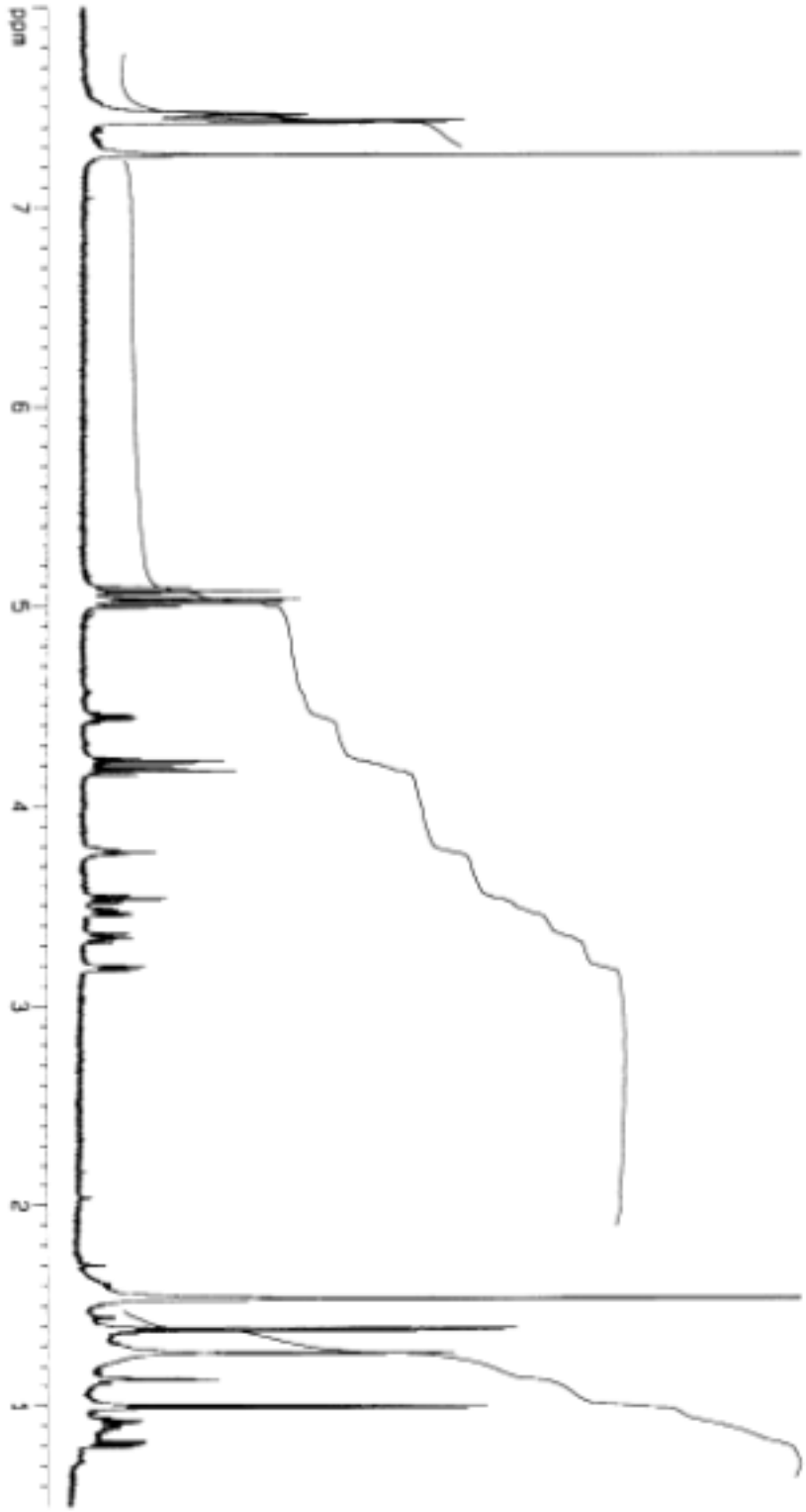
Oxazolidine 26c (R = ^{i}Pr). From **23c** (100 mg, 0.33 mmol), 2,2-dimethoxypropane (0.33 mL, 2.68 mmol), and PPTS (83 mg, 0.33 mmol) by General Procedure G was obtained *cis*-**26c** (92 mg, 82% yield) after recrystallization from hexane as a colorless solid: mp 97-99 °C; $[\alpha]_D^{29}$ +52.8°, (*c* 0.69, $CHCl_3$); IR (film) 2980, 1589, 1491, 1258, 1176, 1029, 746 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28-7.26 (m, 4H), 7.26-7.25 (m, 4H), 7.18-7.16 (m, 2H), 6.11 (ddd, *J* = 17.3, 10.0, 10.0 Hz, 1H), 5.20 (d, *J* = 10.0 Hz, 1H), 5.15 (d, *J* = 17.3 Hz, 1H), 4.05 (dd, *J* = 8.8, 7.9 Hz, 1H), 3.77 (dd, *J* = 7.8, 7.8 Hz, 1H), 1.94-1.86 (m, 1H), 1.42 (s, 3H), 1.23 (s, 3H), 1.11 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 137.0, 128.7, 118.6, 94.3, 82.0, 62.7, 28.7, 28.1, 23.3, 19.7, 19.0; MS (CI) *m*/*z* (relative intensity) 337 ($[M+H]^+$, 100%), 168 (33%); Anal. Calcd for $C_{22}H_{28}N_2O$: C, 78.53; H, 8.39; N, 8.33. Found: C, 78.95; H, 8.51; N, 8.12.

