



Supporting Information

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Kinetic Resolution of 1,2-Diols Through Highly Site- and Enantioselective Catalytic Silylation

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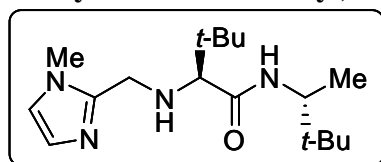
General information. Infrared (**IR**) spectra were recorded on a Perkin Elmer 781 spectrophotometer, ν_{\max} in cm^{-1} . Bands are characterized as broad (br), strong (s), medium (m), and weak (w). **^1H NMR** spectra were recorded on a Varian GN-400 (400 MHz). Chemical shifts are reported in ppm with the solvent reference as the internal standard (CHCl_3 : δ 7.26). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), and coupling constants (Hz). **^{13}C NMR** spectra were recorded on a Varian GN-400 (100 MHz) with complete proton decoupling. Melting points (**mp**) were taken with a Laboratory Devices Melt-Temp and were uncorrected. Enantiomeric ratios were determined by chiral gas liquid chromatography (GLC) on a Hewlett Packard HP 6890 with a Beta Dex 120 (30 m x 0.25

mm x 0.25 μ m film thickness) or a Gamma Dex 120 (30 m x 0.25 mm x 0.25 μ m film thickness) column by Supelco in comparison with authentic racemic materials. **Optical rotations** were measured on a Rudolph Research Analytical Autopol IV Automatic Polarimeter. High resolution mass spectrometry (**HRMS**) was performed by mass spectrometry facility at Boston College.

All reactions were conducted under open atmosphere in 10 x 75 mm borosilicate test tubes. All commercially available reagents listed below were used as received for the reactions without any purification. Liquid reagents were handled with a Gilson Pipetman. THF was dried on alumina columns using a solvent dispensing system. The catalyst **1** was synthesized following the reported procedure;¹ an optimized procedure is given below. *tert*-Butyldimethylsilyl chloride (TBSCl), diisopropylethylamine (DIPEA) and 3,3-dimethylbutane-1,2-diol (*rac*-**5c**) were purchased from Aldrich. 4-Methylpentane-2,3-diol (*rac*-**2a**), pentane-2,3-diol (*rac*-**2d**), 3,3-diethoxypropane-1,2-diol (*rac*-**5b**), 2-methylheptane-1,2-diol (*rac*-**6a**), 2,3-dimethylbutane-1,2-diol (*rac*-**6b**) and 2,3,3-trimethylbutane-1,2-diol (*rac*-**6c**) were synthesized by *cis*-dihydroxylation of the corresponding commercially available *cis*-alkenes.² 1-phenylpropane-1,2-diol (*rac*-**2c**), 1,1-diethoxybutane-2,3-diol (*rac*-**2f**), ethyl 2,3-dihydroxybutanoate (*rac*-**2g**) and *tert*-butyl 2,3-dihydroxybutanoate (*rac*-**2h**) were synthesized by Lindlar reduction of the corresponding commercially available alkynes followed by *cis*-dihydroxylation; the synthesis of (*rac*-**2f**) is detailed as a representative example (Page SI 20). 1-Cyclohexylpropane-1,2-diol (*rac*-**2b**) was synthesized by Lindlar reduction of the corresponding alkyne (synthesized from ethynylcyclohexane and ethyl iodide) followed by *cis*-dihydroxylation. 3,4-Dihydroxypentan-2-one (*rac*-**2e**) was synthesized by a four-step procedure: transformation of methyl 2-butyrate to the corresponding Weinreb amide, methyl magnesium chloride addition followed by Lindlar reduction and *cis*-dihydroxylation. 3-*tert*-Butoxypropane-1,2-diol (*rac*-**5a**) was synthesized according to literature procedure.³

For the kinetic resolution, selectivity factors (k_{rel}) were calculated according to Kagan's equation: $k_{rel} = \ln((1-c)(1-ee_{rsm}))/\ln((1-c)(1+ee_{rsm})) = \ln(1-c(1+ee_{prod}))/\ln(1-c(1-ee_{prod}))$, wherein *c* is conversion of the reaction, ee_{prod} is the enantiomeric excess of the mono silyl ether product and ee_{rsm} is the enantiomeric excess of the recovered diol. Conversions (*c*) were calculated by the following equation: $c = ee_{rsm}/(ee_{prod} + ee_{rsm})$, which is equivalent to eq 7 ($ee_{rsm}/ee_{prod} = c/(1-c)$) in Kagan's review on kinetic resolution⁴.

Procedure for the synthesis of (*S*)-N-((*R*)-3,3-dimethylbutan-2-yl)-3,3-dimethyl-2-((1-methyl-1H-imidazol-2-yl)methylamino)butanamide (1**).⁵**



Boc-*tert*-Leucine (2.3 g, 10 mmol) and (*R*)-3,3-dimethyl-2-butylamine (1.3 mL, 10 mmol) were dissolved in 40 mL CH₂Cl₂ in a 100 mL round bottom flask. To this solution were added EDC (2.1 g, 11 mmol),

¹ Zhao Y.; Rodrigo, J.; Hoveyda, A. H.; Snapper, M. L. *Nature* **2006**, *443*, 67-70.

² VanRheenen, V.; Kelly R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, *17*, 1973-1976.

³ Takano, S.; Ohkawa, T.; Gasawara, K. *Tetrahedron Lett.* **1988**, *29*, 1823-1824.

⁴ Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1998**, *18*, 249-330.

⁵ Catalyst **1** is available from Sigma-Aldrich (# 680826).

HOBt (1.7 g, 11 mmol) and DIPEA (4.4 mL, 25 mmol). The mixture was allowed to stir for 16 h at 22 °C after which time 15 mL of 10 % citric acid was added. The organic layer was separated and washed with 15 mL of a saturated solution of NaHCO₃ and then 15 mL of brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to yield a white solid. This white solid was placed in a round-bottom flask and cooled to 0 °C, HCl/dioxane (7.5 mL of 4.0 M solution) was added through a syringe. The mixture was allowed to warm to 22 °C over 1 h and was concentrated. The unpurified product was dissolved in water and basified with 3 N NaOH until pH 12. The product was extracted with CH₂Cl₂ (3 x 15 mL), the combined organic layer was washed with brine (1 x 10 mL), and then dried over anhydrous Na₂SO₄. After filtration and removal of the solvent, the unpurified amine was dissolved in 5 mL of CH₂Cl₂, followed by the addition of 1-methyl-2-imidazolecarboxaldehyde (1.1 g, 10 mmol) and MgSO₄. The mixture was allowed to stir for 12 h at 22 °C, filtered and concentrated to give a white solid, which was dissolved in MeOH and cooled to 0 °C. To this solution was added NaBH₄ (1.1 g, 30 mmol) and conc. HCl (~10 µL). The solution was allowed to stir for 0.5 h at 0 °C and then 1 h at 22 °C, after which time 10 mL of a saturated solution of NaHCO₃ was slowly added to quench the reaction. The product was extracted with CH₂Cl₂ (3 x 15 mL), the combined organic layer was washed with brine (1 x 10 mL), dried over anhydrous Na₂SO₄ and concentrated to yield a white solid (2.5 g, 81%). ***This unpurified product is of sufficient purity and can be used directly for the asymmetric silylation.*** If necessary, purification by chromatography (CH₂Cl₂ to 98:2 CH₂Cl₂:MeOH) yielded the catalyst as a white solid. **mp:** 130.8-132.0 °C. **IR:** 3362 (br), 3267 (br), 3060 (m), 3025, (m), 2921 (s), 1660 (s), 1366 (w), 1034 (w) cm⁻¹. **¹H NMR** (CDCl₃, 400 MHz): δ 6.94 (1H, d, *J* = 1.2 Hz), 6.82 (1H, d, *J* = 1.2 Hz), 6.51 (1H, d, *J* = 10.0 Hz), 3.91 (1H, dq, *J* = 9.6, 6.8 Hz), 3.80 (1H, d, *J* = 14.0 Hz), 3.62 (3H, s), 3.61 (1H, d, *J* = 14.0 Hz), 2.68 (1H, s), 2.15 (1H, br, s), 1.06 (3H, d, *J* = 6.8 Hz), 0.97 (9H, s), 0.92 (9H, s). **¹³C NMR** (CDCl₃, 100 MHz): δ 171.9, 146.1, 127.5, 121.2, 72.5, 52.9, 44.8, 34.3, 34.2, 32.9, 27.5, 26.7, 16.8. **HRMS** (*m/z* + H): Calculated: 309.2654; Found: 309.2652. **Optical Rotation:** [α]_D²⁵ -95 (*c* = 3.0, CHCl₃).


General procedure for the kinetic resolution of 1,2-diols through catalytic asymmetric silylation

Catalyst **1** (93 mg, 0.300 mmol or 62 mg, 0.200 mmol) and the diol substrate (1.00 mmol) were weighed into a 10 x 75 mm test tube. DIPEA (217 µL, 1.25 mmol) was added with a Gilson Pipetman. The contents were dissolved in THF (200 µL for 1.4 M solution or 500 µL for 1.0 M solution), the tube was capped with a septum, and the mixture was cooled to -78 °C. TBSCl (151 mg, 1.00 mmol) was dissolved in 100 µL THF (total volume ~ 250 µL) and added to the test tube with a Gilson Pipetman. The test tube was capped with a septum, wrapped with Teflon tape and the mixture was allowed to stir at the appropriate temperature (see below for details) in a cryocool apparatus for the reported period of time. The reaction was quenched by addition of methanol (50 µL). The mixture was allowed to warm to 22 °C, diluted with ethyl acetate (15 mL) and washed with 10% citric acid (20 mL). The aqueous layer was washed with ethyl acetate (2 x 15 mL) and the combined organic layer

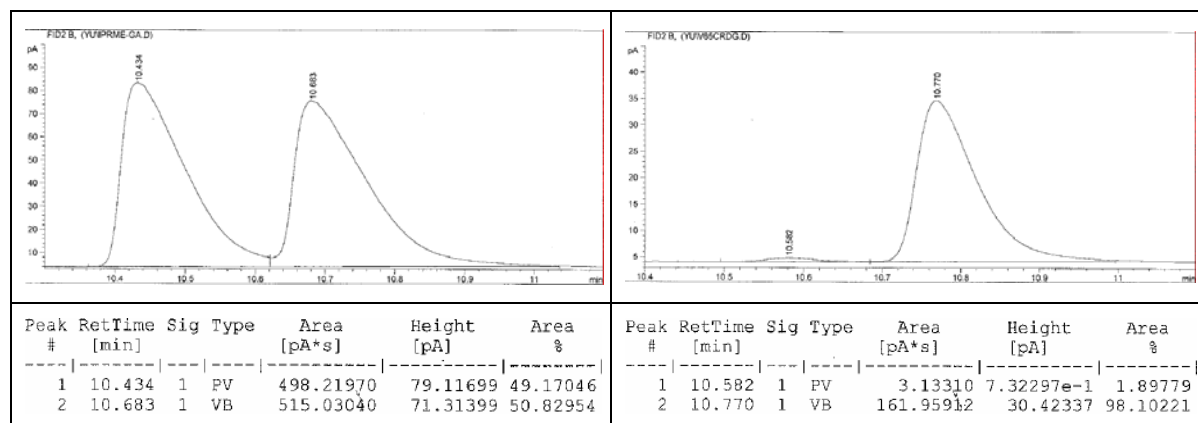
was dried over MgSO_4 , filtered and concentrated to afford a yellow oil. The product and unreacted starting material were purified by silica gel chromatography (load column with hexanes, 100 mL CH_2Cl_2 followed by 100 mL 2 % MeOH in CH_2Cl_2) and analyzed by chiral GLC (Supelco Beta, or Gamma Dex 120).

The aqueous layer was basified with 3 N NaOH until pH 12 and washed with CH₂Cl₂ (3 x 15 mL). The combined organic layer was dried over MgSO₄, filtered and concentrated under high vacuum to provide the recovered catalyst **1** as a white solid (mass recovery > 90%). The recovered catalyst was used directly for the silylation reactions with the same efficiency and selectivity.

(2*S*,3*R*)-4-methylpentane-2,3-diol (2a, Entry 1, Table 2). The general procedure was followed (0.3 equiv. **1**, substrate concentration = 1.4 M, $-50\text{ }^{\circ}\text{C}$ for 72 h) to yield the product as a colorless oil and the unreacted diol as a white solid.


 Recovered starting material: 52 mg, 44 %. **mp**: 51.0-52.5 °C. **¹H NMR** (CDCl₃, 400 MHz): δ 3.91 (1H, m), 3.29 (1H, m), 1.91 (1H, d, *J* = 4.0 Hz), 1.73 (1H, d, *J* = 6.0 Hz), 1.66 (1H, m), 1.16 (3H, d, *J* = 6.4 Hz), 1.02 (3H, d, *J* = 6.8 Hz), 0.88 (3H, d, *J* = 6.8 Hz). **¹³C NMR** (CDCl₃, 100 MHz): δ 80.2, 68.5, 30.6, 19.5, 19.1, 16.3. **Optical Rotation**: [α]_D²⁵ -1.8 (*c* = 0.76, CHCl₃).⁶

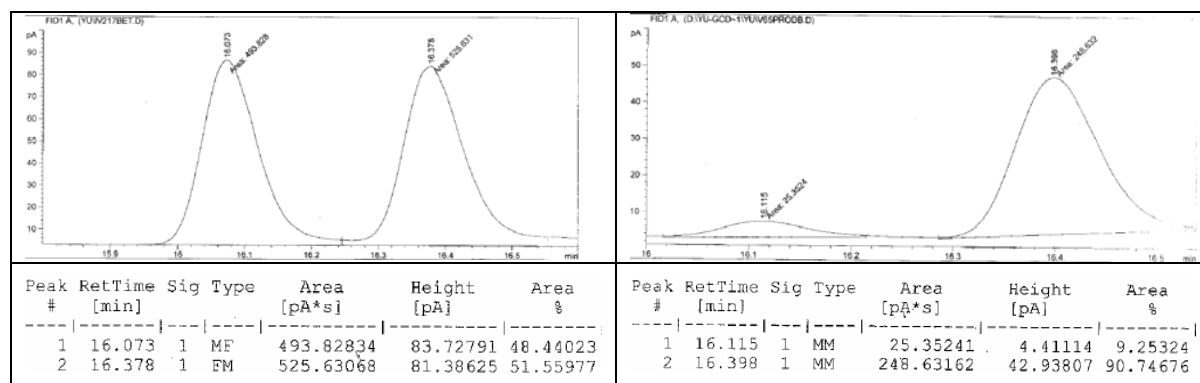
Optical purity was established by chiral GLC analysis (Supelco Gamma Dex 120 (30 m x 0.15 mm x 0.25 μ m film thickness), 80 °C to 125 °C, 2 °C/min. 25 psi.); chromatograms are illustrated below for a 96 % ee sample:



Product: 112 mg, 48 %. **IR** (neat, thin film): 3584 (w), 3496 (br), 2961 (s), 2930 (s), 2860 (m), 1480 (m), 1390 (m), 1256 (s), 1067 (s), 947 (m), 834 (s), 784 (s), 677 (m) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 3.90 (1H, m), 3.16 (1H, dd, $J = 8.4, 3.6$ Hz), 2.41 (1H, s), 1.60 (1H, m), 1.07 (3H, d, $J = 6.0$ Hz), 1.01 (3H, d, $J = 6.4$ Hz), 0.89 (9H, s), 0.83 (3H, d, $J = 7.6$ Hz), 0.07 (3H, s), 0.06 (3H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 80.4, 69.6, 30.1, 26.1, 19.8, 18.8, 18.4, 16.3, -4.09, -4.51. **HRMS** ($m/z + \text{Na}$): Calculated: 255.1756; Found: 255.1759. **Optical Rotation**: $[\alpha]_D^{25} +0.53$ ($c = 0.76, \text{CHCl}_3$).

⁶ Absolute configuration was assigned by analogy to other substrates in Table 2.

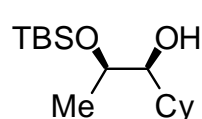
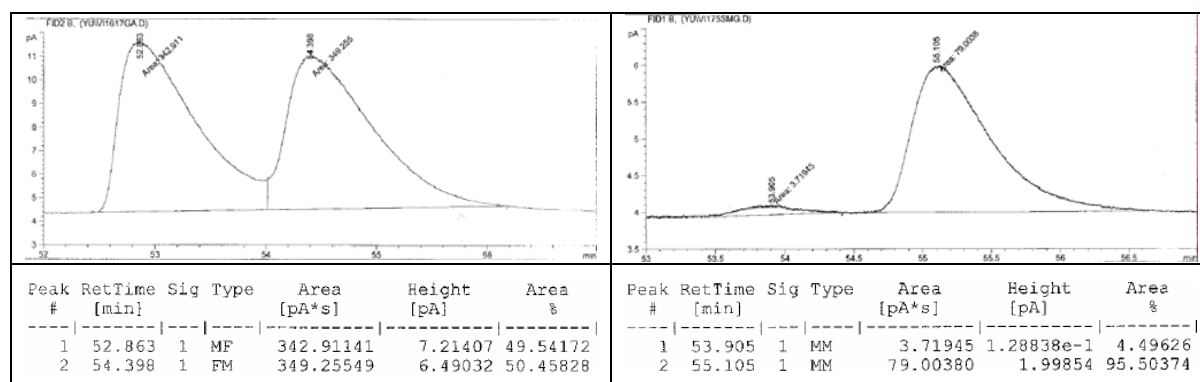
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μ m film thickness), 80 $^{\circ}$ C to 125 $^{\circ}$ C, 2 $^{\circ}$ C/min. 25 psi.); chromatograms are illustrated below for an 81 % ee sample:



(1R,2S)-1-cyclohexylpropane-1,2-diol (2b, Entry 2, Table 2). The general procedure was followed (0.3 equiv. **1**, substrate concentration = 1.4 M, -50° C for 48 h) to yield the product and the unreacted diol as colorless oil.

Recovered starting material: 76 mg, 48 %. ^1H NMR (CDCl_3 , 400 MHz): δ 3.94–3.86 (1H, m), 3.34 (1H, dd, $J = 8.4, 3.6$ Hz), 2.77 (1H, br), 2.10–0.80 (12H, m), 1.14 (3H, d, $J = 6.4$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz): δ 79.1, 68.2, 40.2, 29.6, 29.0, 26.6, 26.2, 26.0, 16.2. **Optical Rotation:** $[\alpha]_D^{25} +4.3$ ($c = 0.76$, CHCl_3).⁷

Optical purity was established by chiral GLC analysis (Supelco Gamma Dex 120 (30 m x 0.15 mm x 0.25 μ m film thickness), 110 $^{\circ}$ C for 66 min, 25 psi.); chromatograms are illustrated below for a 91 % ee sample:

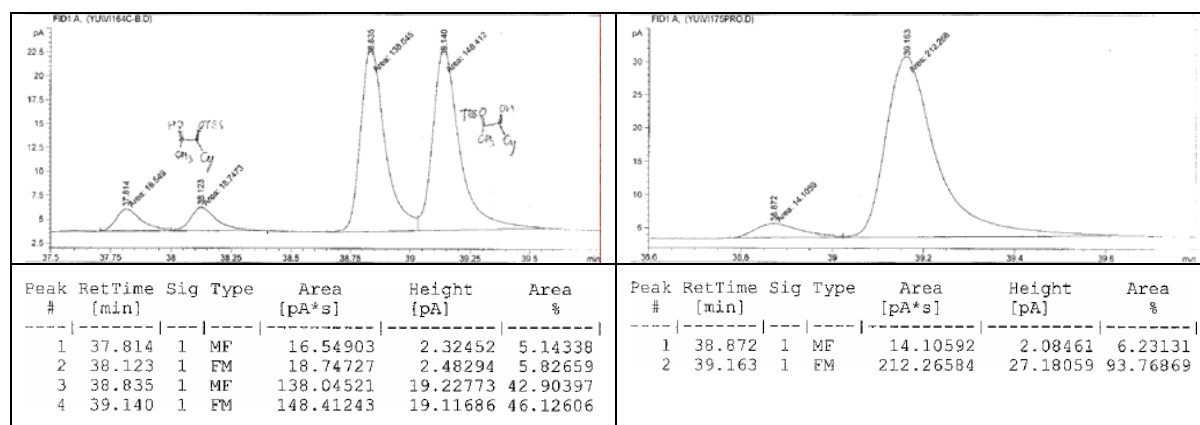


Product: 136 mg, 50 %. **IR** (neat, thin film): 3584 (w), 3490 (br), 2930 (s), 2855 (m), 1457 (w), 1388 (w), 1262 (m), 1134(m), 1080 (m), 954 (m), 840 (s), 777 (m), 677 (w) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 3.87–3.83 (1H, m), 3.23 (1H, dt, $J = 8.4, 1.6$ Hz), 2.39 (1H, d, $J = 1.6$ Hz), 2.07 (1H,

⁷ Absolute configuration of the recovered diol was assigned as (1R,2R) by comparing optical rotation to what was reported. See: Cervinka, O.; Struzka, V. *Collect. Czech. Chem. Commun.* **1990**, 55, 2685–2691.

m), 1.8-0.9 (10H, m), 1.06 (3H, d, $J = 6.0$ Hz), 0.88 (9H, s), 0.06 (3H, s), 0.05 (3H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 79.3, 69.3, 39.7, 29.9, 28.8, 26.8, 26.2, 26.1, 18.3, 16.2, -4.2, -4.6. **HRMS** ($m/z - \text{H}$): Calculated: 271.2093; Found: 271.2106. **Optical Rotation**: $[\alpha]_D^{25}$ -5.99 ($c = 1.00$, CHCl_3).

