Total synthesis of (-)-conocarpan and assignment of the absolute configuration by chemical methods

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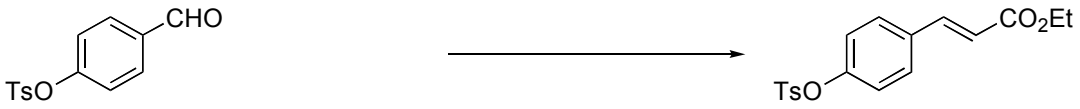
SUPPORTING INFORMATION

In ^{1}H NMR spectra the *J* values quoted are spacings measured directly from the spectrum.

All experiments were done under an inert atmosphere (N_2 or Ar). Column sizes are quoted as diameter x height.

2-Propenoic acid, 3-phenyl-, ethyl ester, (2E)-

(2*E*)-3-[4-(Toluene-4-sulfonyloxy)phenyl]-2-propenoic Acid Ethyl Ester (6).

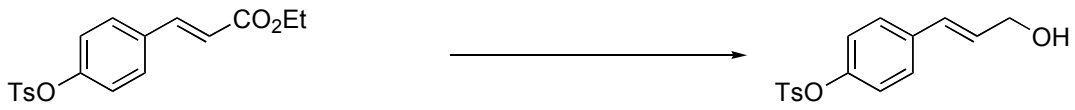


5 **6**

$(EtO)_2P(O)CH_2CO_2Et$ (11.6 mL, 58.47 mmol), followed by Et_3N (8.2 mL, 8.2 mmol), were added to a suspension of LiBr (5.27 g, 61.11 mmol) in THF (136 mL) and the mixture was stirred for 15 min. Aldehyde **5** (13.69 g, 49.55 mmol) was then added in one portion and stirring was continued for 4 h. Et_2O (250 mL) was added and the organic layer was washed with water, saturated aqueous Na_2CO_3 and brine, dried ($MgSO_4$) and evaporated. The residue was dissolved in EtOH (150 mL) and, after a few min, the product crystallized and was collected. A second crop was obtained when the filtrate was allowed to stand for several h. The total product, which was a white crystalline solid, weighed 13.88 g (81%): mp 75-78 °C; FTIR (CH_2Cl_2 cast) 3068, 2982, 1710, 1415,

1200, 1177 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.35 (t, *J* = 7.1 Hz, 3 H), 2.47 (s, 3 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 6.38 (d, *J* = 16.1 Hz, 1 H), 7.02 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.33 (apparent d as part of AA'BB' system, *J* = 8.1 Hz, 2 H), 7.45 (apparent d as part of AA'BB' system, *J* = 8.8 Hz, 2 H), 7.62 (d, *J* = 16.1 Hz, 1 H), 7.73 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.3 (q), 21.7 (q), 60.6 (t), 119.3 (d), 122.9 (d), 128.5 (d), 129.2 (d), 129.8 (d), 132.3 (s), 133.4 (s), 142.8 (d), 145.6 (s), 150.7 (s), 166.6 (s); exact mass *m/z* calcd for $C_{18}H_{18}O_5S$ 346.08749, found 346.08836. Anal. Calcd for $C_{18}H_{18}SO_5$: C 62.40; H 5.24; S 9.26. Found: C 62.38; H 5.10; S 9.10.

Toluene-4-sulfonic Acid 4-[(1*E*)-3-Hydroxy-1-propenyl]phenyl Ester (7).

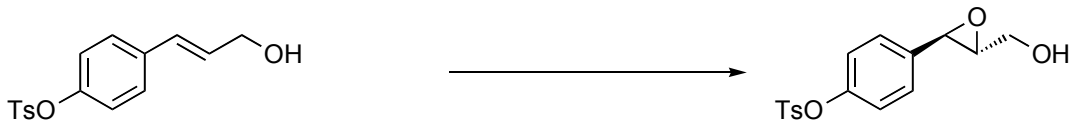


6 **7**

A three-necked flask was equipped with a stopper, a septum, a magnetic stirring bar and an addition funnel. The flask was charged with **6** (20.20 g, 58.32 mmol) and THF (200 mL) was added. The resulting solution was cooled to 0 °C in an ice bath, and the addition funnel was charged with DIBAL-H (1 M in hexane, 128 mL), which was then added dropwise over 1 h with stirring. After the addition, stirring at 0 °C was continued for 1 h, and the mixture was then quenched by addition of aqueous NaOH (1 M, 50 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL) and the combined organic extracts were washed with aqueous NaOH (1 M, 2 x 50 mL) and brine (1x 50 mL). The ethereal solution was allowed to stand overnight, during which time an aluminum hydrate precipitated. $MgSO_4$ and Celite were added and the mixture was filtered. Evaporation of the filtrate and flash chromatography of the residue over silica gel (5 x 30 cm), using 30-50% EtOAc-