Chemical Correlation of 26c and 14c via Oxazolidine 27. A solution of diastereomerically pure **26c** (186.6 mg, 0.56 mmol) and OsO_4 (84 mg, 0.33 mmol) in dioxane/water (3:1, 18 mL) was stirred at room temperature for 1 h, and sodium periodate (230.0 mg, 1.12 mmol) was added. After 1 d the solution was diluted with EtOAc, washed with water, then brine, dried (Na_2SO_4), and concentrated. A solution of the crude aldehyde in MeOH (2.03 mL) was treated with $NaBH_4$ (53.4 mg, 1.40 mmol) at 0

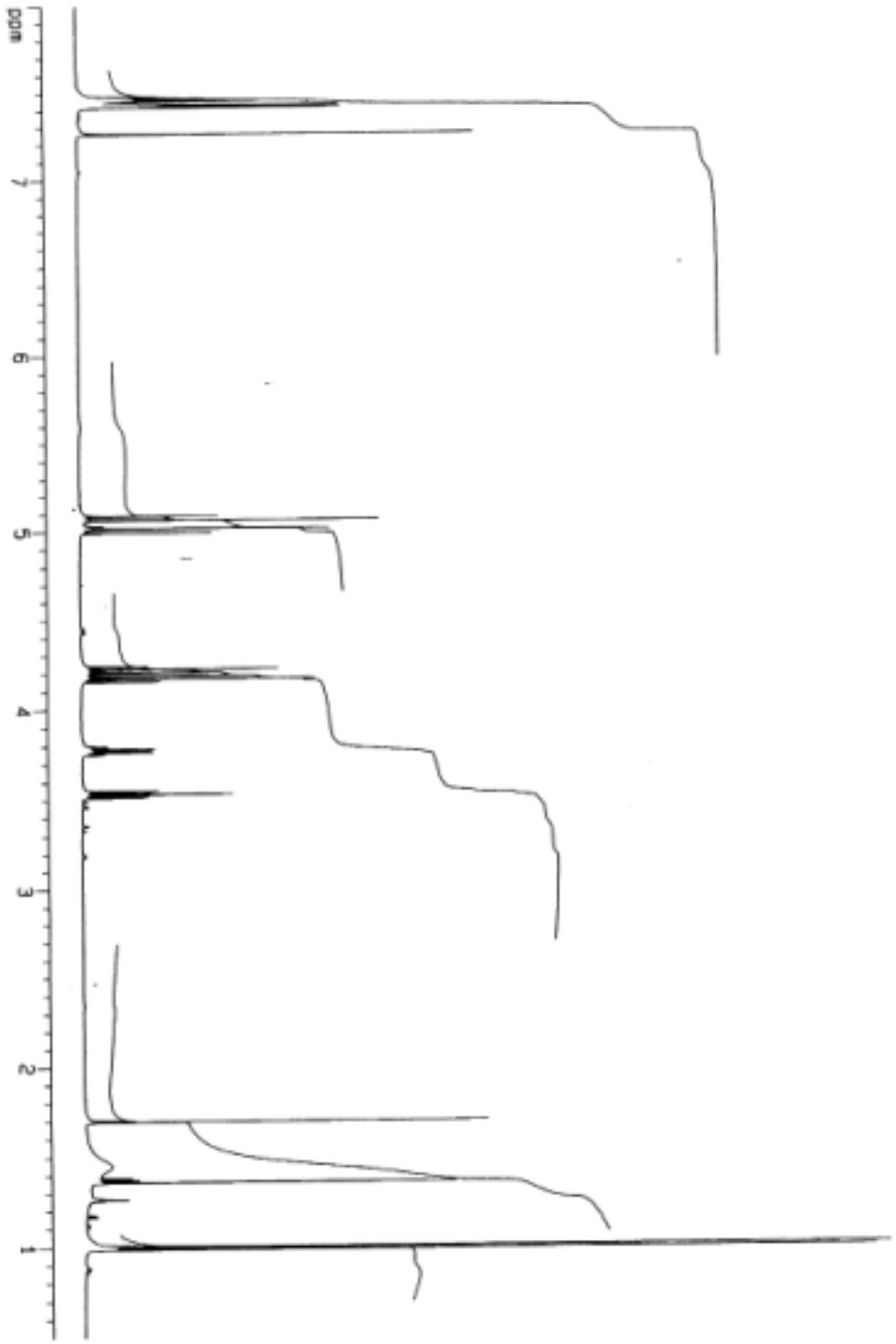
°C. After 12 h the solution was diluted with ether, washed with water, dried (Na_2SO_4) and concentrated. Flash chromatography (10:1 hexane/EtOAc) furnished oxazolidine **27** (20 mg, 10% yield) as a colorless oil; $[\alpha]_D^{26}$ +20.4° (*c* 0.51, ether); IR (film) 3481, 2960, 1588, 1490, 1270, 1029, 747 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.30-7.29 (m, 4H), 7.10-7.06 (m, 4H), 6.81-6.79 (m, 2H), 4.00 (d, *J* = 9.0 Hz, 2H), 3.72 (ddd, *J* = 8.3, 8.3, 5.4 Hz, 1H), 3.50 (dd, *J* = 9.3, 5.4 Hz, 1H), 1.72-1.69 (m, 1H), 1.61 (d, *J* = 3.9 Hz, 1H), 1.37 (s, 6H), 0.73 (d, *J* = 6.8 Hz, 3H), 0.67 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 128.9, 97.8, 76.6, 64.0, 59.1, 30.5, 27.4, 23.4, 19.1, 16.9; MS (CI) *m*/*z* (relative intensity) 341 ($[M+H]^+$, 60%), 170 (100%); Anal. Calcd for $C_{21}H_{28}N_2O_2$: C, 74.08; H, 8.29; N, 8.23. Found: C, 73.90; H, 8.42; N, 8.27.

A solution of **27** (10 mg, 0.03 mmol) obtained above, 2,2-dimethoxypropane (0.035 mL, 0.28 mmol), and PPTS (7.3 mg, 0.029 mmol) in $CHCl_3$ (0.15 mL) was stirred for 1 d at room temperature, then partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Flash chromatography with 10:1 hexane/EtOAc furnished **14c** (7.2 mg, 70% yield) as a colorless oil, identical to the sample prepared from **11c** using General Procedures C and D.