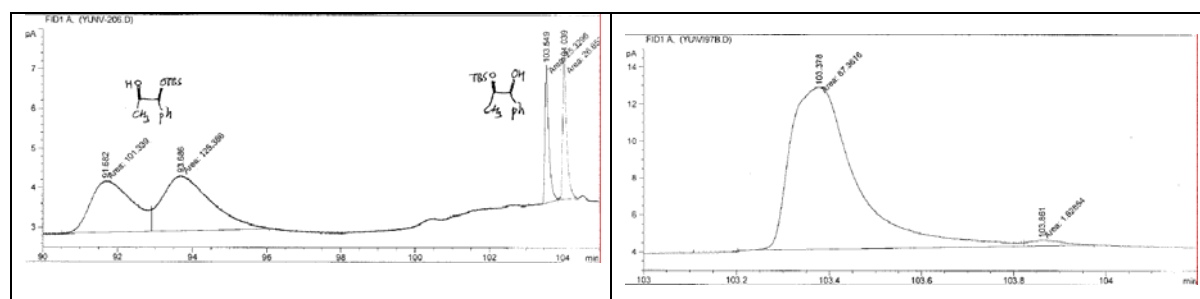
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 $^\circ\text{C}$ to 180 $^\circ\text{C}$, 2 $^\circ\text{C}/\text{min}$, 25 psi.); chromatograms are illustrated below for an 88 % ee sample:



(1R,2S)-1-phenylpropane-1,2-diol (2c, Entry 3, Table 2). The general procedure was followed (0.3 equiv. **1**, substrate concentration = 1.4 M, -40 $^\circ\text{C}$ for 48 h) to yield the product and the unreacted diol as colorless or pale yellow oil.

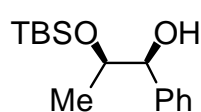
Recovered starting material: 46 mg, 30 %. ^1H NMR (CDCl_3 , 400 MHz): δ 7.37-7.27 (5H, m), 4.68 (1H, d, $J = 4.4$ Hz), 4.01 (1H, dq, $J = 6.4, 4.4$ Hz), 2.7-2.6 (2H, m), 1.08 (3H, d, $J = 6.4$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz): δ 140.5, 128.5, 128.0, 126.8, 71.5, 46.2, 17.5. **Optical Rotation**: $[\alpha]_D^{25}$ -39.4 ($c = 1.00$, CHCl_3).⁸

Optical purity was established by chiral GLC analysis after conversion to the mono silyl ether (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 110 $^\circ\text{C}$ for 98 min, 25 psi.); chromatograms are illustrated below for a 96 % ee sample:



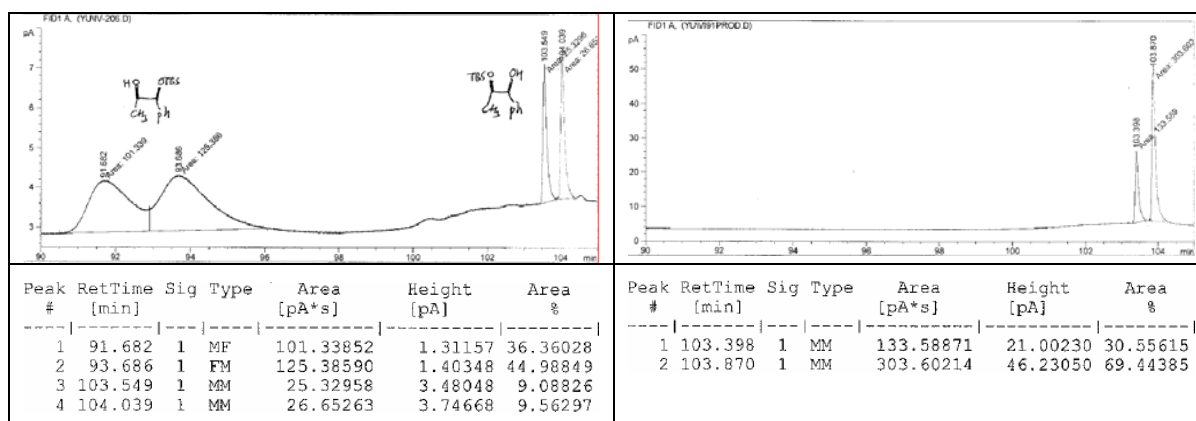
⁸ Absolute configuration of the recovered diol was assigned as (1R,2R) by comparing optical rotation to what was reported. See: Kreutz, O. C.; Moran, P. J. S.; Rodrigues, J. A. R. *Tetrahedron Asymmetry*. **1997**, 8, 2649-2653.

Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %	Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	91.682	1	MF	101.33852	1.31157	36.36028	1	103.378	1	MF	87.36164	8.77907	98.16998
2	93.686	1	FM	125.38590	1.40348	44.98849	2	103.861	1	FM	1.62854	3.16785e-1	1.83002
3	103.549	1	MM	25.32958	3.48048	9.08826							
4	104.039	1	MM	26.65263	3.74668	9.56297							



Product: 181 mg, 68 %. **IR** (neat, thin film): 3446 (br), 2955 (m), 2936 (m), 2886 (m), 2861 (m), 1476 (w), 1382 (w), 1262 (m), 1142 (m), 1092 (s), 979 (m), 897 (w), 834 (s), 777 (s), 702 (s) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 7.35-7.23 (5H, m), 4.67 (1H, dd, $J = 4.0, 2.0$ Hz), 4.00 (1H, dq, $J = 6.0, 4.0$ Hz), 2.61 (1H, d, $J = 2.0$ Hz), 0.98 (3H, d, $J = 6.0$ Hz), 0.91 (9H, s), 0.07 (3H, s), 0.04 (3H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 140.8, 128.2, 127.5, 126.6, 77.6, 72.7, 26.1, 18.3, 17.3, -4.29, -4.76. **HRMS** ($m/z + \text{Na}$): Calculated: 289.1600; Found: 289.1597.

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 110 $^\circ\text{C}$ for 98 min, 25 psi.); chromatograms are illustrated below for a 39 % ee sample:

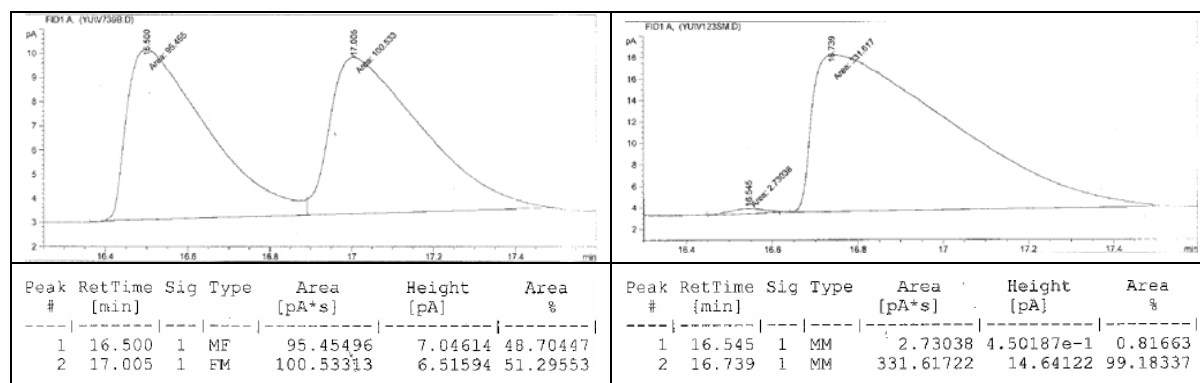


(2S,3R)-pentane-2,3-diol (2d, Entry 4, Table 2). The general procedure was followed (0.3 equiv. **1**, substrate concentration = 1.4 M, -40 $^\circ\text{C}$ for 48 h) to yield the product and the unreacted diol as colorless or pale yellow oil.

Recovered starting material: 38 mg, 36 %. **^1H NMR** (CDCl_3 , 400 MHz): δ 3.78 (1H, dq, $J = 6.8, 3.2$ Hz), 3.51 (1H, m), 1.95-1.80 (2H, m), 1.41 (2H, m), 1.11 (3H, d, $J = 6.4$ Hz), 0.96 (3H, t, $J = 7.6$ Hz). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 76.7, 70.4, 25.0, 16.8, 10.8. **Optical Rotation:** $[\alpha]_D^{25} +8.4$ ($c = 0.76$, CHCl_3).⁹

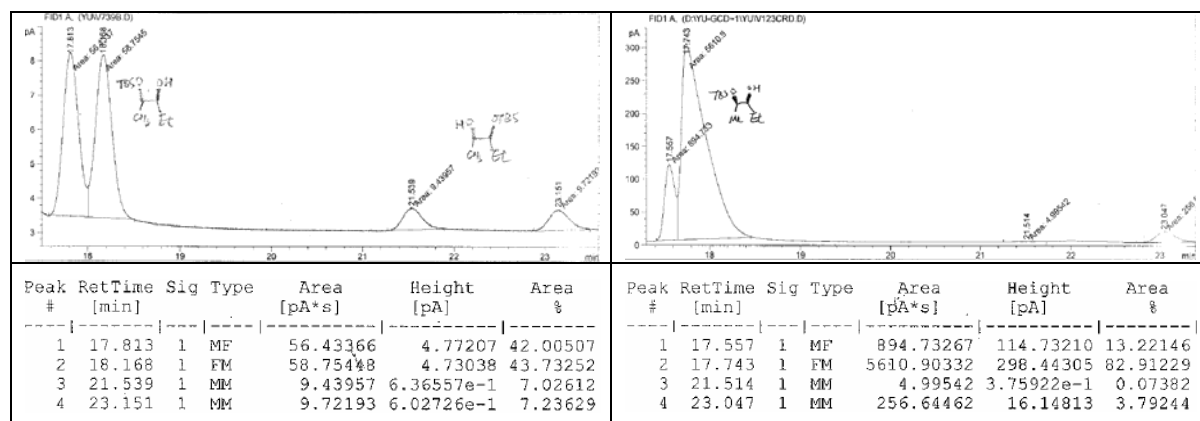
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 90 $^\circ\text{C}$ for 30 min, 25 psi.); chromatograms are illustrated below for a 98 % ee sample:

⁹ Absolute configuration was assigned by analogy to other substrates in Table 2.



Product: 109 mg, 50 % (as a 97:3 mixture of regioisomers, with the major isomer shown). ¹H NMR (CDCl₃, 400 MHz): δ 3.77 (1H, m), 3.44 (1H, m) [3.53 (1H, m) for minor regioisomer], 2.20 (1H, br) [2.08 (1H, m) for minor regioisomer], 1.40 (2H, m), 1.05 (3H, d, *J* = 6.0 Hz), 0.96 (3H, t, *J* = 7.2 Hz), 0.88 (9H, s), 0.06 (6H, s). ¹³C NMR (CDCl₃, 100 MHz): δ 76.9, 71.2, 26.1, 25.2, 18.4, 17.0, 10.8, -4.07, -4.48. **Optical Rotation:** [α]_D²⁵ -8.2 (*c* = 0.76, CHCl₃).

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μ m film thickness), 90 °C for 30 min, 25 psi.); chromatograms are illustrated below for a 73 % ee sample (96 % ee for minor isomer):

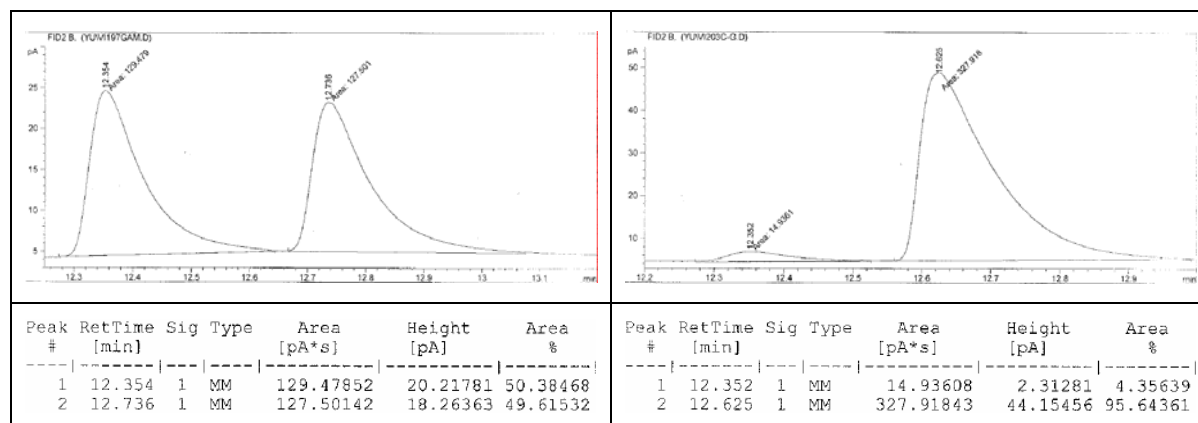


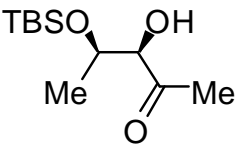
(3R,4R)-3,4-dihydroxypentan-2-one (2e, Entry 5, Table 2). The general procedure was followed (0.3 equiv. **1**, substrate concentration = 1.4 M, -50 °C for 48 h) to yield the product and the unreacted diol as colorless oil.

Recovered starting material: 40 mg, 34 %. **IR** (neat, thin film): 3396 (br), 2980 (m), 2924 (m), 1715 (s), 1476 (w), 1363 (m), 1294 (m), 1237 (m), 1136 (m), 1086 (m), 1004 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 4.29 (1H, d, *J* = 3.6 Hz), 4.11 (1H, dq, *J* = 6.4, 4.0 Hz), 2.25 (3H, s), 1.12 (3H, d, *J* = 6.4 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 207.9, 80.9, 68.8, 27.0, 17.8. **Optical Rotation:**

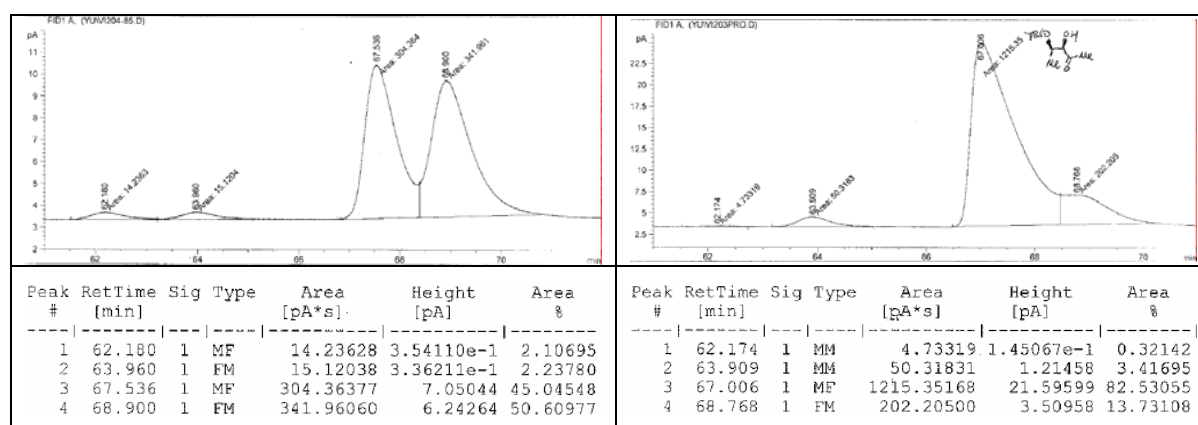
$$[\alpha]_D^{25} +131 (c = 1.00, \text{CHCl}_3)^{10}$$

Optical purity was established by chiral GLC analysis (Supelco Gamma Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 °C to 120 °C, 2 °C/min. 25 psi.); chromatograms are illustrated below for a 91 % ee sample:




 Product: 104 mg, 45 %. **IR** (neat, thin film): 3478 (br), 2961 (m), 2930 (m), 2854 (m), 1721 (m), 1476 (w), 1363 (w), 1262 (m), 1099 (s), 834 (s), 778 (s), 664 (w) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 4.06-3.98 (2H, m), 3.24 (1H, d, $J = 4.8$ Hz), 2.27 (3H, s), 1.21 (3H, d, $J = 6.4$ Hz), 0.88 (9H, s), 0.08 (3H, s), 0.06 (3H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 209.4, 81.5, 71.2, 28.3, 26.0, 19.8, 18.3, -4.29, -4.56. **HRMS** (m/z - H): Calculated: 231.1416; Found: 231.1418. **Optical Rotation**: $[\alpha]_D^{25} -138 (c = 1.00, \text{CHCl}_3)$.

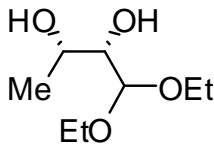
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 85 °C for 75 min, 25 psi.); chromatograms are illustrated below for a 71 % ee sample:



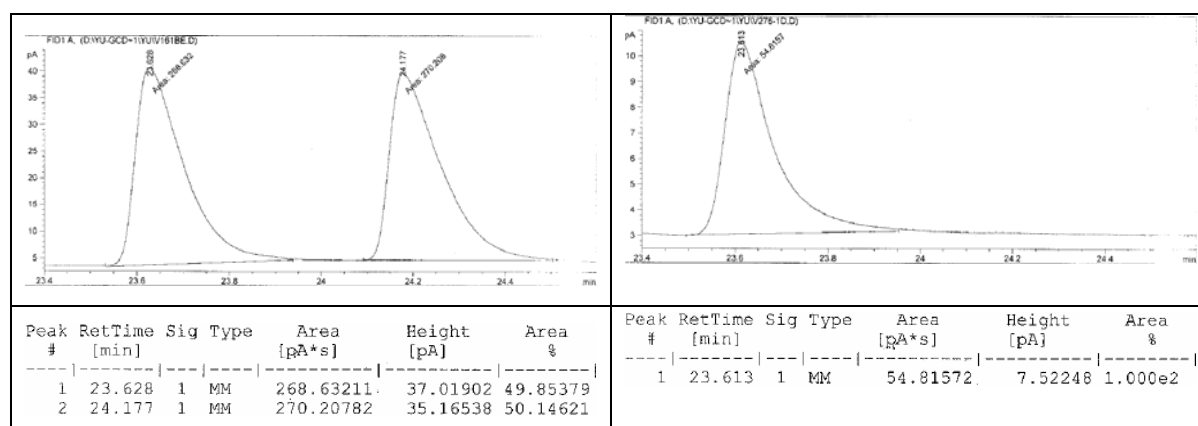
(2S,3S)-1,1-diethoxybutane-2,3-diol (2f, Entry 6, Table 2). The general procedure

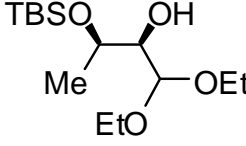
¹⁰ Absolute configuration was assigned as (3R,4R) by converting the recovered diol to the corresponding TIPS ether and comparing optical rotation to what was reported. See: Nicolaou, K. C.; Mitchell, H. J.; Jain, N. F.; Bando, T.; Hughes, R.; Winssinger, N.; Natarajan, S.; Koumbis, A. E. *Chem. Eur. J.* **1999**, 5, 2648-2667.

was followed (0.3 equiv. **1**, substrate concentration = 1.4 M, $-30\text{ }^{\circ}\text{C}$ for 24 h) to yield the product and the unreacted diol as pale yellow oil.


 Recovered starting material: 78 mg, 44 %. **IR** (neat, thin film): 3434 (br), 2980 (s), 2930 (s), 2905 (m), 1451 (w), 1375 (w), 1130 (m), 1067 (s), 1004 (w), 840 (w), 784 (w) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 4.49 (1H, d, $J = 5.6$ Hz), 3.88 (1H, dq, $J = 6.4, 6.4$ Hz), 3.82-3.74 (2H, m), 3.66-3.54 (2H, m), 3.46 (1H, dd, $J = 5.6, 5.6$ Hz), 1.26-1.20 (9H, m). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 103.7, 74.3, 68.3, 63.8, 63.7, 18.7, 15.7, 15.5. **HRMS** ($m/z + \text{Na}$): Calculated: 201.1103; Found: 201.1093. **Optical Rotation**: $[\alpha]^{25}_{\text{D}} -15.3$ ($c = 0.76$, CHCl_3).¹¹

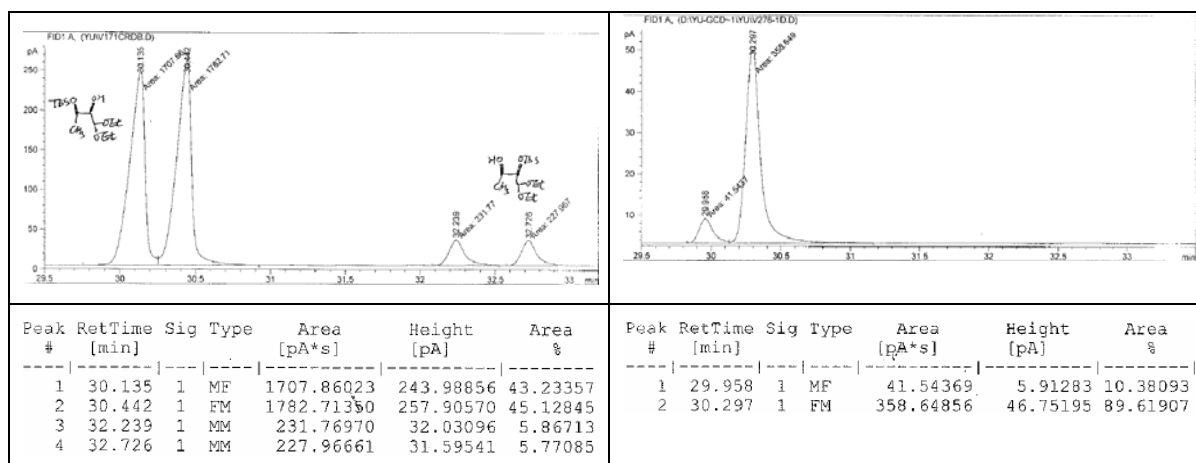
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), $80\text{ }^{\circ}\text{C}$ to $180\text{ }^{\circ}\text{C}$, $2\text{ }^{\circ}\text{C}/\text{min}$, 25 psi.); chromatograms are illustrated below for a $>98\%$ ee sample:




 Prod: 152 mg, 52 %. **IR** (neat, thin film): 3578 (br), 3490 (br), 2980 (s), 2961 (s), 2936 (s), 2899 (m), 2861 (m), 1480 (w), 1380 (w), 1260 (m), 1099 (s), 1067 (s), 840 (s), 784 (s), cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 4.47 (1H, d, $J = 5.2$ Hz), 3.91 (1H, dq, $J = 6.4, 5.2$ Hz), 3.82-3.52 (4H, m), 3.49 (1H, dd, $J = 5.2, 5.2$ Hz), 2.36 (1H, d, $J = 4.0$ Hz), 1.24 (3H, t, $J = 7.2$ Hz), 1.21 (3H, t, $J = 7.2$ Hz), 1.16 (3H, d, $J = 6.4$ Hz), 0.88 (9H, s), 0.07 (3H, s), 0.06 (3H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 102.0, 75.7, 68.9, 63.2, 63.1, 26.1, 18.8, 18.3, 15.6, 15.59, -4.07, -4.60. **HRMS** ($m/z + \text{Na}$): Calculated: 315.1968; Found: 315.1965. **Optical Rotation**: $[\alpha]^{25}_{\text{D}} -3.7$ ($c = 0.76$, CHCl_3).

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), $80\text{ }^{\circ}\text{C}$ to $180\text{ }^{\circ}\text{C}$, $2\text{ }^{\circ}\text{C}/\text{min}$, 25 psi.); chromatograms are illustrated below for an 80 % ee sample:

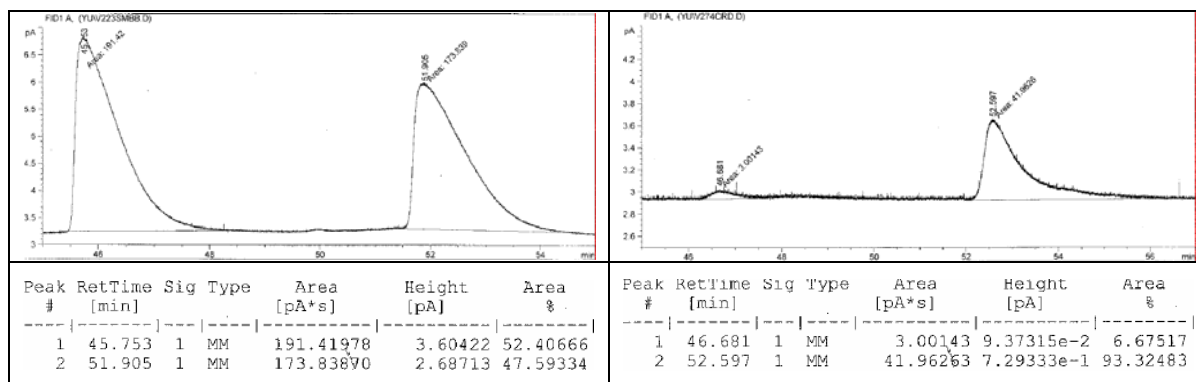
¹¹ Absolute configuration was assigned by analogy to other substrates in Table 2.



(2S,3S)-ethyl 2,3-dihydroxybutanoate (2g, Entry 7, Table 2). The general procedure was followed (0.3 equiv. **1**, substrate concentration = 1.4 M, $-30\text{ }^{\circ}\text{C}$ for 72 h) to yield the product and the unreacted diol as colorless oil.

Recovered starting material: 47 mg, 32 %. $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 4.28-4.16 (3H, m), 4.04 (1H, m), 3.70 (1H, br), 3.20 (1H, br), 1.26 (3H, t, $J = 6.8$ Hz), 1.15 (3H, d, $J = 6.4$ Hz). $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): δ 172.7, 74.6, 69.2, 61.9, 17.4, 14.3. **Optical Rotation:** $[\alpha]_D^{25} +3.9$ ($c = 0.76$, CHCl_3).¹²

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), $90\text{ }^{\circ}\text{C}$ for 90 min, $10\text{ }^{\circ}\text{C}/\text{min}$ to $180\text{ }^{\circ}\text{C}$, 25 psi.); chromatograms are illustrated below for an 87 % ee sample:

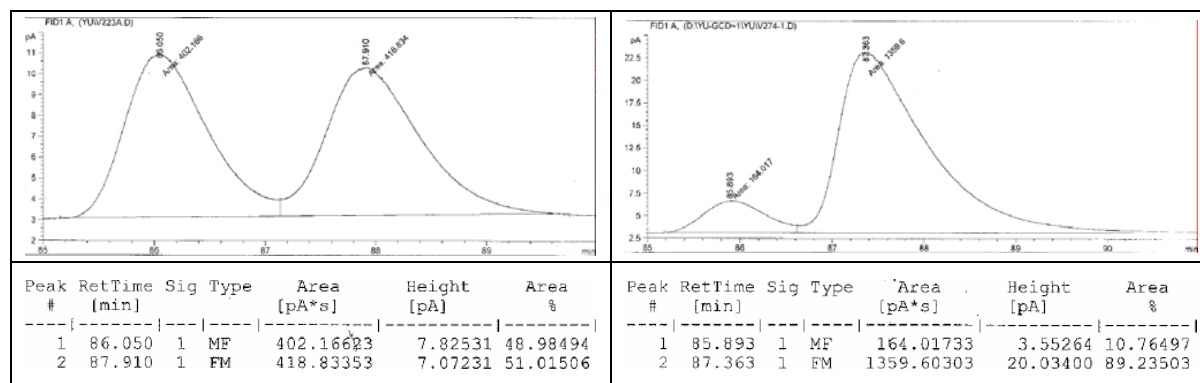


Major product: 89 mg, 34 %. **IR** (neat, thin film): 3484 (br), 2961 (s), 2930 (s), 2898 (m), 2861 (m), 1746 (s), 1469 (w), 1375 (w), 1262 (s), 1212 (m), 1150 (m), 1092 (s), 985 (m), 840 (w), 784 (w) cm^{-1} . $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 4.30-4.20 (2H, m), 4.12-4.02 (2H, m), 2.92 (1H, d, $J = 6.4$ Hz), 1.31 (3H, t, $J = 7.2$ Hz), 1.21 (3H, d, $J = 6.4$ Hz), 0.86 (9H, s), 0.08 (3H, s), 0.07 (3H, s). $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): δ 172.4, 75.7, 71.2, 61.6, 26.0, 19.4, 18.2, 14.5, -4.30, -4.62.

¹² Absolute configuration of the recovered diol was assigned as (2S,3S) by comparing optical rotation to what was reported. See: Solladie, G.; Gressot, L.; Colobert, F. *Eur. J. Org. Chem.* **2000**, 357-364.

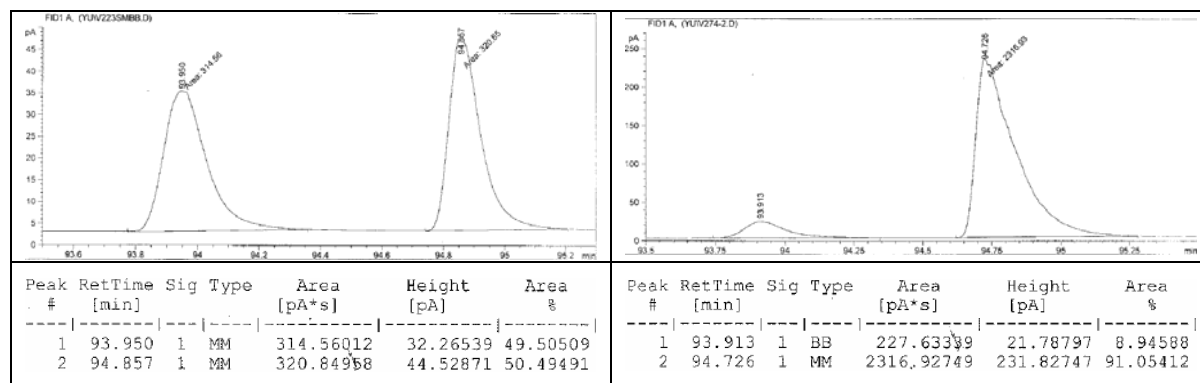
HRMS (m/z + Na): Calculated: 285.1498; Found: 285.1495. **Optical Rotation**: $[\alpha]_D^{25}$ -17.9 ($c = 0.76$, CHCl₃).

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μ m film thickness), 90 °C for 90 min, 10 °C/ min to 180 °C, 25 psi.); chromatograms are illustrated below for a 78 % ee sample:

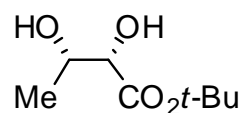


CC(C)(O)C(=O)OCC Minor product: 16 mg, 6 %. **IR** (neat, thin film): 3490 (br), 2958 (m), 2930 (s), 2898 (m), 2857 (m), 1735 (s), 1473 (w), 1375 (w), 1257 (s), 1187 (m), 1154 (s), 1112 (s), 1030 (s), 940 (m), 838 (s), 779 (s) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 4.25-4.15 (2H, m), 4.12 (1H, d, $J = 4.0$ Hz), 4.03-3.97 (1H, m), 2.34 (1H, br), 1.42 (3H, t, $J = 7.2$ Hz), 1.18 (3H, d, $J = 6.0$ Hz), 0.92 (9H, s), 0.09 (3H, s), 0.08 (3H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 171.9, 76.3, 69.7, 61.2, 26.0, 18.6, 18.2, 14.5, -4.56, -4.98. **HRMS** (m/z): Calculated: 263.1679; Found: 263.1689. **Optical Rotation**: $[\alpha]_D^{25}$ -36.9 ($c = 0.50$, CHCl_3).

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μ m film thickness), 90 °C for 90 min, 10 °C/ min to 180 °C, 25 psi.); chromatograms are illustrated below for an 82 % ee sample:

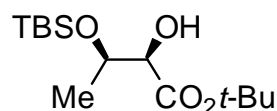
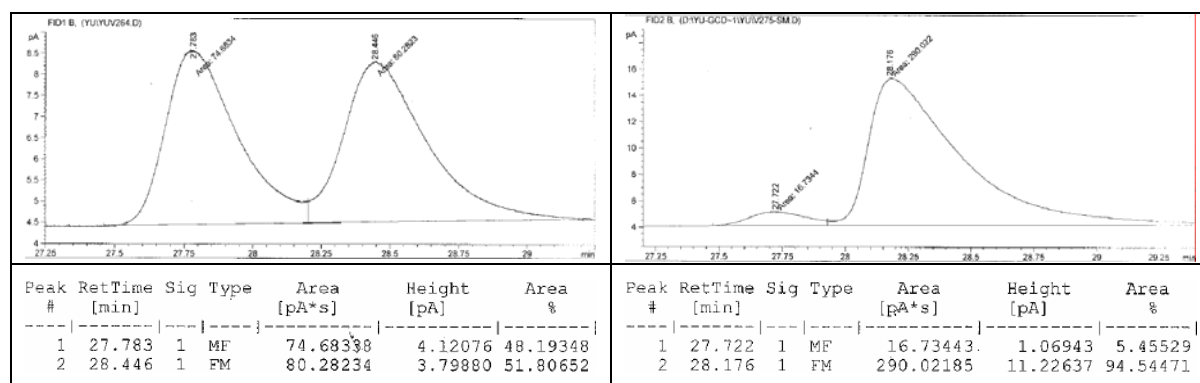


(2*S*,3*S*)-tert-butyl 2,3-dihydroxybutanoate (2h, Entry 8, Table 2). The general procedure was followed (0.3 equiv. **1**, substrate concentration = 1.4 M, -30 °C for 72 h) to yield the product and the unreacted diol as colorless or pale yellow oil.



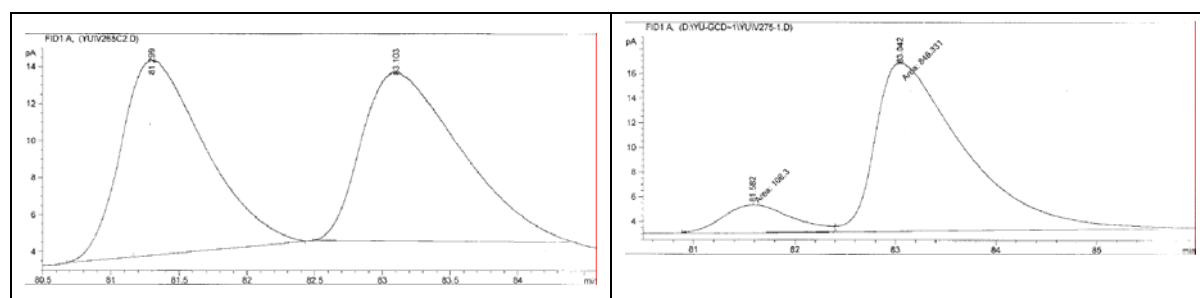
Recovered starting material: 60 mg, 34 %. **¹H NMR** (CDCl₃, 400 MHz): δ 4.09 (1H, m), 4.02 (1H, m), 3.08 (1H, br), 2.30 (1H, br), 1.50 (9H, s), 1.18 (3H, d, *J* = 6.4 Hz). **¹³C NMR** (CDCl₃, 100 MHz): δ 172.1, 83.5, 74.4, 69.3, 28.3, 17.5. **Optical Rotation:** $[\alpha]^{25}_D$ +1.6 (*c* = 0.76, CHCl₃).¹³

Optical purity was established by chiral GLC analysis (Supelco Gamma Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 90 °C for 30 min, 25 psi.); chromatograms are illustrated below for a 90 % ee sample:



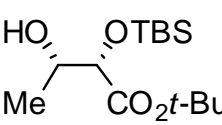
Major product: 128 mg, 44 %. **IR** (neat, thin film): 3515 (br), 2961 (s), 2936 (s), 2898 (m), 2861 (m), 1734 (s), 1476 (w), 1380 (m), 1262 (s), 1150 (m), 1089 (s), 991 (m), 840 (w), 784 (w) cm⁻¹. **¹H NMR** (CDCl₃, 400 MHz): δ 4.06 (1H, dq, *J* = 6.8, 2.0 Hz), 3.95 (1H, dd, *J* = 6.8, 2.0 Hz), 3.05 (1H, d, *J* = 6.8 Hz), 1.50 (9H, s), 1.21 (3H, d, *J* = 6.4 Hz), 0.88 (9H, s), 0.08 (3H, s), 0.06 (3H, s). **¹³C NMR** (CDCl₃, 100 MHz): δ 171.5, 82.6, 75.7, 71.6, 28.4, 26.0, 19.6, 18.3, -4.40, -4.56. **HRMS** (*m/z* + Na): Calculated: 313.1811; Found: 313.1807. **Optical Rotation:** $[\alpha]^{25}_D$ -15.0 (*c* = 0.76, CHCl₃).

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 90 °C for 30 min, 10 °C/ min to 100 °C, then 100 °C for 54 min, 25 psi.); chromatograms are illustrated below for a 77 % ee sample:

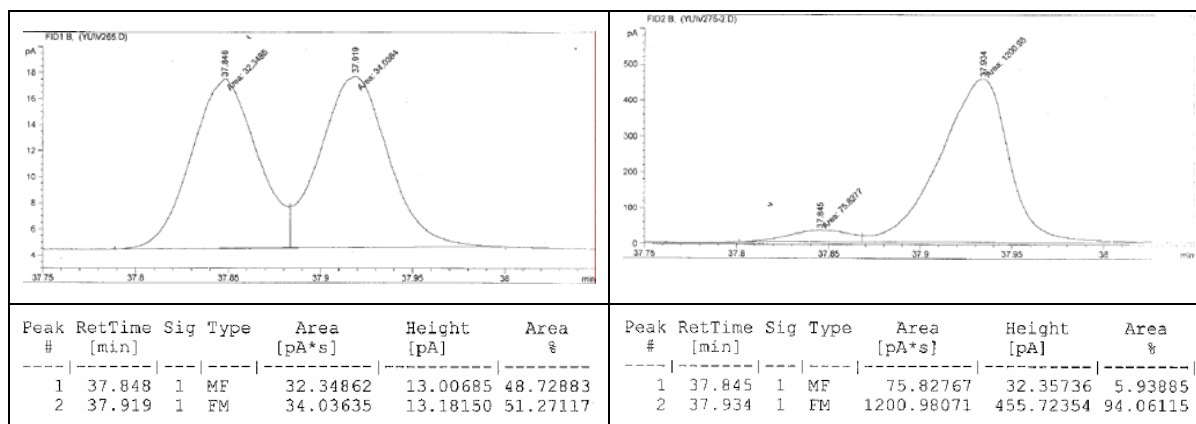


¹³ Absolute configuration of the recovered diol was assigned as (2*S*,3*S*) by comparing optical rotation to what was reported. See: d'Angelo, J. ; Pagès, O.; Maddaluno, J.; Dumas F.; Revial, G. *Tetrahedron Lett.* **1983**, 24, 5869-5872.

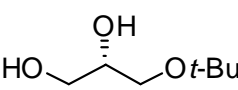
Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %	Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	81.299	1	BB	451.16891	10.57283	49.20727	1	81.582	1	MF	108.29951	2.29563	11.34465
2	83.103	1	BB	465.70566	9.11461	50.79273	2	83.042	1	FM	846.33148	13.71864	88.65535


 Minor product: 23 mg, 8 %. **IR** (neat, thin film): 3469 (br), 2955 (s), 2930 (s), 2857 (m), 1749 (s), 1473 (w), 1368 (m), 1254 (s), 1145 (s), 1032 (w), 876 (m), 837 (s), 780 (w) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 4.22-4.00 (1H, m), 4.00-3.94 (1H, m), 2.32 (1H, d, $J = 6.4$ Hz), 1.48 (9H, s), 1.17 (3H, d, $J = 6.4$ Hz), 0.92 (9H, s), 0.11 (3H, s), 0.07 (3H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 171.0, 81.9, 76.5, 69.8, 28.4, 26.0, 18.6, 18.1, -4.40, -5.00. **HRMS** (m/z): Calculated: 291.1992; Found: 291.1995. **Optical Rotation**: $[\alpha]_D^{25} -32.8$ ($c = 0.5$, CHCl_3).