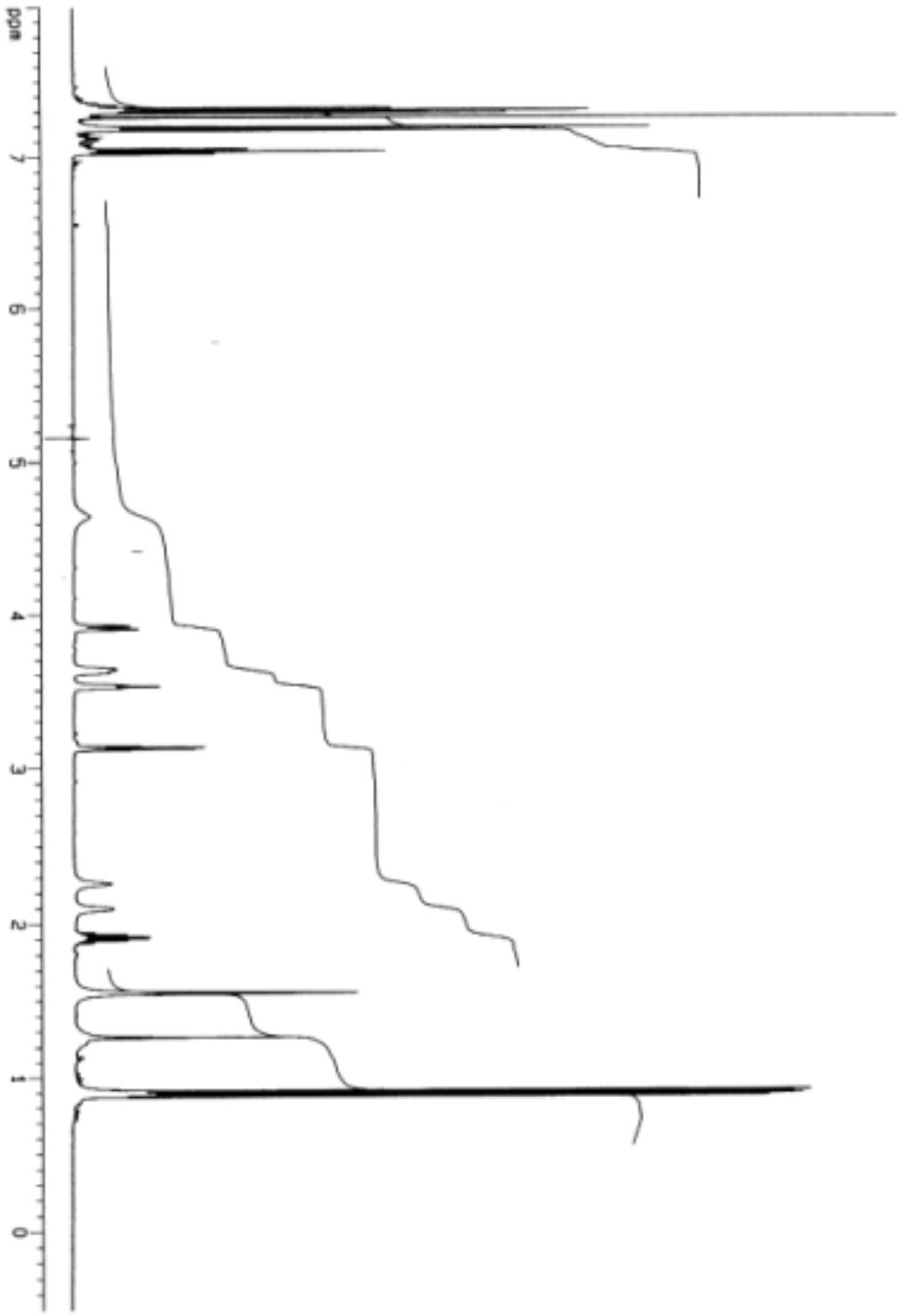
^{1}H NMR spectrum of *trans*-**6** (500 MHz, $CDCl_3$), as a 1:1.2 mixture with **7**



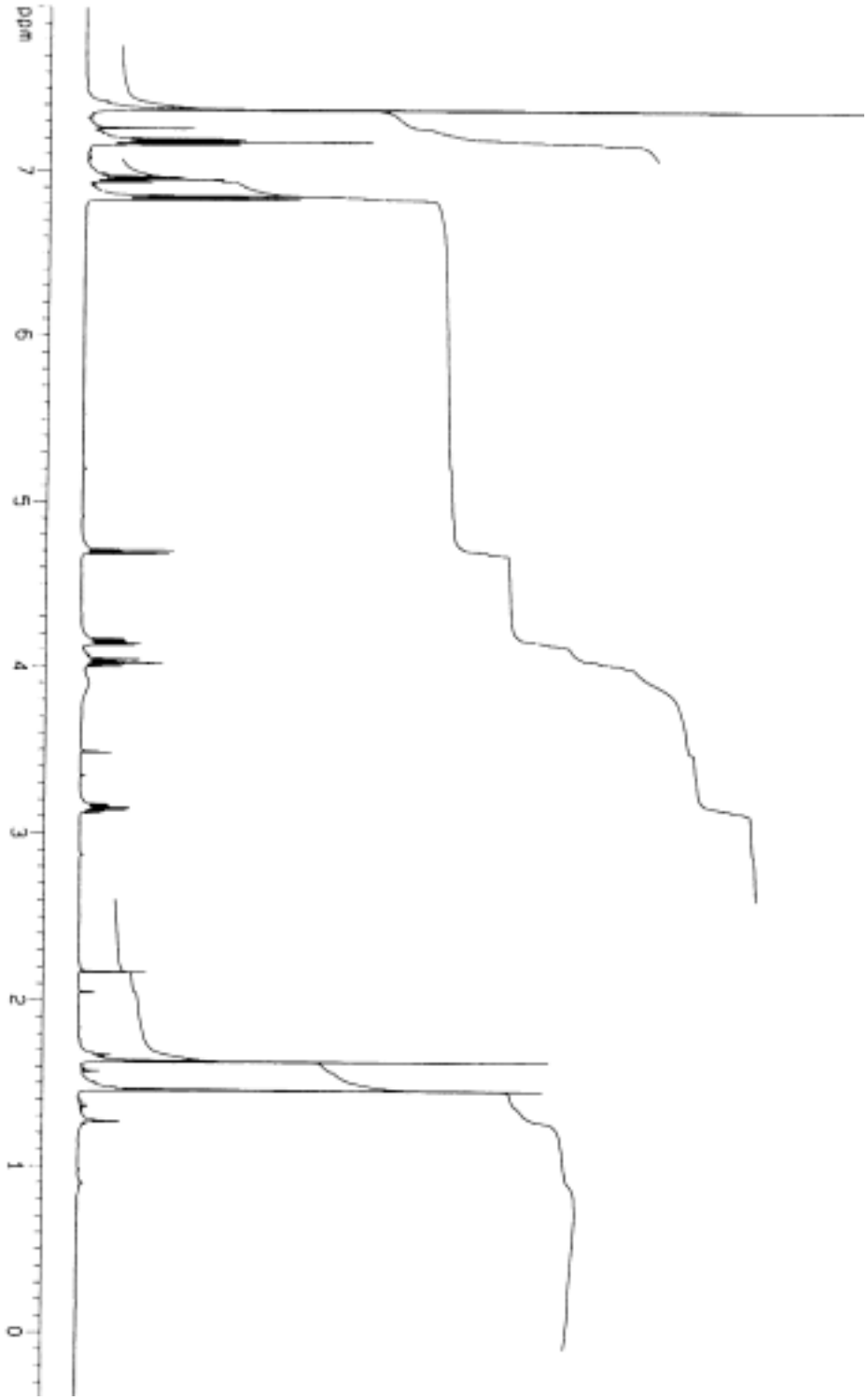