Optical purity was established by chiral GLC analysis (Supelco Gamma Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 90 $^\circ\text{C}$ for 30 min, 10 $^\circ\text{C}/\text{min}$ to 100 $^\circ\text{C}$, 25 psi); chromatograms are illustrated below for an 88 % ee sample:

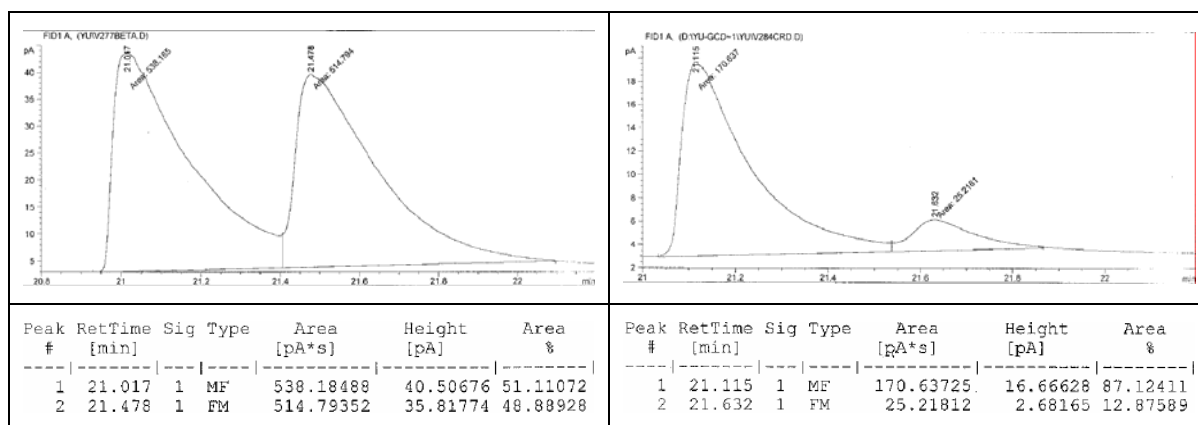


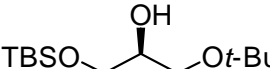
(S)-3-tert-butoxypropane-1,2-diol (5a, Entry 1, Table 3). The general procedure was followed (0.2 equiv. **1**, 0.75 equiv. TBSCl, substrate concentration = 1.0 M, -78 $^\circ\text{C}$ for 24 h) to yield the product and the unreacted diol as colorless or pale yellow oil.


 Recovered starting material: 56 mg, 38 %. **^1H NMR** (CDCl_3 , 400 MHz): δ 3.81-3.75 (1H, m), 3.74-3.60 (2H, m), 3.50-3.41 (2H, m), 1.20 (9H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 73.8, 70.8, 64.8, 64.0, 27.7. **Optical Rotation**: $[\alpha]_D^{25} -1.0$ ($c = 0.76$, CHCl_3).¹⁴

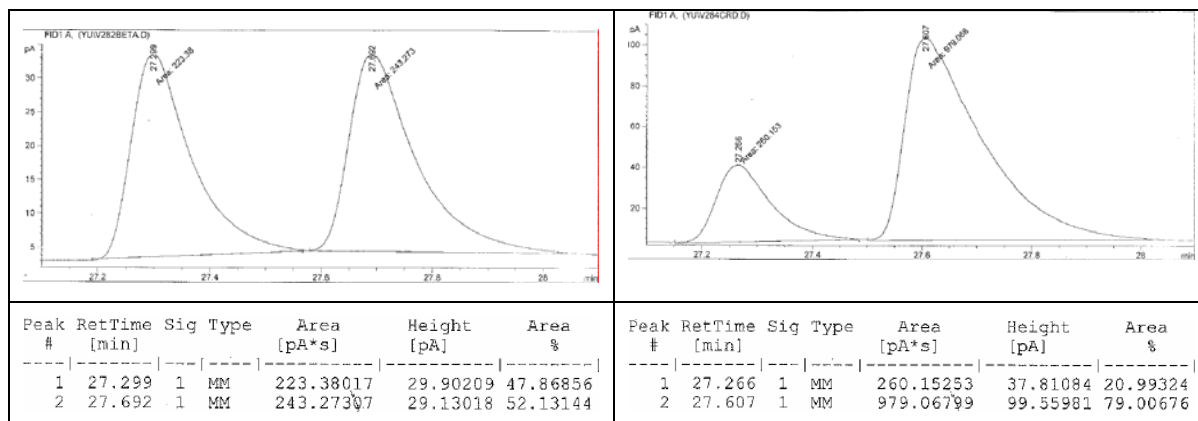
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 $^\circ\text{C}$ to 180 $^\circ\text{C}$, 2 $^\circ\text{C}/\text{min}$, 25 psi); chromatograms are illustrated below for a 74 % ee sample:

¹⁴ Absolute configuration of the recovered diol was assigned as (*S*) by comparing optical rotation to what was reported. See: Verheij et al. *Chem. Phys. Lipids*. **1971**, 6, 46.

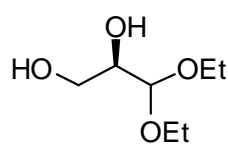



 Product: 121 mg, 46 %. **IR** (neat, thin film): 3584 (w), 3459 (br), 2960 (s), 2930 (s), 2854 (m), 1476 (m), 1369 (m), 1268 (m), 1200 (m), 1092 (s), 941 (w), 840 (s), 777 (s), 671 (w) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 3.76-3.68 (1H, m), 3.66-3.58 (2H, m), 3.43-3.34 (2H, m), 2.49 (1H, br), 1.18 (9H, s), 0.89 (9H, s), 0.07 (3H, s), 0.06 (3H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 73.2, 71.3, 64.2, 62.6, 27.8, 26.1, 18.6, -5.10, -5.10. **HRMS** (m/z + Na): Calculated: 285.1862; Found: 285.1863.

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 $^\circ\text{C}$ to 180 $^\circ\text{C}$, 2 $^\circ\text{C}/\text{min}$, 25 psi.); chromatograms are illustrated below for a 58 % ee sample:



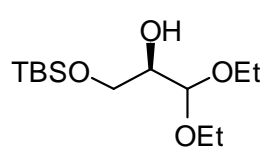
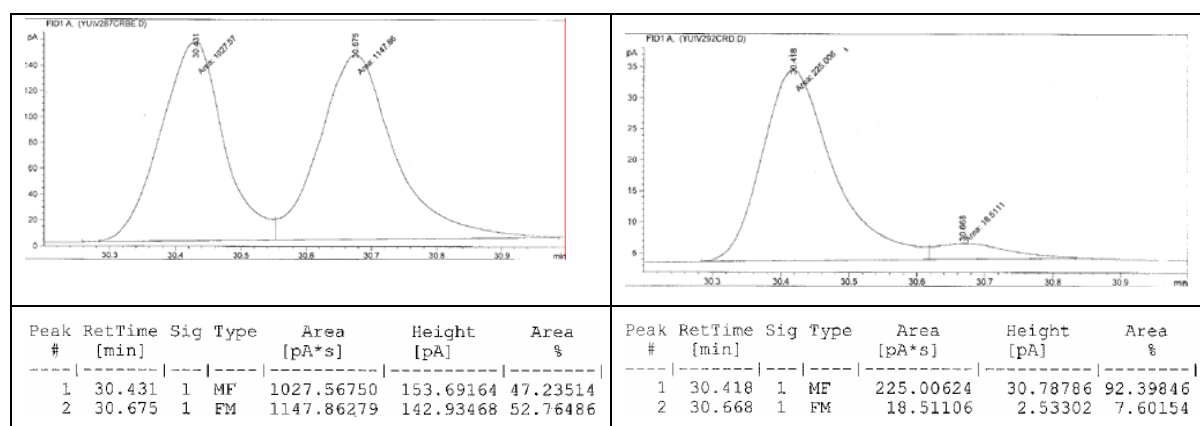
(S)-3,3-diethoxypropane-1,2-diol (5b, Entry 2, Table 3). The general procedure was followed (0.2 equiv. **1**, 0.75 equiv. TBSCl, substrate concentration = 1.0 M, -78 $^\circ\text{C}$ for 24 h) to yield the product and the unreacted diol as pale yellow oil.



Recovered starting material: 41 mg, 25 %. **^1H NMR** (CDCl_3 , 400 MHz): δ 4.45 (1H, d, J = 6.0 Hz), 3.80-3.50 (7H, m), 1.21 (3H, t, J = 7.2 Hz), 1.19 (3H, t, J = 7.2 Hz). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 103.5, 71.9, 64.4, 63.7, 62.6, 15.5. **Optical Rotation**: $[\alpha]_D^{25}$ -8.4 (c = 0.76,

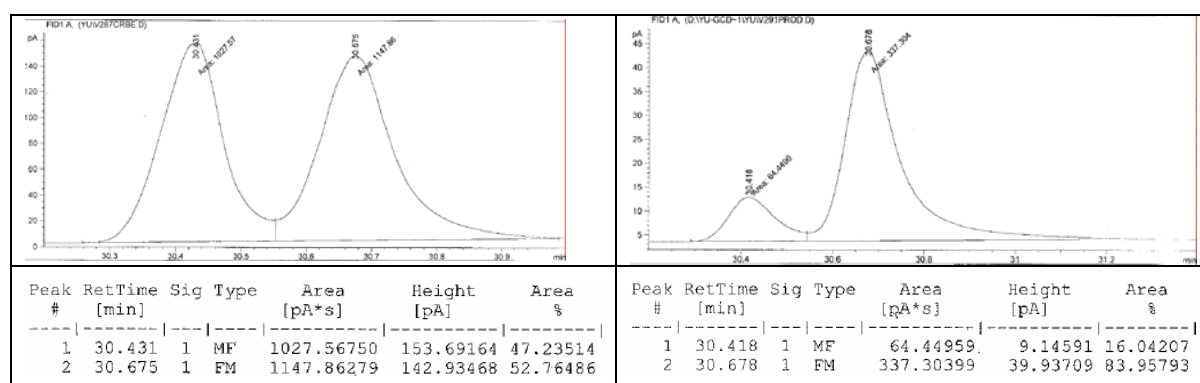
CHCl₃).¹⁵

Optical purity was established by chiral GLC analysis after conversion to the mono silyl ether (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 °C to 180 °C, 2 °C/min, 25 psi.); chromatograms are illustrated below for an 84 % ee sample:



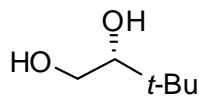
Product: 153 mg, 55 %. **IR** (neat, thin film): 3490 (br), 2930 (s), 2886 (m), 2861 (m), 1470 (m), 1376 (w), 1256 (s), 1123 (s), 1067 (s), 840 (s), 777 (m), 677 (w) cm⁻¹. **¹H NMR** (CDCl₃, 400 MHz): δ 4.47 (1H, d, *J* = 5.6 Hz), 3.80-3.50 (7H, m), 2.44 (1H, d, *J* = 4.4 Hz), 1.22 (3H, t, *J* = 4.0 Hz), 1.20 (3H, t, *J* = 4.0 Hz), 0.89 (9H, s), 0.06 (6H, s). **¹³C NMR** (CDCl₃, 100 MHz): δ 102.3, 72.4, 63.7, 63.4, 62.9, 26.1, 18.5, 15.6, 15.5, -5.13, -5.19. **HRMS** (m/z + Na): Calculated: 301.1811; Found: 301.1824. **Optical Rotation**: [α]_D²⁵ +8.9 (*c* = 0.76, CHCl₃).

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 °C to 180 °C, 2 °C/min, 25 psi.); chromatograms are illustrated below for a 68 % ee sample:



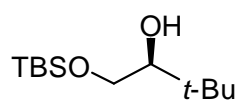
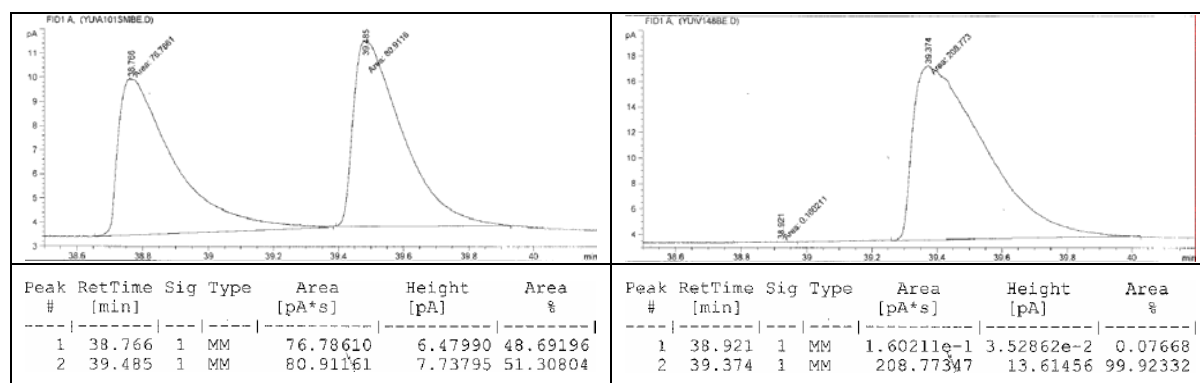
(R)-3,3-dimethylbutane-1,2-diol (5c, Entry 3, Table 3). The general procedure was followed (0.2 equiv. **1**, 0.75 equiv. TBSCl, substrate concentration = 1.0 M, -78 °C for 24 h) to yield the product and the unreacted diol as colorless or pale yellow oil.

¹⁵ Absolute configuration of the recovered diol was assigned as (*S*) by comparing optical rotation to what was reported. See: Page, P.; Blonski, C.; Périé, J. *Tetrahedron*. **1996**, 52, 1557-1572.



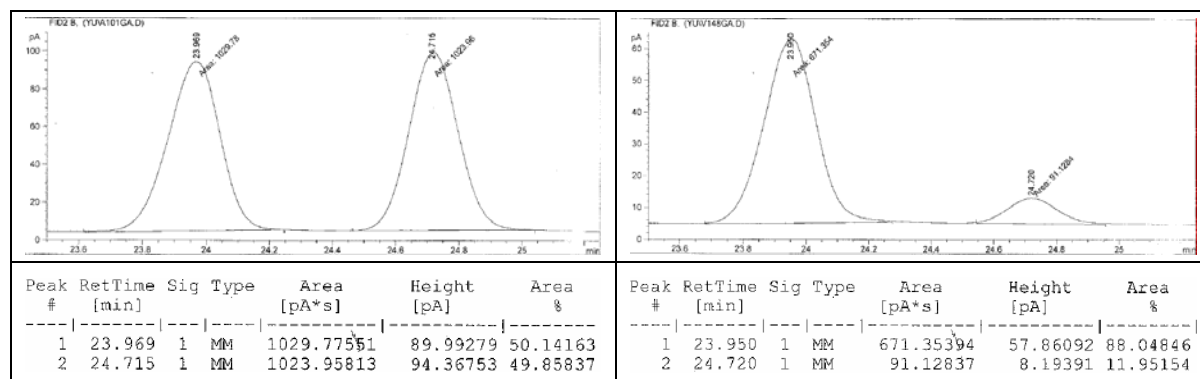
Recovered starting material: 69 mg, 42 %. ^1H NMR (CDCl_3 , 400 MHz): δ 3.75-3.68 (1H, m), 3.50-3.43 (1H, m), 3.39-3.33 (1H, m), 0.91 (9H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 79.9, 63.4, 33.9, 26.2. **Optical Rotation:** $[\alpha]_D^{25}$ -26.0 ($c = 1.00$, CHCl_3).¹⁶

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 $^\circ\text{C}$ for 20 min, then 2 $^\circ\text{C}/\text{min}$ to 145 $^\circ\text{C}$, 25 psi.); chromatograms are illustrated below for a > 99 % ee sample:



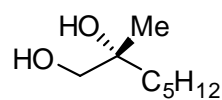
Product: 102 mg, 44 %. **IR** (neat, thin film): 3584 (br), 2960 (s), 2867 (m), 1476 (m), 1376 (w), 1268 (m), 1117 (s), 1080 (s), 1010 (m), 885 (w), 847 (s), 784 (m) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 3.71 (1H, dd, $J = 9.6, 2.80$ Hz), 3.46 (1H, t, $J = 9.2$ Hz), 3.31 (1H, m), 2.64 (1H, d, $J = 2.0$ Hz), 0.91 (9H, s), 0.90 (9H, s), 0.08 (6H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 78.8, 63.9, 33.5, 26.3, 26.2, 18.6, -4.91, -4.97. **HRMS** ($m/z + \text{Na}$): Calculated: 255.1756; Found: 255.1749. **Optical Rotation:** $[\alpha]_D^{25}$ +21.3 ($c = 0.76$, CHCl_3).

Optical purity was established by chiral GLC analysis (Supelco Gamma Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 $^\circ\text{C}$ for 20 min, then 2 $^\circ\text{C}/\text{min}$ to 145 $^\circ\text{C}$, 25 psi.); chromatograms are illustrated below for a 76 % ee sample:



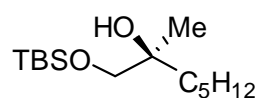
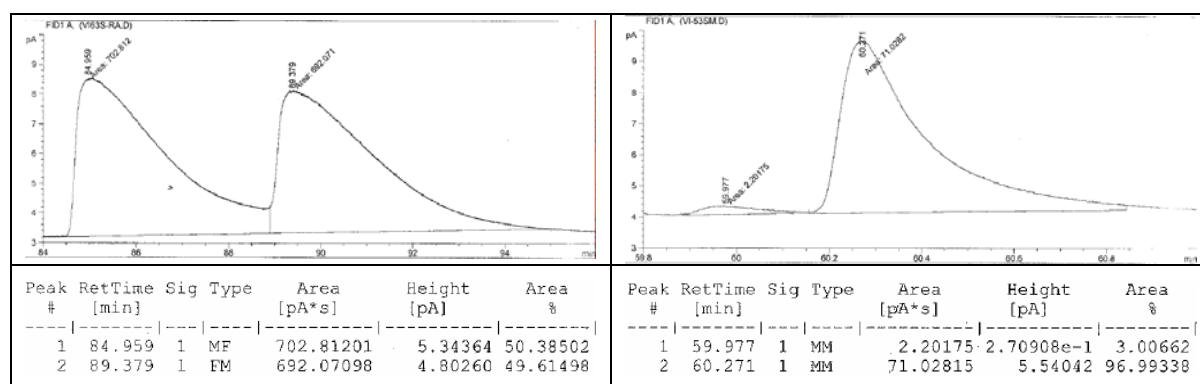
¹⁶ Absolute configuration of the recovered diol was assigned as (*R*) by comparing optical rotation to what was reported. See: Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, 124, 1307-1315.

(R)-2-methylheptane-1,2-diol (6a, Entry 4, Table 3). The general procedure was followed (0.3 equiv. **1**, substrate concentration = 1.0 M, $-78\text{ }^{\circ}\text{C}$ for 96 h) to yield the product and the diol as colorless oil.



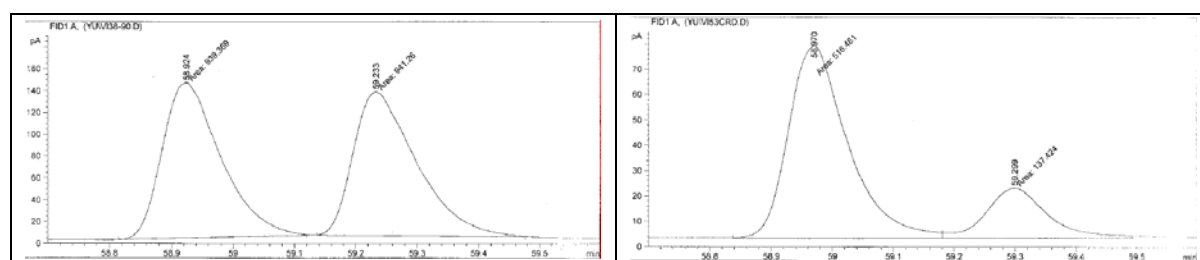
Recovered starting material: 61 mg, 42 %. $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 3.43 (1H, d, $J = 11.0$ Hz), 3.37 (1H, d, $J = 11.0$ Hz), 1.50-1.20 (8H, m), 1.13 (3H, s), 0.87 (3H, t, $J = 6.8$ Hz). $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): δ 73.3, 69.9, 38.9, 32.6, 23.7, 23.3, 22.8, 14.2. **Optical Rotation:** $[\alpha]_D^{25} +3.2$ ($c = 0.76$, CHCl_3).¹⁷

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), $100\text{ }^{\circ}\text{C}$ for 100 min, 25 psi.); chromatograms are illustrated below for a 94 % ee sample:



Product: 130 mg, 50 %. **IR** (neat, thin film): 3578 (br), 3458 (br), 2955 (s), 2930 (s), 2861 (s), 1470 (m), 1381 (w), 1256 (m), 1099 (s), 1010 (w), 935 (w), 840 (s), 778 (s), 670 (m) cm^{-1} . $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 3.42 (1H, d, $J = 9.6$ Hz), 3.36 (1H, d, $J = 9.6$ Hz), 2.33 (1H, s), 1.46-1.24 (8H, m), 1.10 (3H, s), 0.91-0.85 (12H, m), 0.07 (3H, s), 0.06 (3H, s). $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): δ 72.6, 70.3, 38.9, 32.8, 26.1, 25.9, 23.7, 23.4, 22.9, 14.3, -5.19, -5.19. **HRMS** ($m/z + \text{Na}$): Calculated: 283.2069; Found: 283.2078. **Optical Rotation:** $[\alpha]_D^{25} -0.53$ ($c = 0.76$, CHCl_3).

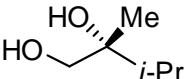
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), $90\text{ }^{\circ}\text{C}$ for 50 min, then $5\text{ }^{\circ}\text{C}/\text{min}$ to $180\text{ }^{\circ}\text{C}$, 25 psi.); chromatograms are illustrated below for a 58 % ee sample:



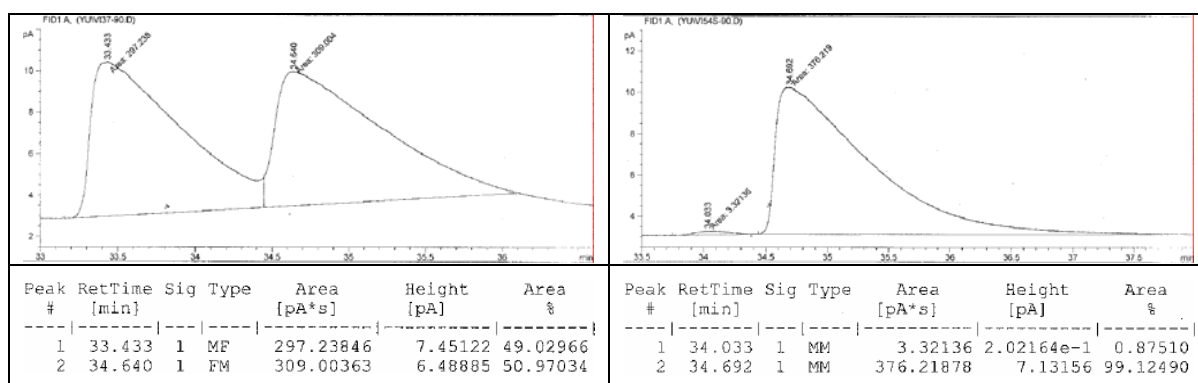
¹⁷ Absolute configuration of the recovered diol was assigned as (*R*) by comparing optical rotation to what was reported. See: Orru, R. V. A.; Mayer, S. F.; Kroutil, W.; Faber, K. *Tetrahedron*. **1998**, 54, 859-874.

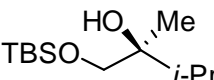
Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %	Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	58.924	1	MM	939.36902	142.19225	49.94973	1	58.970	1	MF	516.46075	76.09501	78.98346
2	59.233	1	MM	941.25989	132.00813	50.05027	2	59.299	1	FM	137.42393	19.88258	21.01654

(R)-2,3-dimethylbutane-1,2-diol (6b, Entry 5, Table 3). The general procedure was followed (0.2 or 0.3 equiv. **1**, substrate concentration = 1.0 M, -78°C for 40 h) to yield the product and the diol as colorless oil.


 Recovered starting material: 52 mg, 44 %. **^1H NMR** (CDCl_3 , 400 MHz): δ 3.52 (1H, d, $J = 7.2$ Hz), 3.40 (1H, d, $J = 7.2$ Hz), 1.80 (1H, qq, $J = 7.2$, 6.8 Hz), 1.03 (3H, s), 0.93 (3H, d, $J = 6.8$ Hz), 0.85 (3H, d, $J = 7.2$ Hz). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 75.4, 68.6, 34.4, 19.0, 17.9, 16.9. **Optical Rotation:** $[\alpha]_D^{25} +11.6$ ($c = 0.76$, CHCl_3).¹⁸

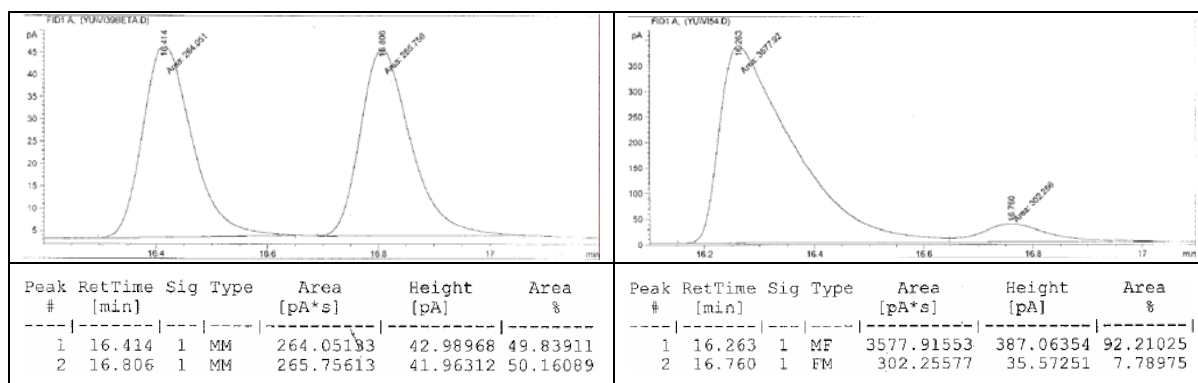
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 90°C for 40 min, 25 psi); chromatograms are illustrated below for a 98 % ee sample:



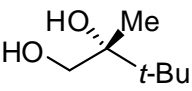

 Product: 121 mg, 52 %. **IR** (neat, thin film): 3578 (br), 3484 (br), 2955 (s), 2930 (s), 2861 (s), 1470 (m), 1388 (m), 1362 (m), 1161 (w), 1099 (s), 941 (w), 916 (w), 840 (s), 778 (s), 670 (m) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 3.51 (1H, d, $J = 9.2$ Hz), 3.37 (1H, d, $J = 9.6$ Hz), 2.37 (1H, s), 1.80 (1H, qq, $J = 6.8$, 6.8 Hz), 1.00 (3H, s), 0.94 (3H, d, $J = 6.8$ Hz), 0.90 (9H, s), 0.84 (3H, d, $J = 6.8$ Hz), 0.06 (6H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 74.6, 69.1, 34.4, 26.1, 19.1, 18.5, 18.0, 17.1, -5.03, -5.03. **HRMS** ($m/z + \text{Na}$): Calculated: 255.1756; Found: 255.1766. **Optical Rotation:** $[\alpha]_D^{25} -5.0$ ($c = 0.76$, CHCl_3).

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80°C to 120°C , $2^{\circ}\text{C}/\text{min}$, 25 psi.); chromatograms are illustrated below for an 84 % ee sample:

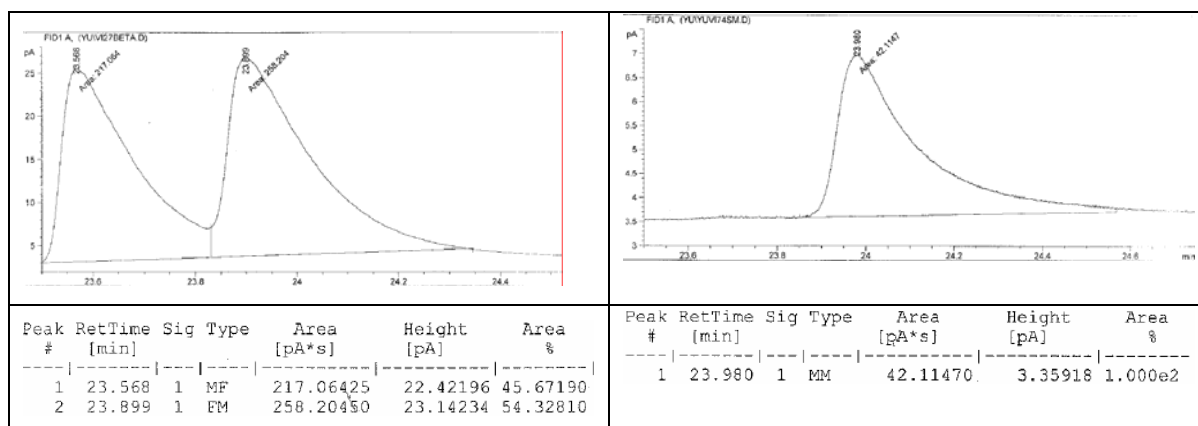
¹⁸ Absolute configuration of the recovered diol was assigned as (*R*) by comparing optical rotation to what was reported. See: Mori, K.; Ebata, T.; Takechi, S. *Tetrahedron*. **1984**, 40, 1761-1766.

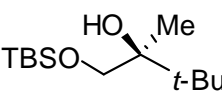


(R)-2,3,3-trimethylbutane-1,2-diol (6c, Entry 6, Table 3). The general procedure was followed (0.2 equiv. **1**, substrate concentration = 1.0 or 1.4 M, $-78\text{ }^{\circ}\text{C}$ for 24 h) to yield the product as colorless oil and the diol as a white solid.


 Recovered starting material: 59 mg, 45 %. **mp**: $59.0\text{--}60.5\text{ }^{\circ}\text{C}$. **IR** (neat, thin film): 3333 (br), 3257 (br), 2955 (s), 2873 (m), 1470 (w), 1370 (w), 1161 (w), 1124 (m), 1055 (s), 1010 (m), 941 (w) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 3.71 (1H, d, $J = 10.8\text{ Hz}$), 3.43 (1H, d, $J = 10.8\text{ Hz}$), 1.19 (3H, s), 0.95 (9H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 76.7, 66.2, 36.6, 25.6, 19.8. **Optical Rotation**: $[\alpha]_D^{25} +6.8$ ($c = 0.76$, CHCl_3).¹⁹

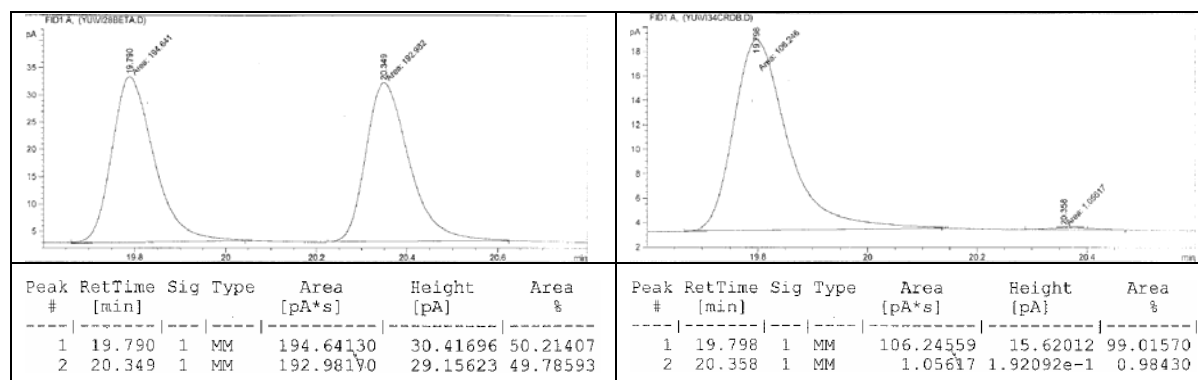
Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), $80\text{ }^{\circ}\text{C}$ to $120\text{ }^{\circ}\text{C}$, $2\text{ }^{\circ}\text{C}/\text{min}$, 25 psi.); chromatograms are illustrated below for a $>98\%$ ee sample:




 Product: 111 mg, 45 %. **IR** (neat, thin film): 3578 (br), 2950 (s), 2930 (s), 2860 (s), 1470 (m), 1375 (m), 1256 (m), 1168 (w), 1080 (s), 1010 (w), 941 (w), 840 (s), 777 (s), 664 (w) cm^{-1} . **^1H NMR** (CDCl_3 , 400 MHz): δ 3.65 (1H, d, $J = 9.6\text{ Hz}$), 3.39 (1H, d, $J = 9.6\text{ Hz}$), 2.51 (1H, s), 1.11 (3H, s), 0.94 (9H, s), 0.91 (9H, s), 0.07 (6H, s). **^{13}C NMR** (CDCl_3 , 100 MHz): δ 75.6, 67.0, 36.4, 26.1, 25.8, 20.6, 18.5, -5.18, -5.18. **HRMS** ($m/z + \text{Na}$): Calculated: 269.1913; Found: 269.1920. **Optical Rotation**: $[\alpha]_D^{25} -1.3$ ($c = 0.76$, CHCl_3).

¹⁹ Absolute configuration was assigned by analogy to other substrates in Table 3.

Optical purity was established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μ m film thickness), 80 °C to 120 °C, 2 °C/min, 25 psi.); chromatograms are illustrated below for a 98 % ee sample:

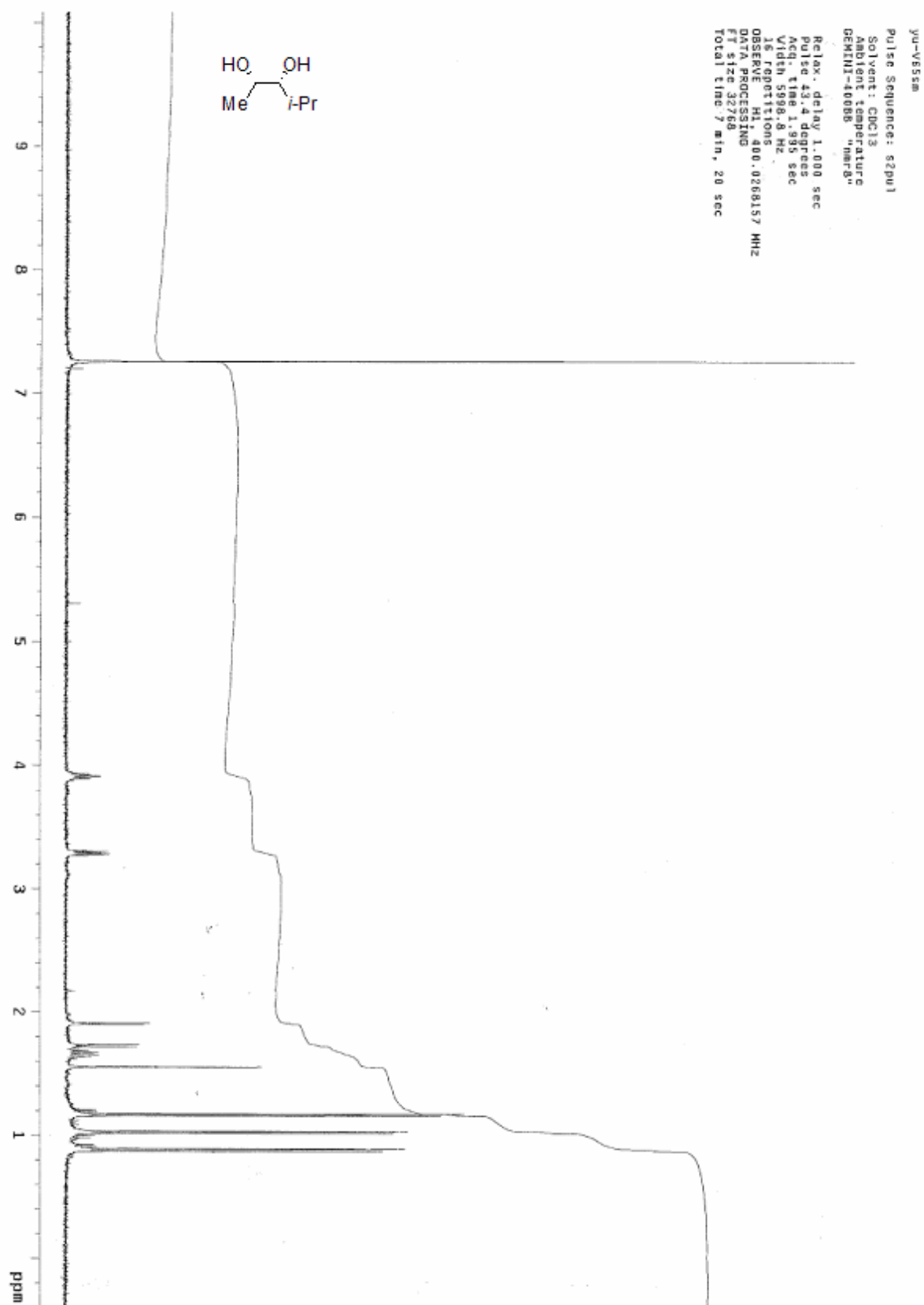


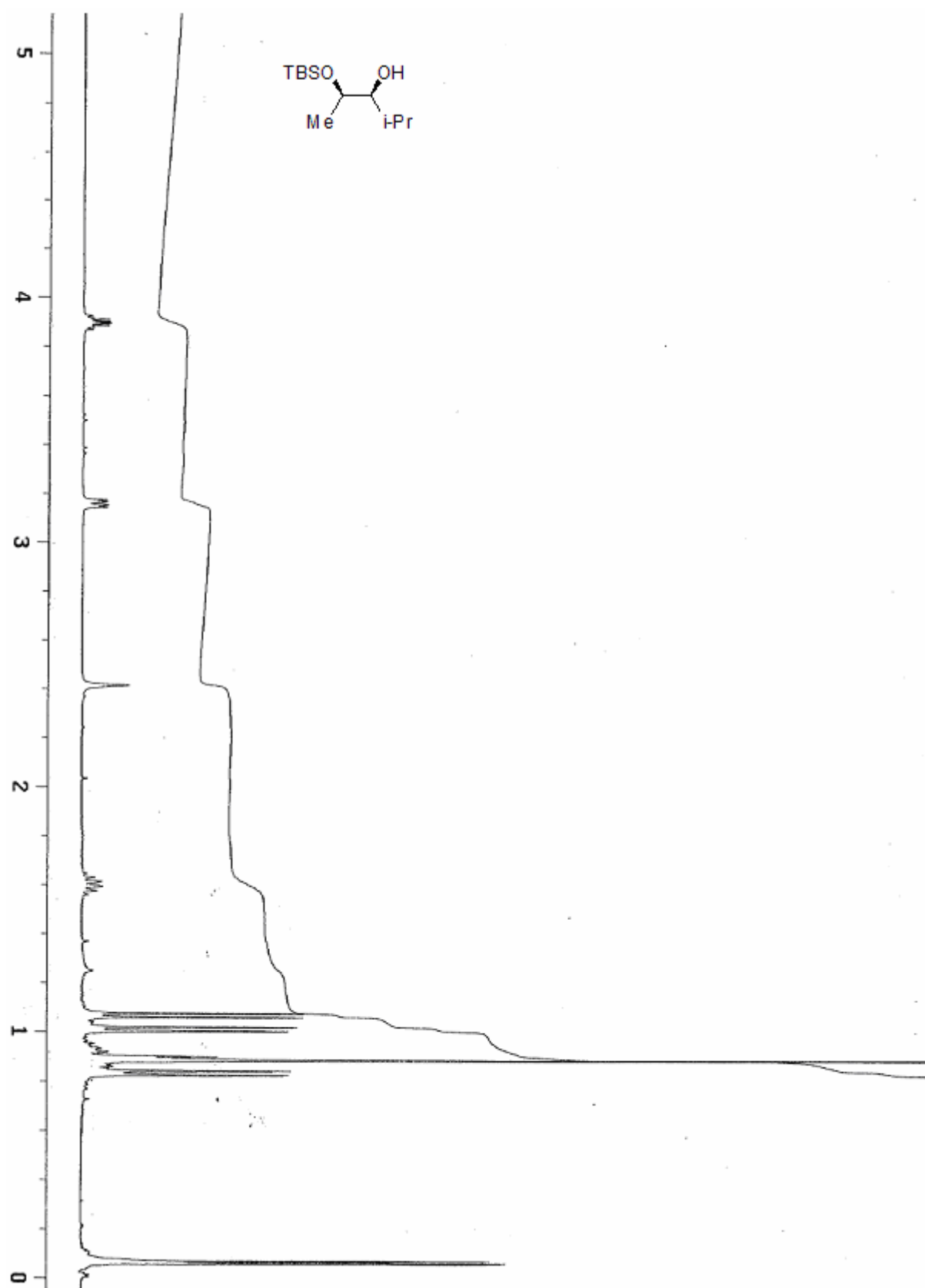
Procedure for the synthesis of 1,1-diethoxybutane-2,3-diol (2f)