^{1}H NMR spectrum of **7** (500 MHz, $CDCl_3$)



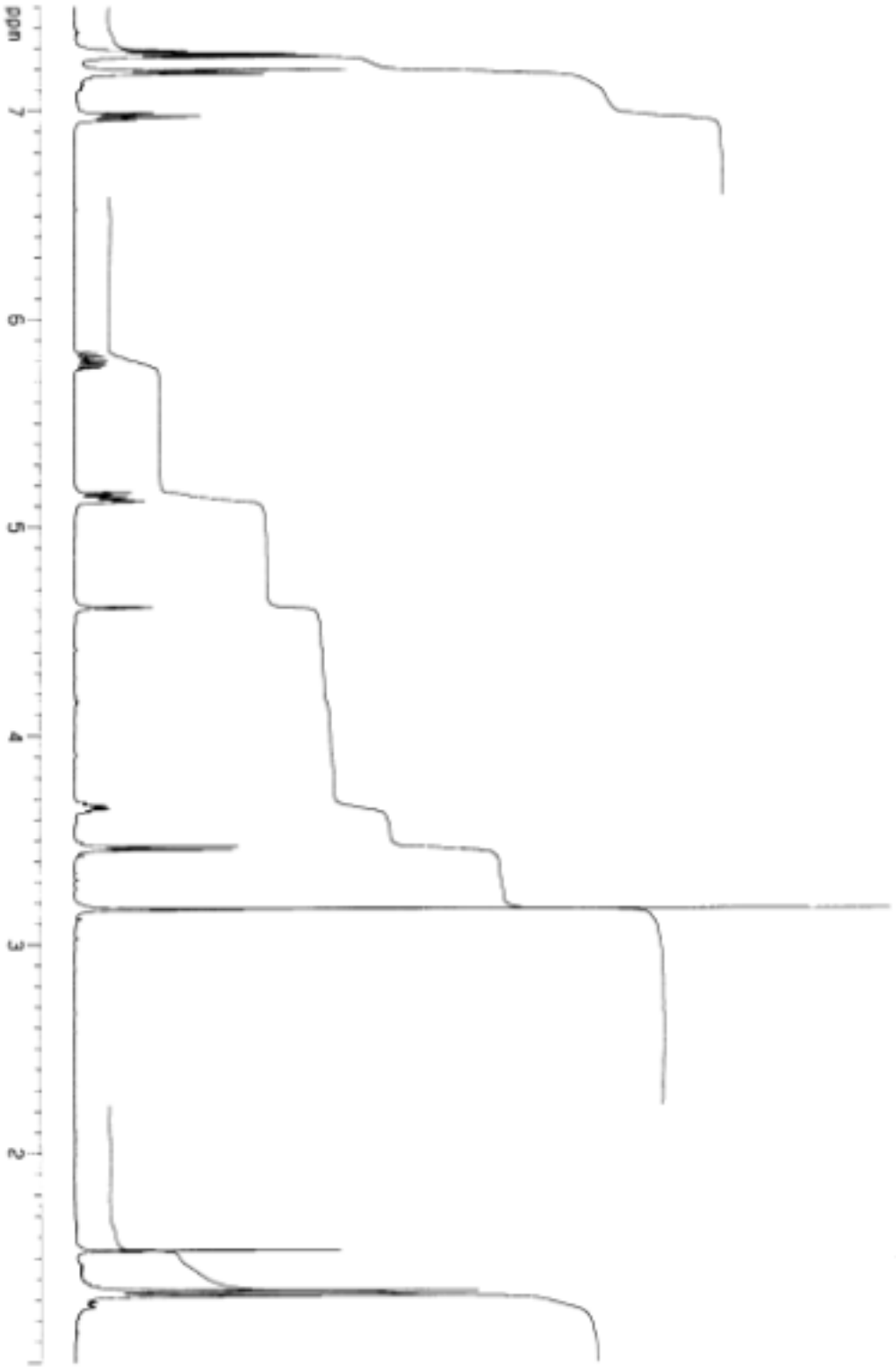
^{1}H NMR spectrum of *syn*-**13c** (500 MHz, $CDCl_3$)