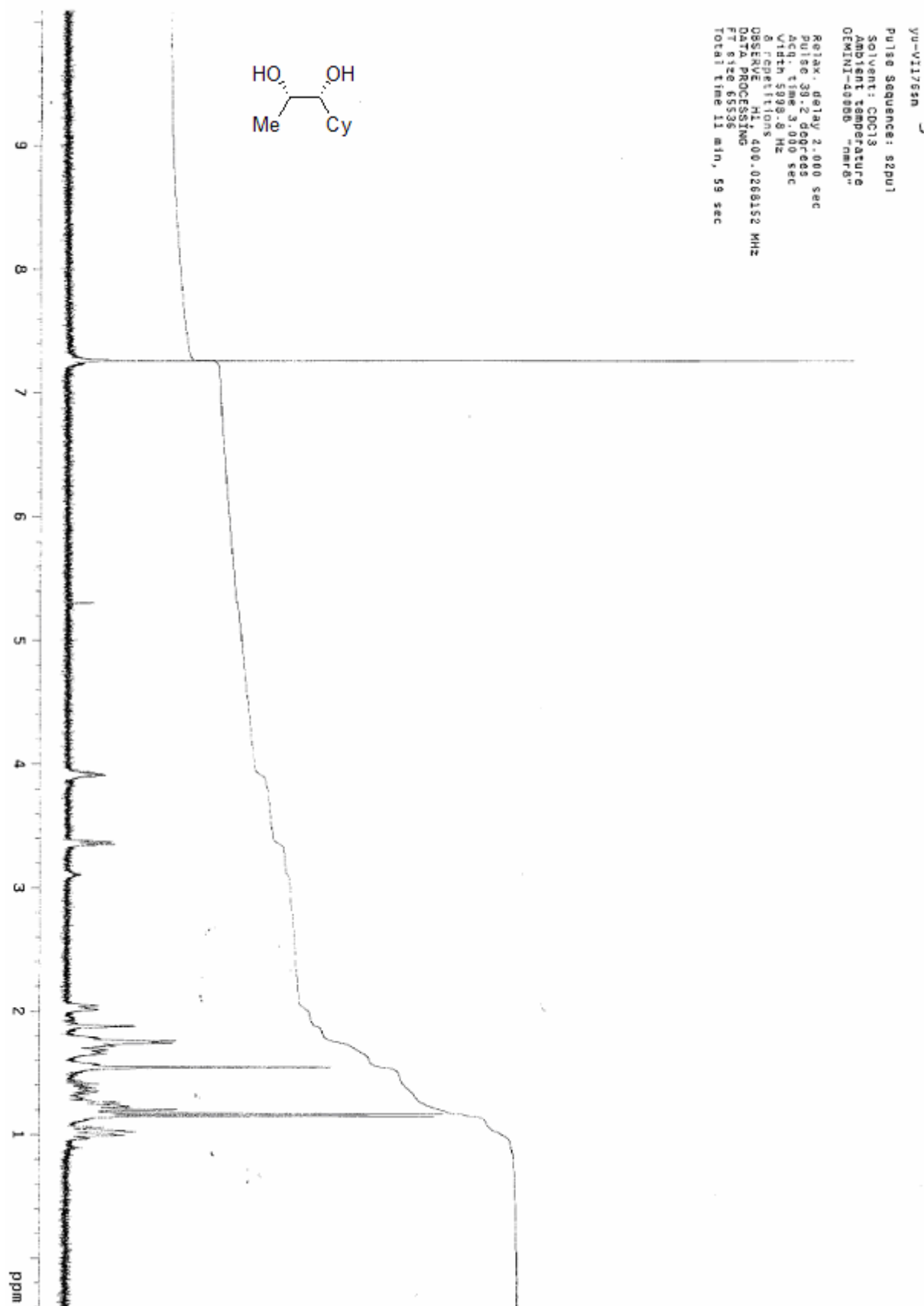
Palladium, 5 wt. % on calcium carbonate, poisoned with lead (Lindlar's catalyst, 0.50 g) was added to a 100 mL flask and diethyl ether (20 mL) was added, followed by quinoline (0.50 mL). This suspension was charged with 2-butyne-1-ol diethyl acetal (3.2 mL, 20 mmol). The solution was purged with H₂ and allowed to stir under a balloon of H₂ for 8-10 h (test NMR shows complete consumption of the starting material). The mixture was filtered through celite. Due to the volatility of the product, diethyl ether was only partially removed under reduced pressure to yield approximately 10 mL of solution.²⁰

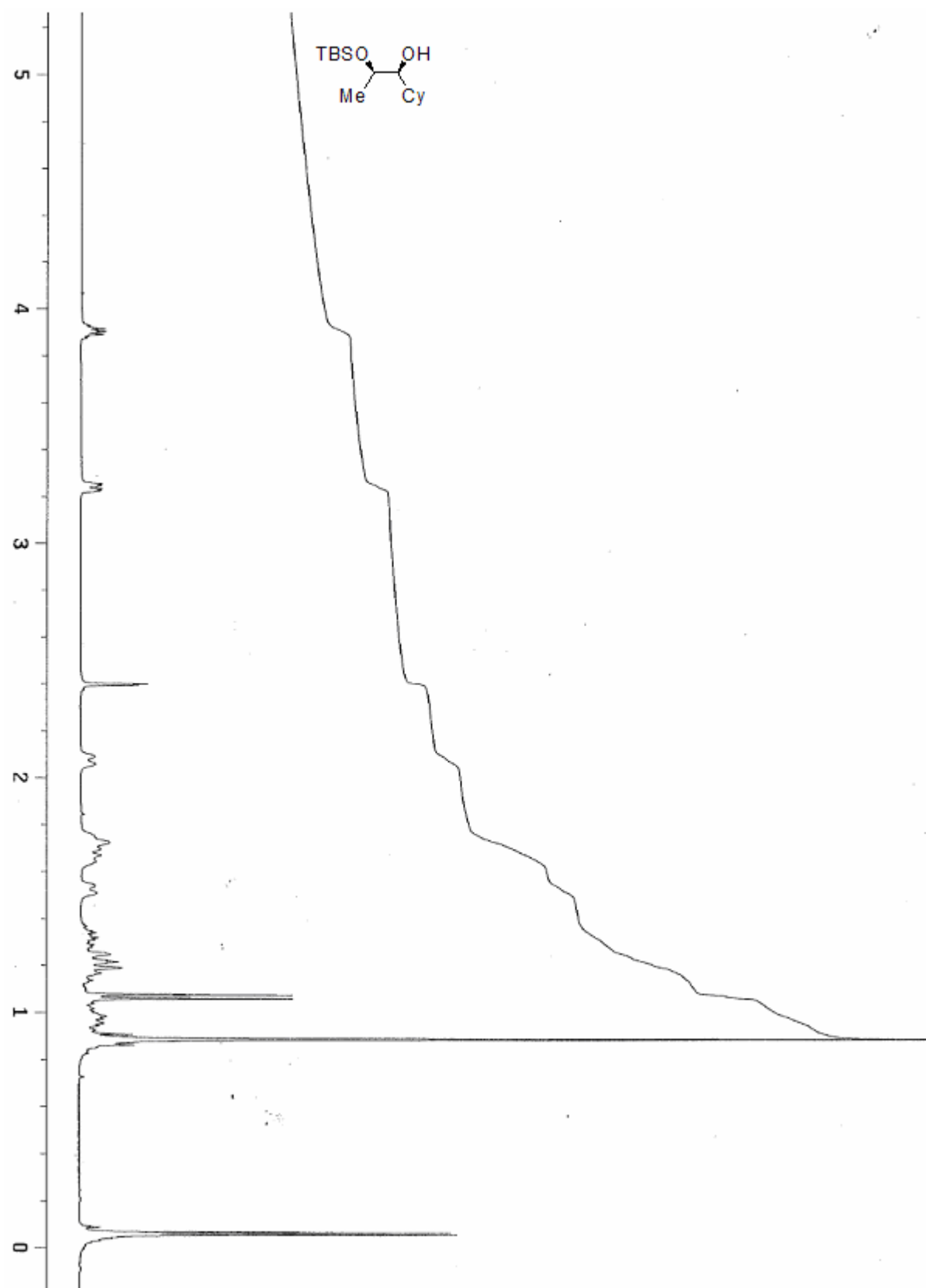
To this mixture was added 12 mL acetone and 5 mL H₂O. 4-Methylmorpholine-*N*-Oxide (2.5 g, 21 mmol) was added, followed by OsO₄, 2.5 wt. % in 2-methyl-2-propanol (1.5 mL, 0.3 wt. %). The solution was allowed to stir for 16 h at 22 °C, after which time 15 mL of saturated Na₂SO₃ solution was added to quench the reaction. The product was extracted with EtOAc (5 x 30 mL), the combined organic layer was dried over anhydrous MgSO₄ and concentrated to afford a yellow oil. Purification by chromatography (10:1 hexanes:EtOAc) yielded the desired diol as a pale yellow oil (2.6 g, 15 mmol, 73 %).

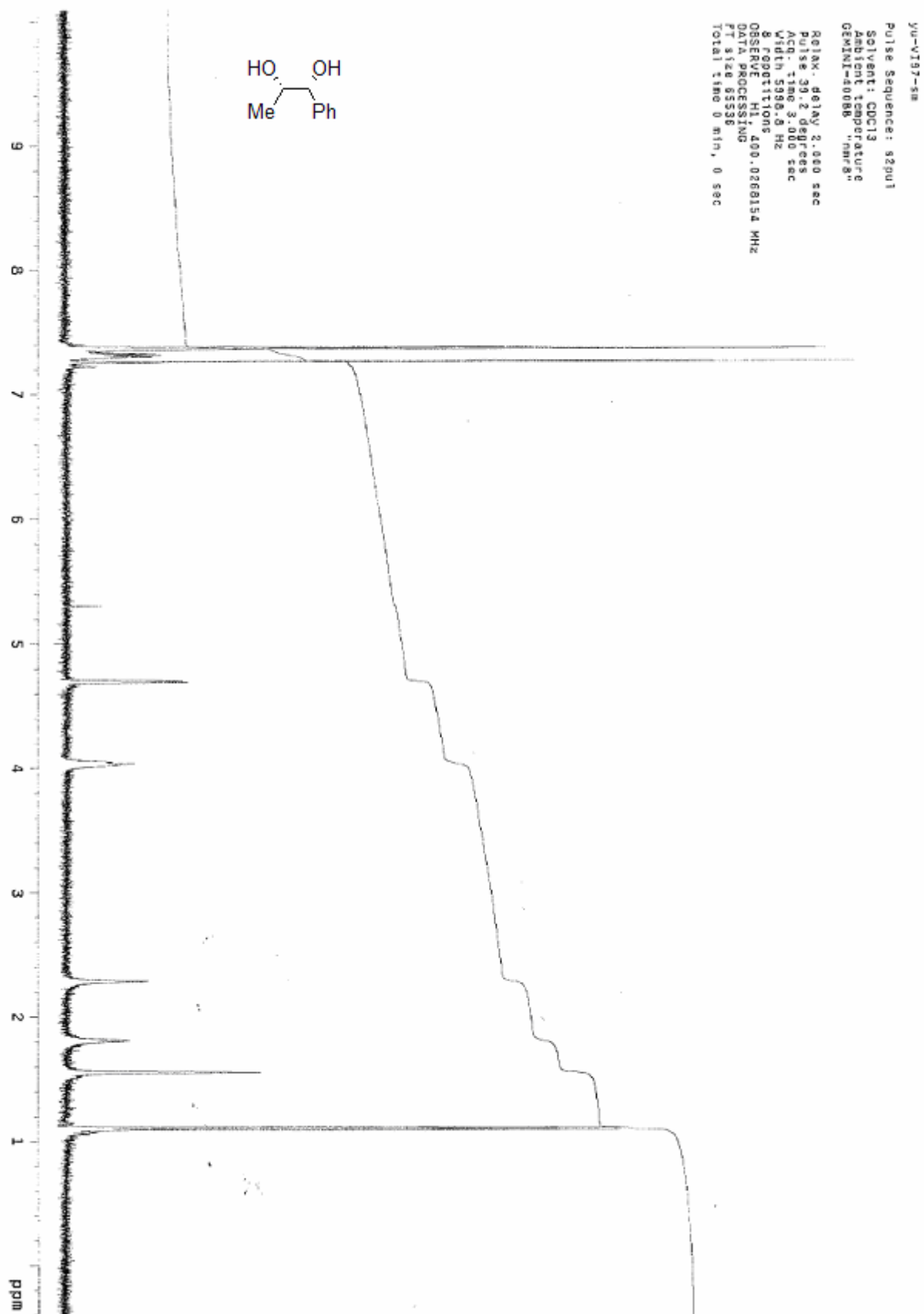
²⁰ For an equally effective procedure for this step using Ni⁰, see: Qiao, L.; Murray, B. W.; Shimazaki, M.; Schultz, J.; Wong, C.-H. *J. Am. Chem. Soc.* **1996**, *118*, 7653-7662.

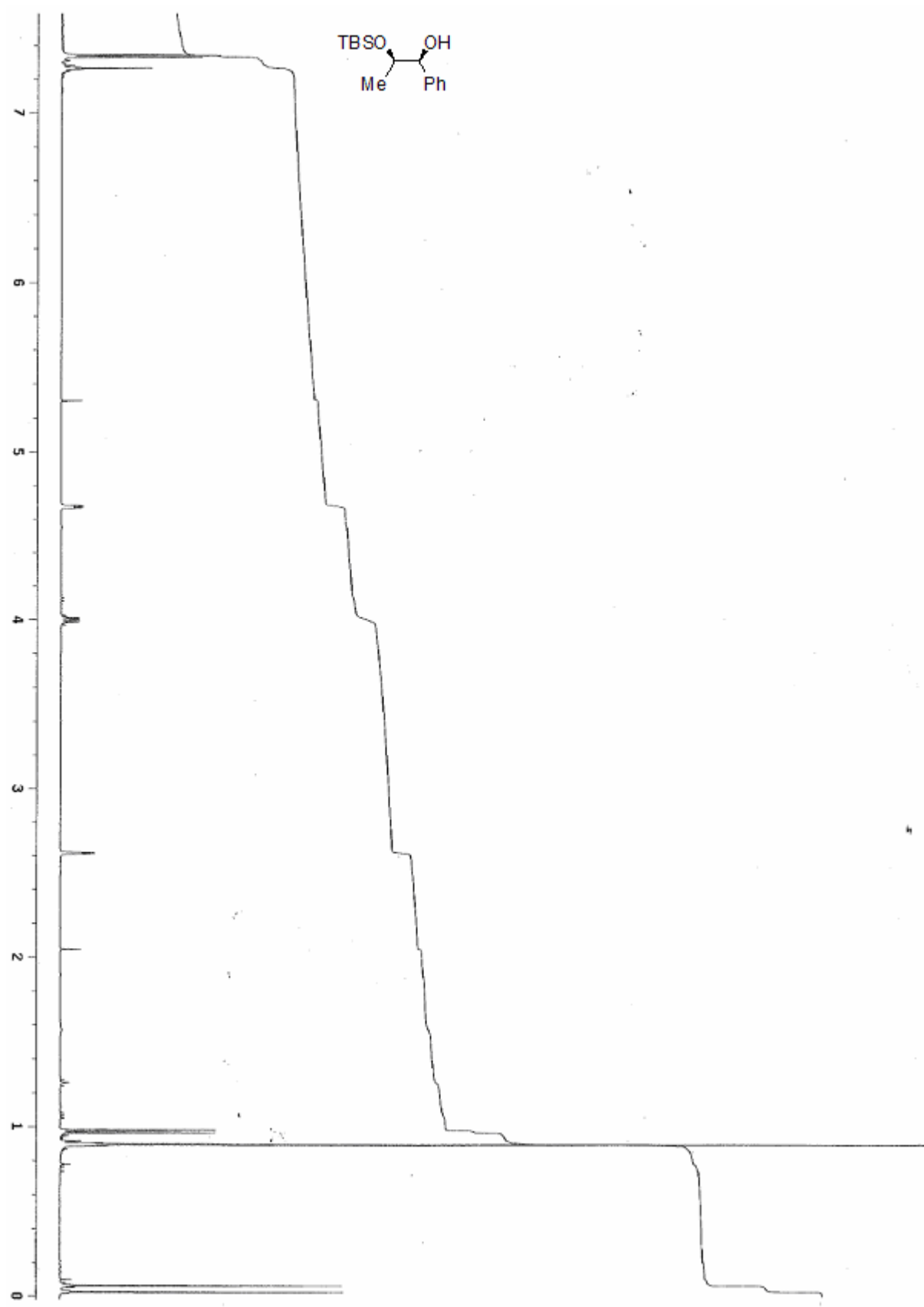














yu-v-90prod

Pulse Sequence: s2pu1

Solvent: CDCl₃
Ambient temperature

GEMINI-400BB "MART"

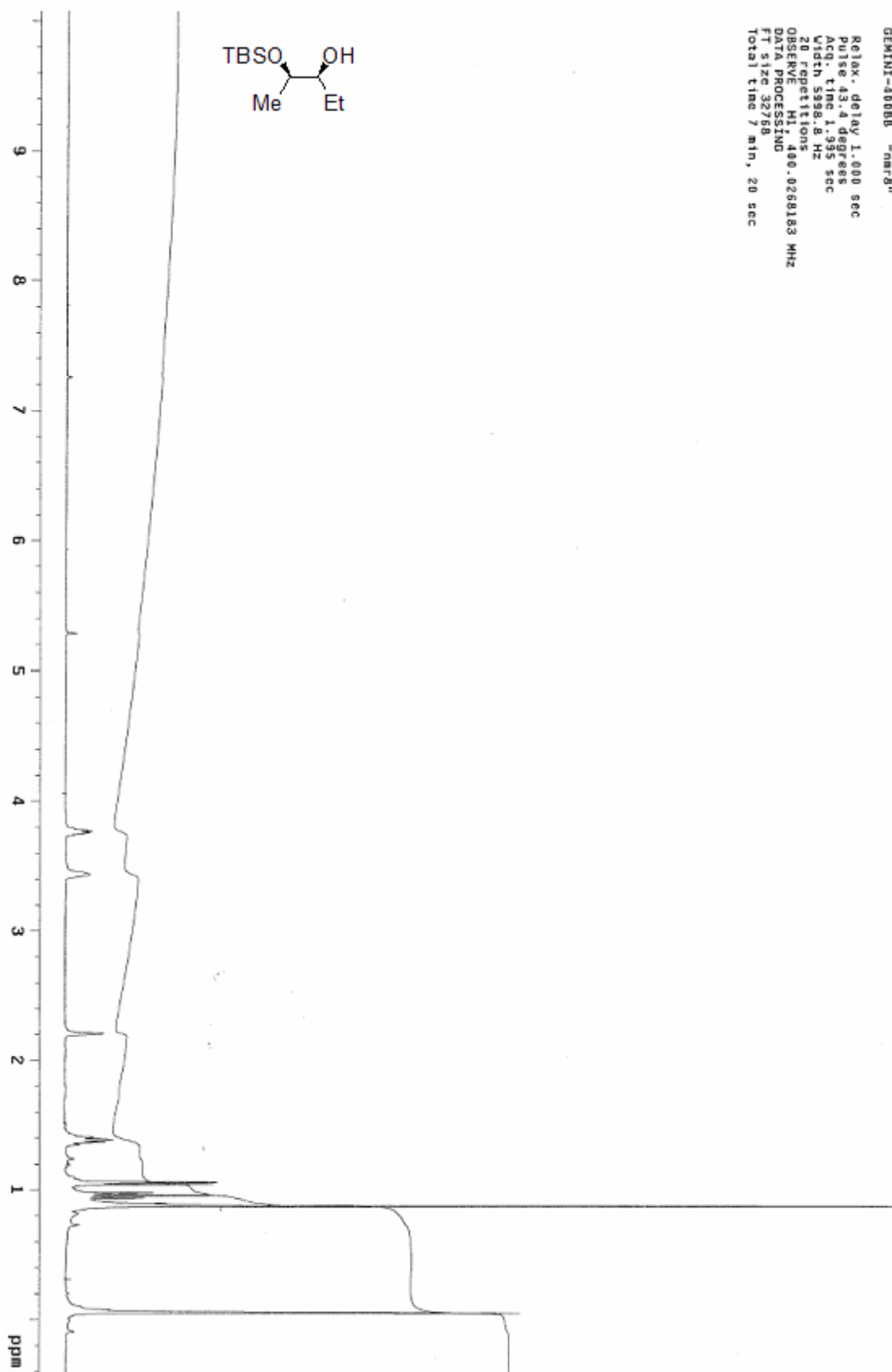
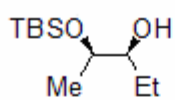
Relax. delay 1.000 s
Pulse 43.4 degrees

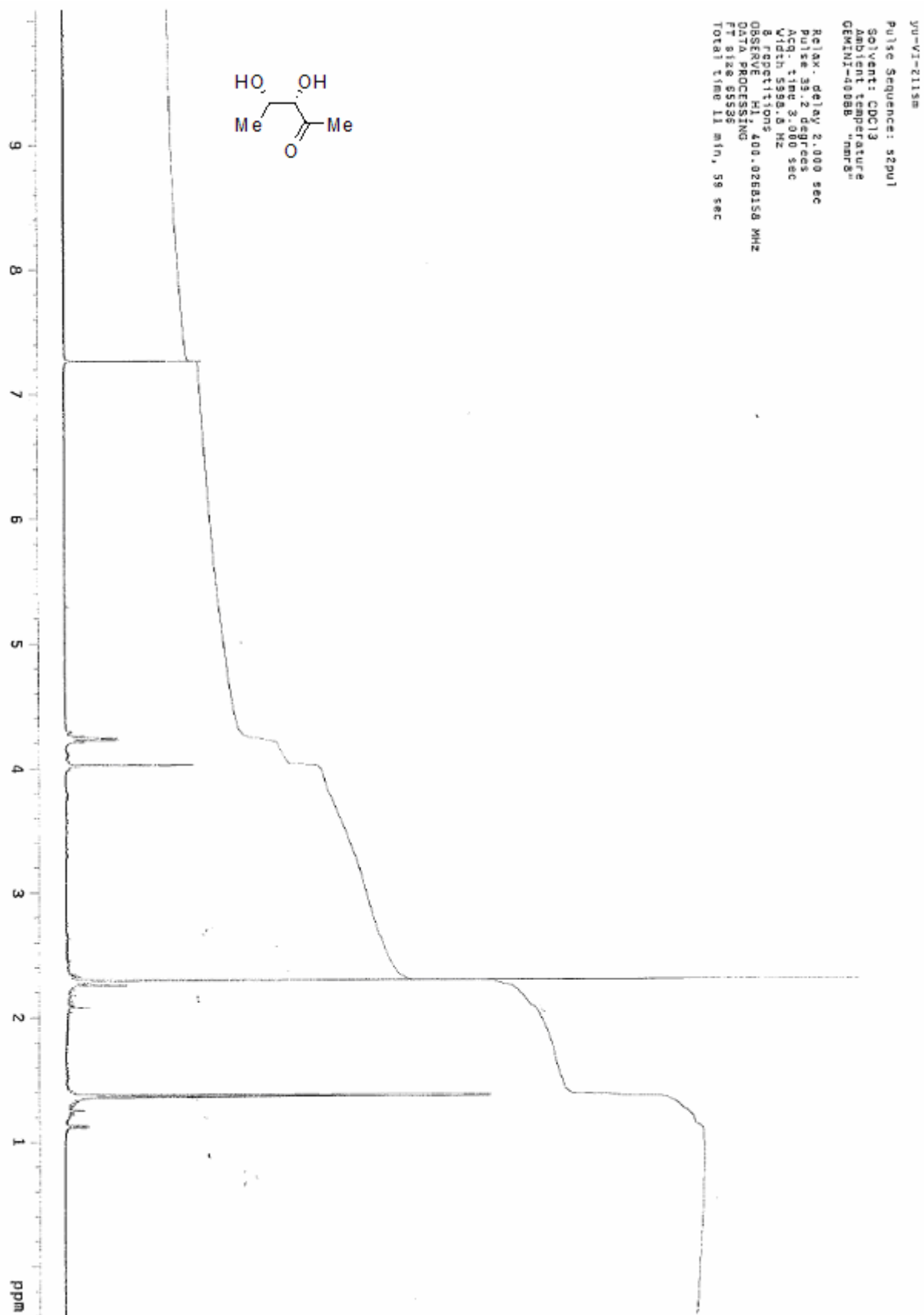
Acq. time 1.995 sec
Width 5998.8 Hz

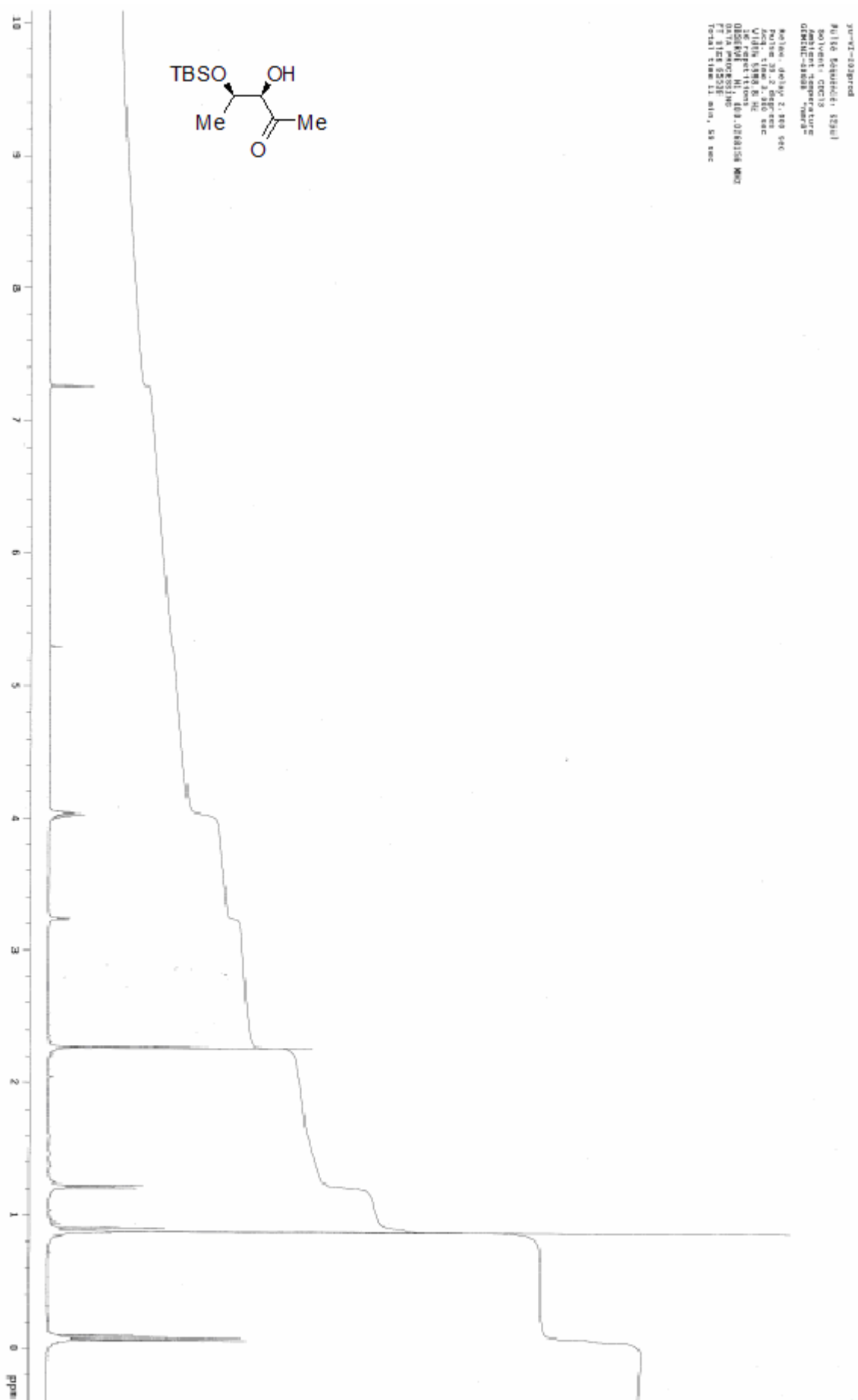
20 repetitions
OBSERVE HI 400-02681

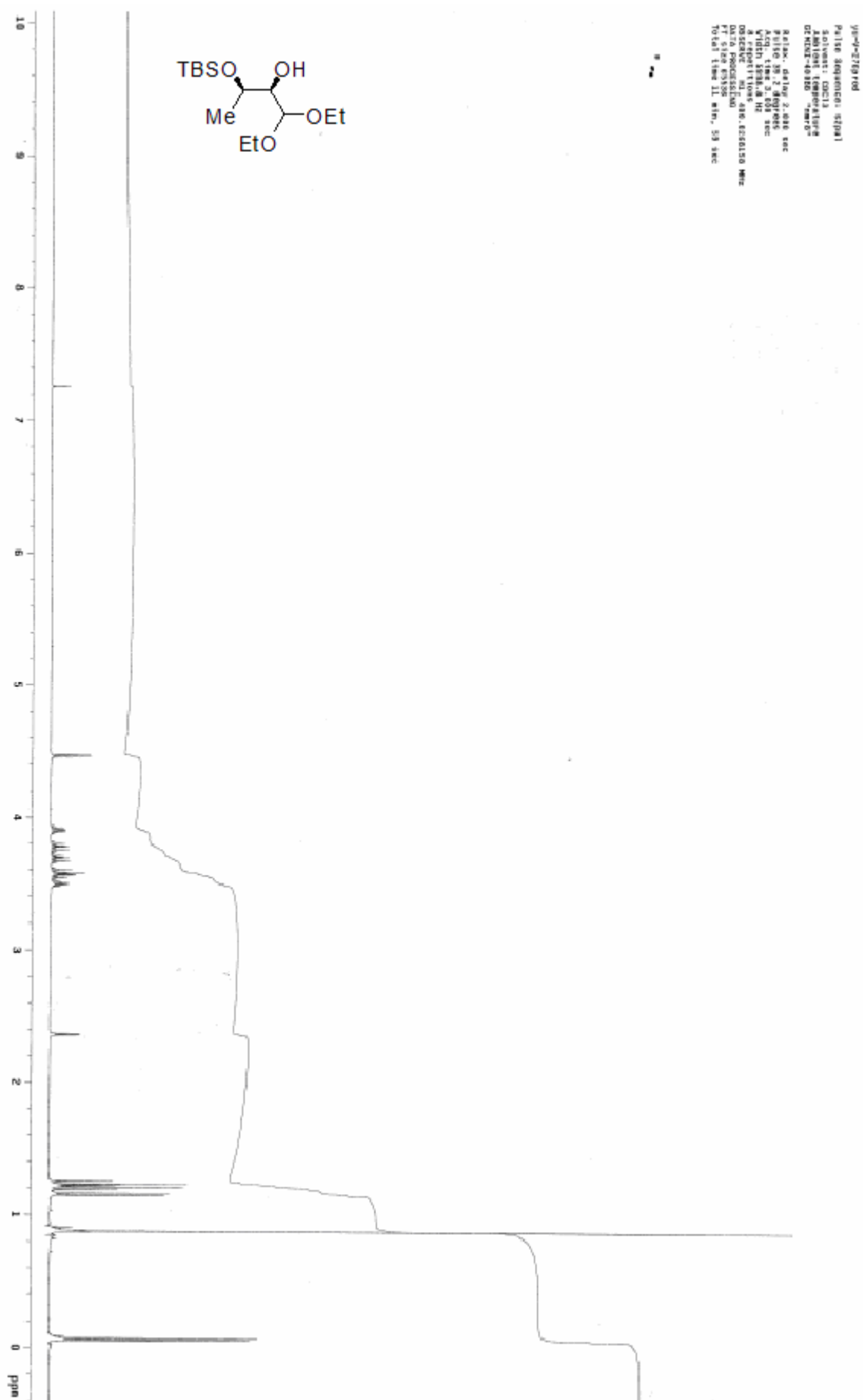
DATA PROCESSING
FT size 32768

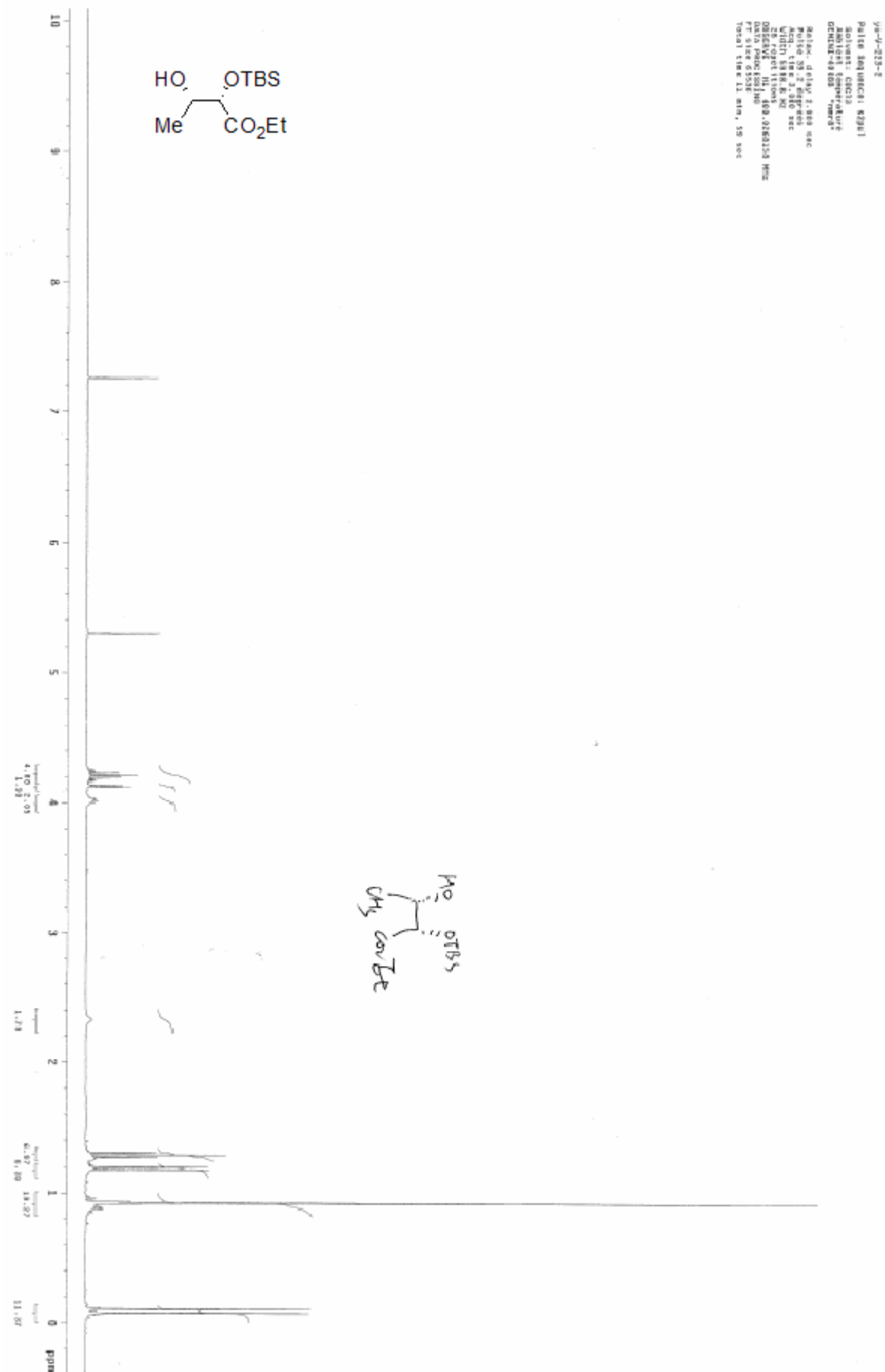
Total time 7 min, 20 sec

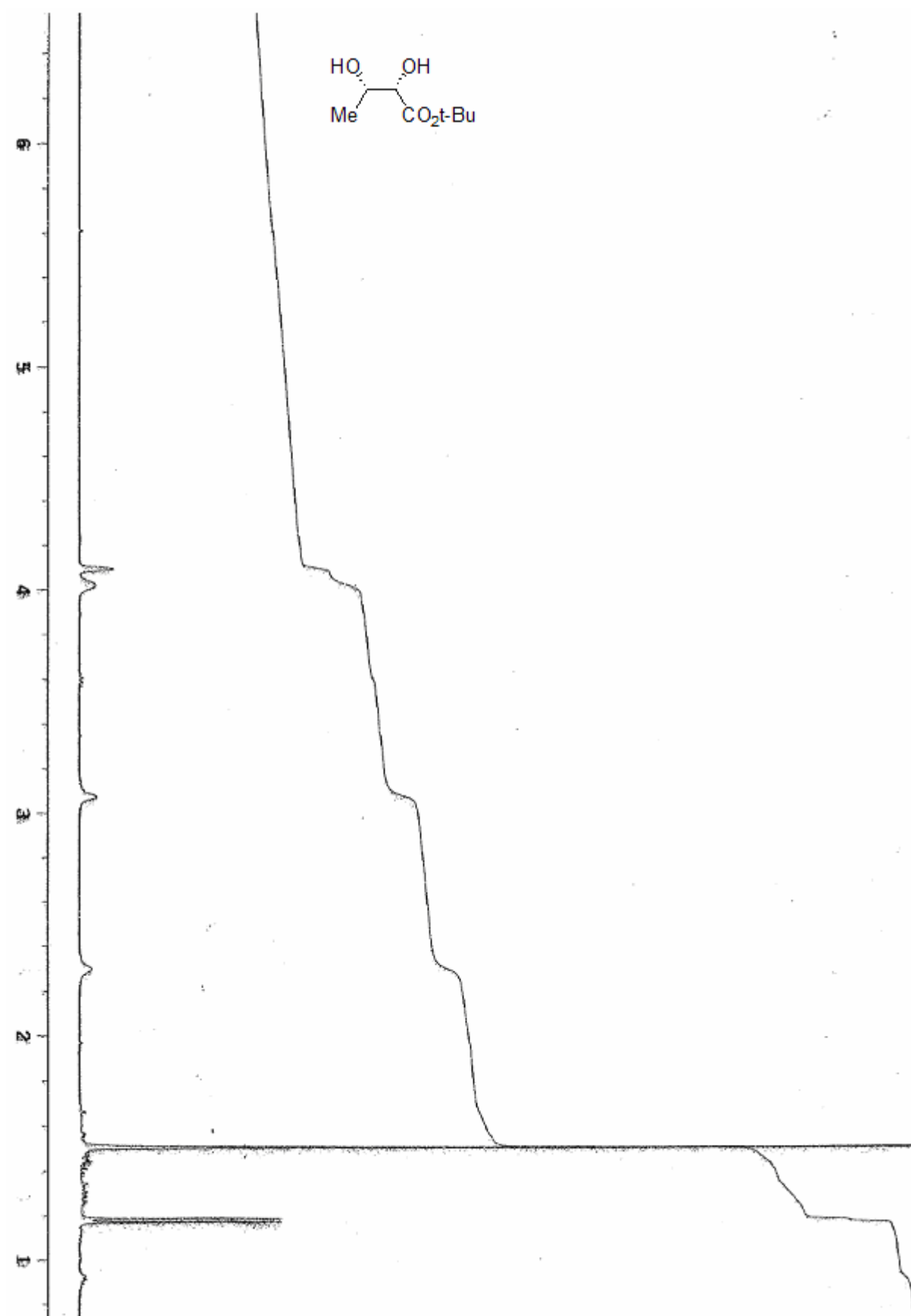


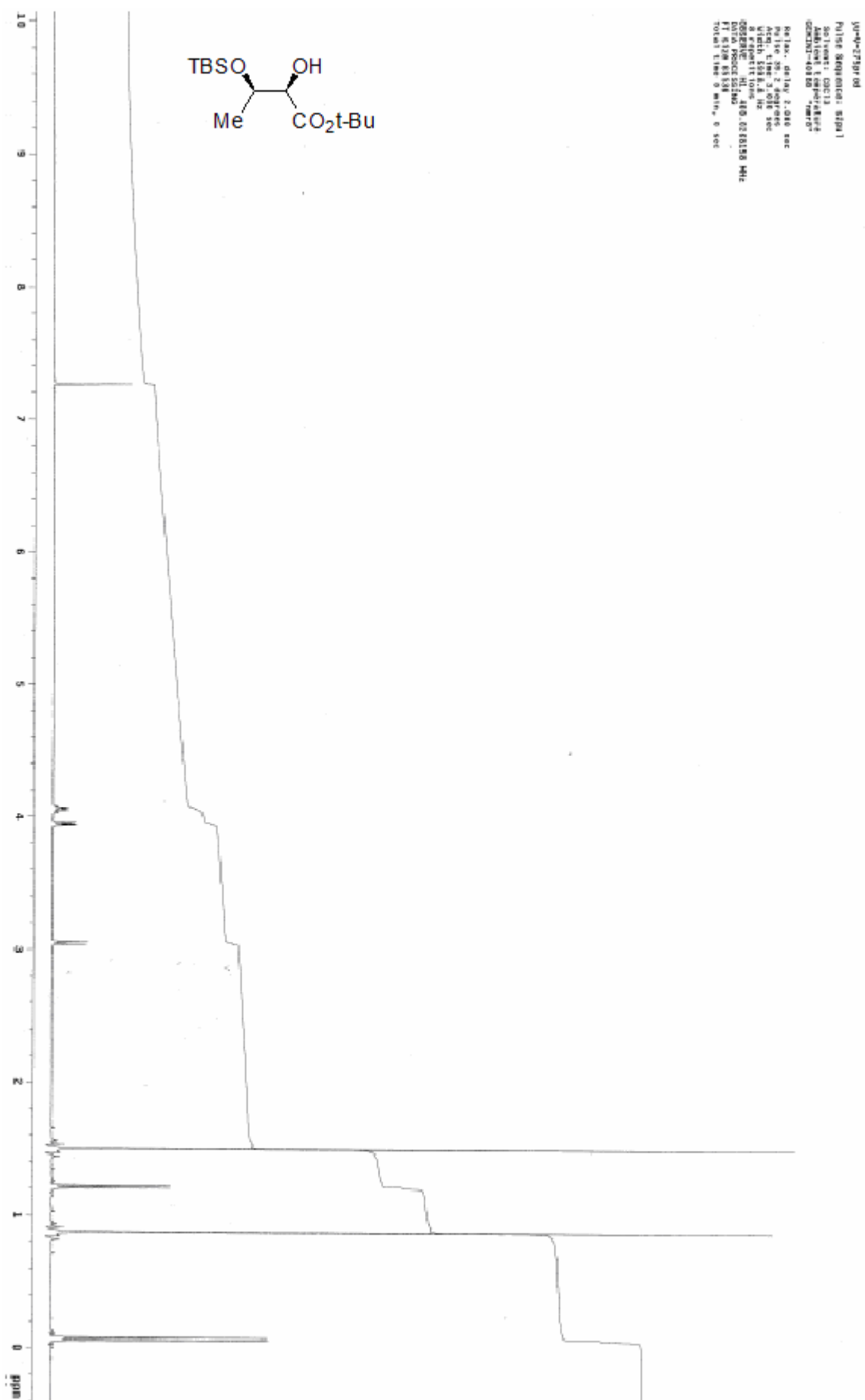


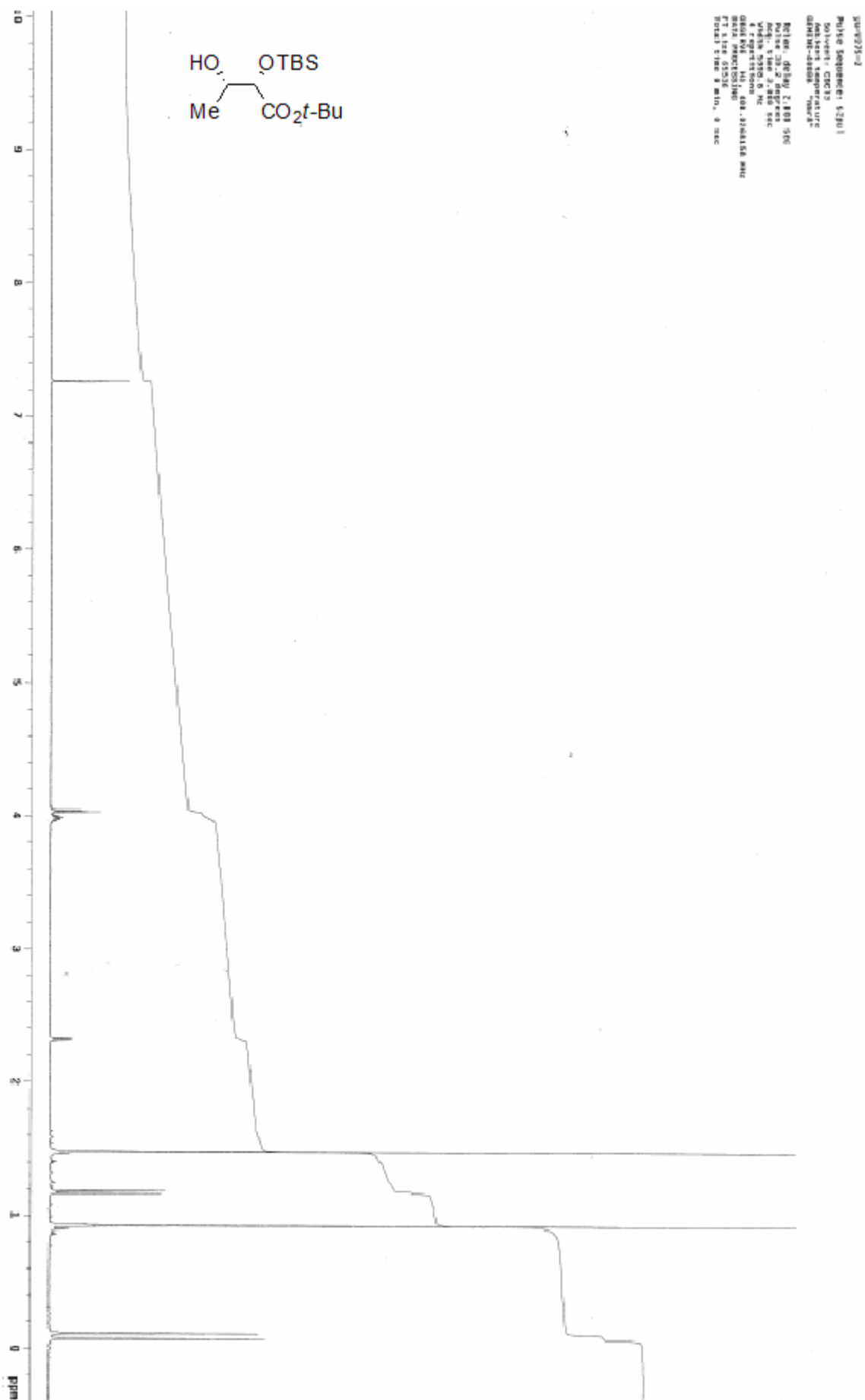