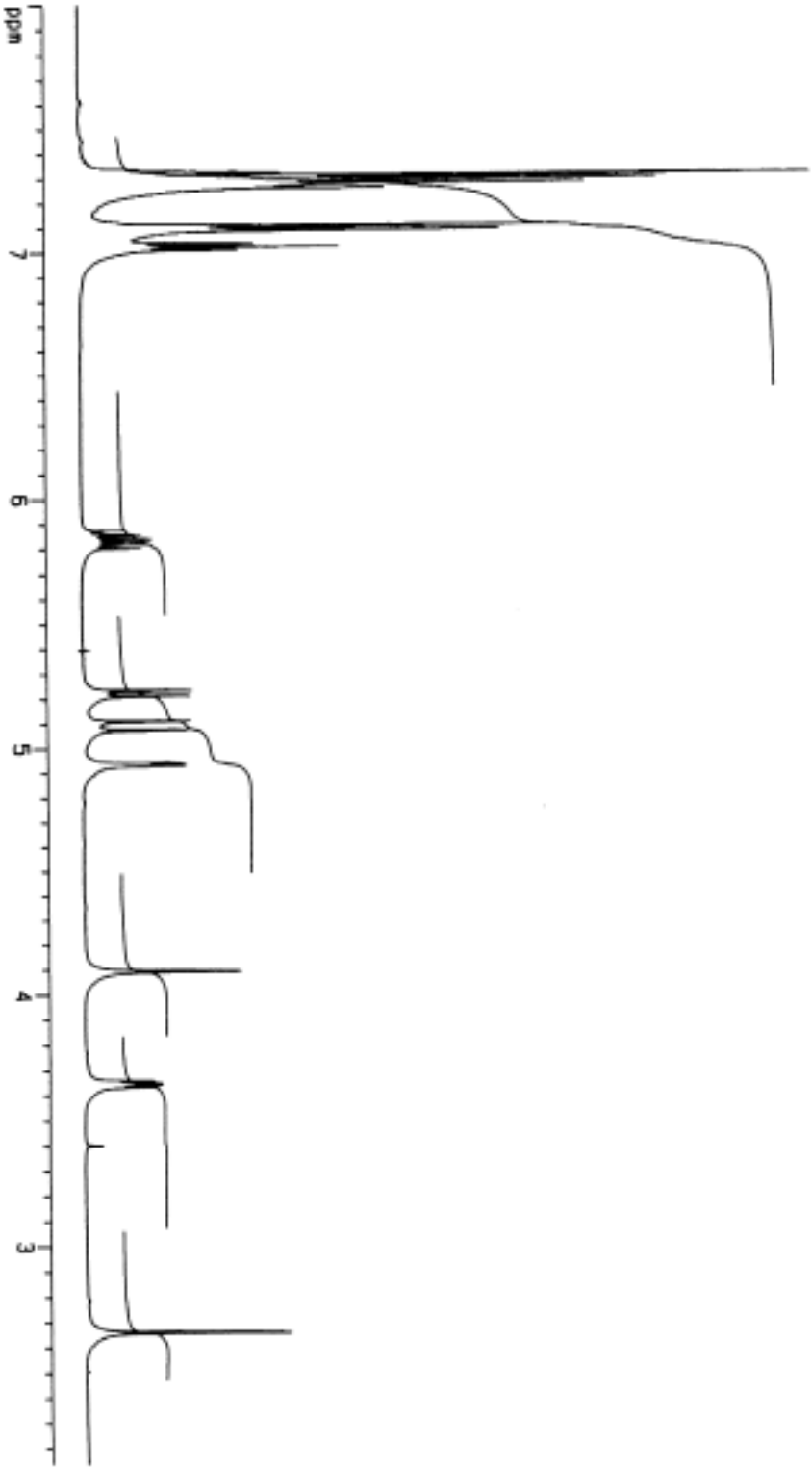
^{1}H NMR spectrum of **14d** (500 MHz, $CDCl_3$)



^{1}H NMR spectrum of **21** (500 MHz, $CDCl_3$)



^{1}H NMR spectrum of **23d** (500 MHz, $CDCl_3$)



^{1}H NMR spectrum of **32** (500 MHz, $CDCl_3$), as a mixture of diastereomers (dr = 91:9)