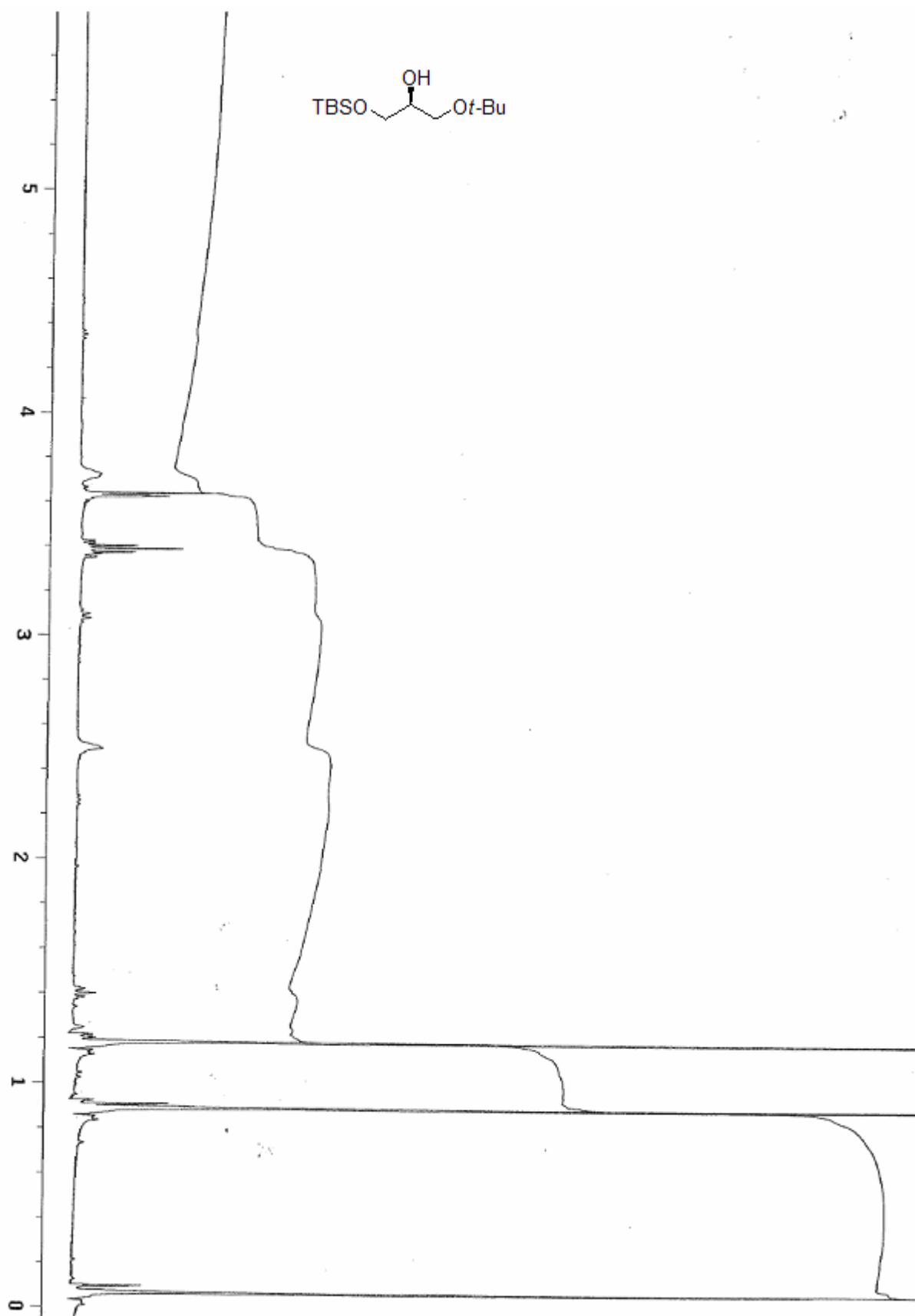


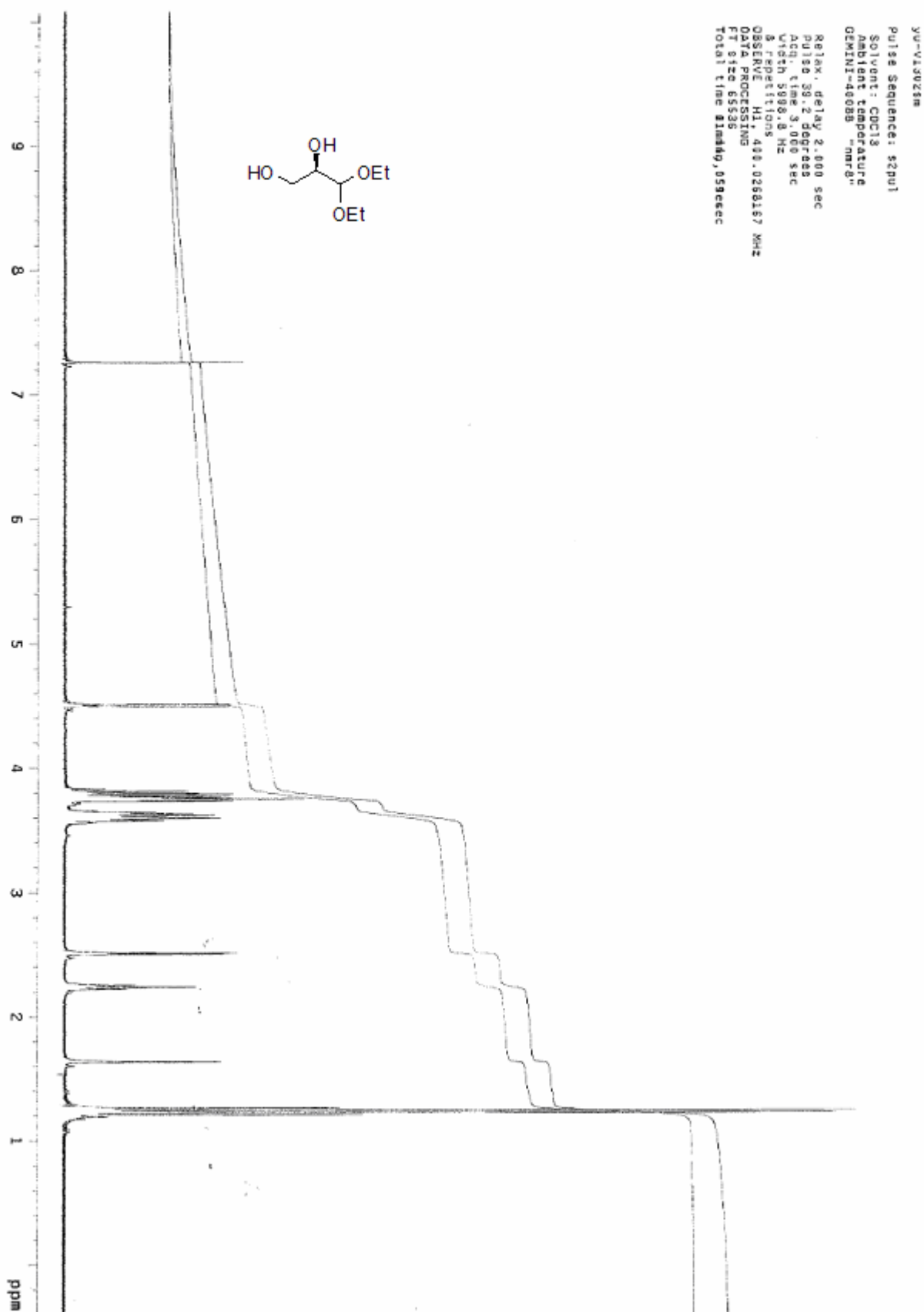


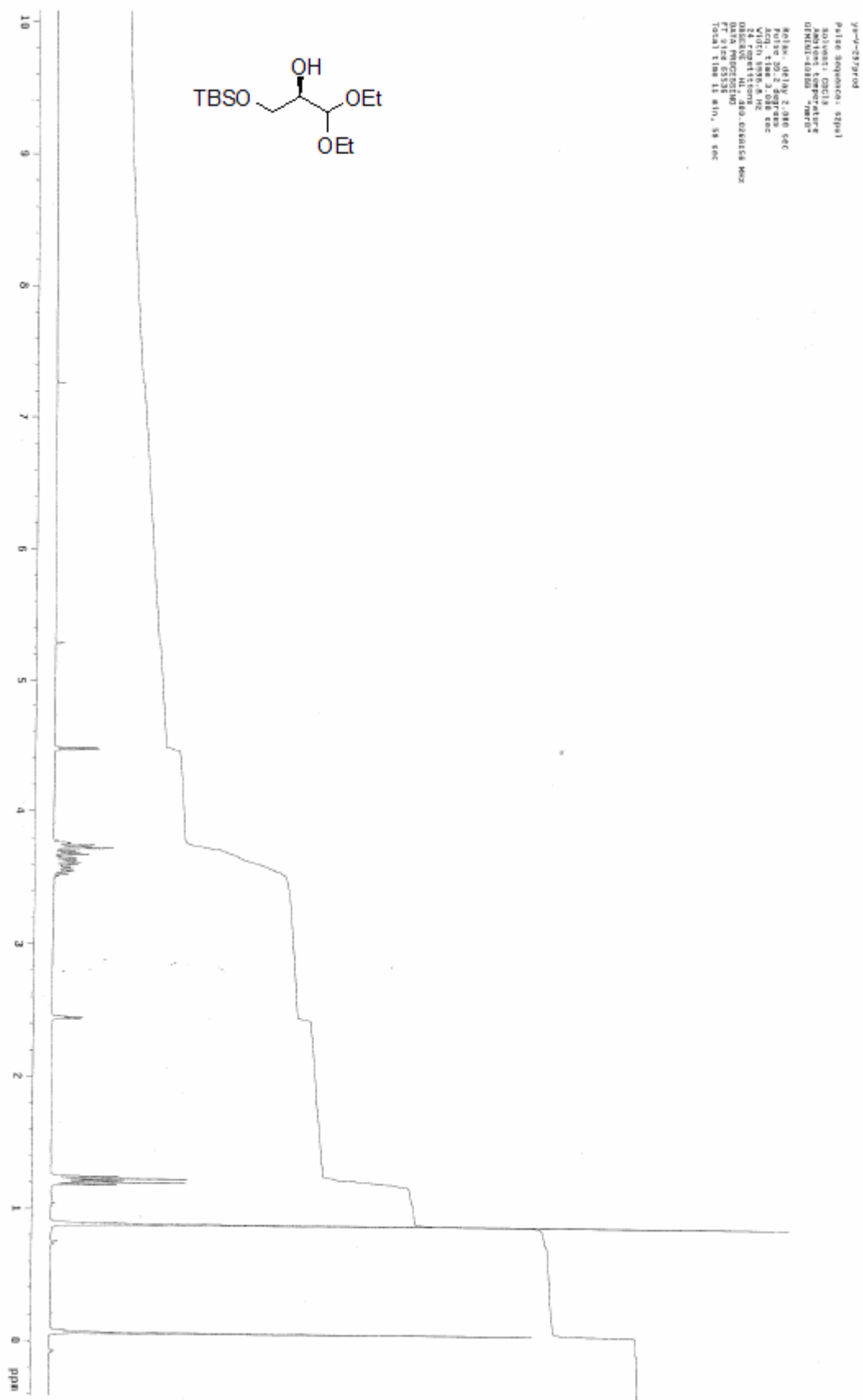


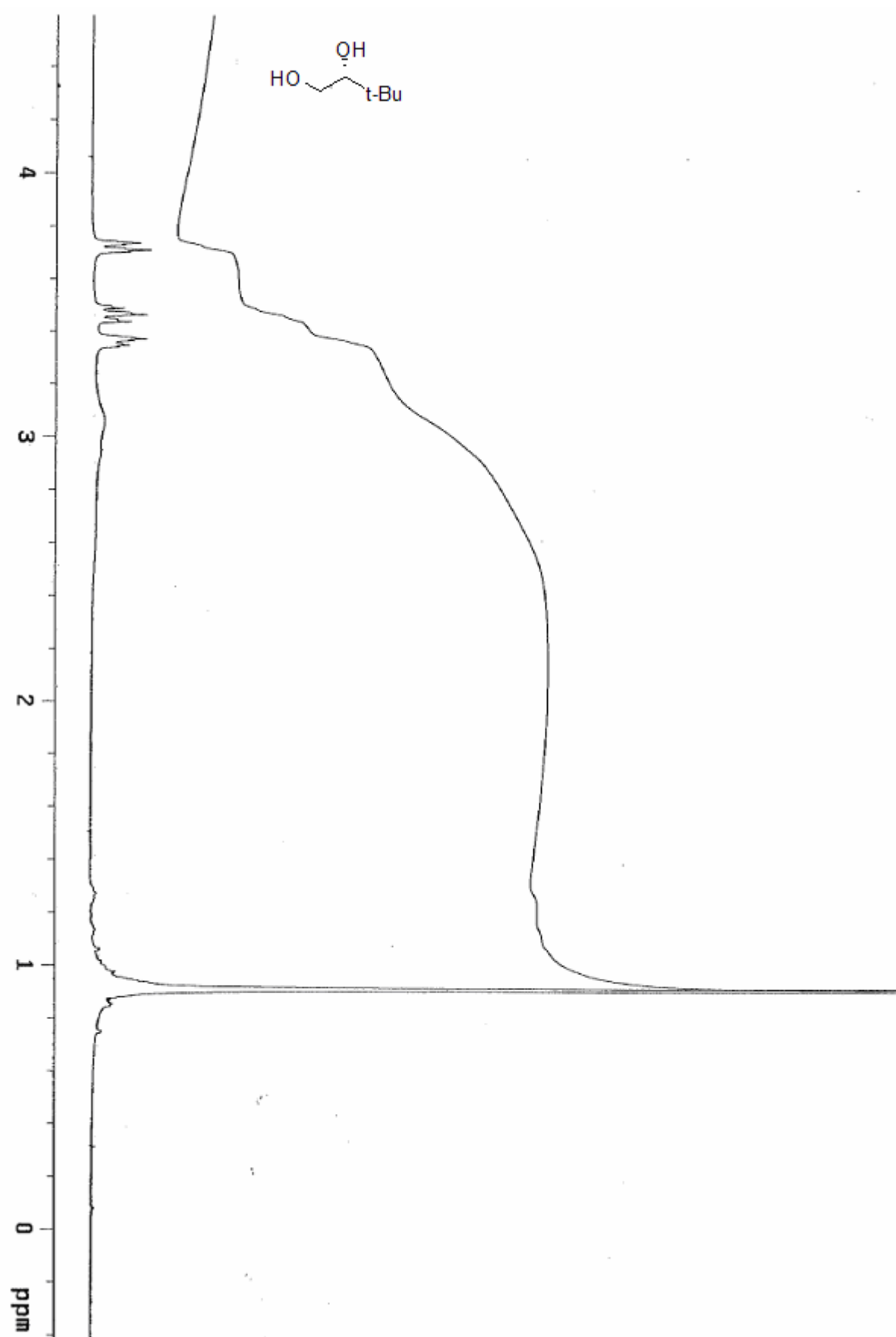












YU-VI-635M

Pulse Sequence: s2pu1

Solvent: CHCl₃
 Ambient Temp

GEMINI-40066 "nmr8"

Relax: getau 2.000

Pulse 38 - 2 degrees

Aug. 11, 1999, B. H. N. 5999, B. H. N.

6 repetitions
OBSERVE HL, 400.02DATA PROCESSING
ET 8426 65536

Total time 11 min, 5