hexane (gradient elution), gave **7** (16.84 g, 95%) as a crystalline solid: mp 64-67 °C; FTIR ($CHCl_3$ cast) 3363, 2868, 1597, 1501, 1371, 1197 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.80 (br s, 1 H), 2.45 (s, 3 H), 4.31 (d, *J* = 5.1 Hz, 2 H), 6.30 (dt, *J* = 15.9, 5.5 Hz, 1 H), 6.56, (d, *J* = 16.0 Hz, 1 H), 6.92 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.27 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.31 (apparent dd as part of AA'BB' system, *J* = 8.6, 0.6 Hz, 2 H), 7.70 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.7 (q), 63.4 (t), 122.5 (d), 127.5 (d), 128.5 (d), 129.4 (d), 129.7 (d), 132.3 (s), 135.8 (s), 145.4 (s), 148.8 (s); exact mass *m/z* calcd for $C_{16}H_{16}O_4S$ 304.07693, found 304.07651.

Toluene-4-sulfonic Acid 4-[(2*S*,3*R*)-3-Hydroxymethyloxyranyl)]-phenyl Ester (8a).



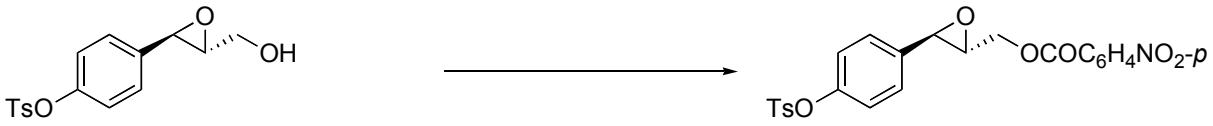
7 **8a**

Crushed 4Å molecular sieves (500 mg), activated at >200 °C and 0.3 torr for 24 h, were added to a solution of (-)-diisopropyl tartrate (0.050 mL, 0.23 mmol) in CH_2Cl_2 (4 mL), and the flask was lowered into a cold bath (-25 °C, CO_2-CCl_4). $Ti(OPr\text{-}i)_4$ (0.10 mL, 0.34 mmol) was then added, followed by *t*-BuOOH (3 M in isooctane, 1.6 mL, 4.8 mmol). The mixture was stirred for 10 min and then **7** (728.4 mg, 2.390 mmol) in CH_2Cl_2 (1.2 mL plus 0.8 mL as a rinse) was added dropwise by syringe. The mixture was stirred for 2 h and then quenched by addition of aqueous NaOH (30%w/v, 0.38 mL) saturated with NaCl. Stirring was continued for 10 min and then $MgSO_4$ (ca 500 mg) and Celite (ca 1 g) were added. The mixture was swirled and the solids were filtered off. Evaporation of the filtrate and flash chromatography of the residue over silica gel (2.5 x 35 cm), using first 50-60% EtOAc-hexane (step gradient elution) and then

6:3:1 EtOAc-hexane-MeOH, gave **8a** (712.4 mg, 93%) as a white solid: mp 51-53 °C; FTIR ($CHCl_3$ cast) 3419, 3069, 2986, 2926, 2872, 1598, 1505, 1372, 1198, 1176, 1150 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.74 (dd, *J* = 5.1, 7.7 Hz, 1 H), 2.49 (s, 3 H), 3.18 (ddd, *J* = 2.3, 2.3, 3.6 Hz, 1 H), 3.83 (ddd, *J* = 3.6, 7.8, 12.64 Hz, 1H), 3.93 (d, *J* = 2.0 Hz, 1 H), 4.06 (ddd, *J* = 2.5, 4.9, 12.9 Hz, 1 H), 6.99 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.21 (apparent d as part of AA'BB' system, *J* = 8.5 Hz, 2 H), 7.30 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H), 7.71 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.0 (t), 55.1 (d), 61.3 (t), 62.8 (d), 122.8 (d), 127.2 (d), 128.7 (d), 130.1 (d), 132.5 (s), 136.1 (s), 145.7 (s), 149.7 (s); exact mass *m/z* calcd for $C_{16}H_{16}NaOS$ 343.06107, found 343.06134.

Samples of the Mosher esters (from the above optically active epoxy alcohol and the corresponding racemic epoxy alcohol) were prepared by adding (+)-MTPA-Cl to a stirred solution of the epoxy alcohol and Et_3N in CH_2Cl_2. Analysis of the derived crude Mosher esters by ^1H NMR showed the diastereomeric ratio of the above epoxy alcohol to be 94:6. Analysis of the epoxy alcohol from another batch (but prepared under the same conditions) by chiral HPLC [Chiralpak AD-RH (150 x 4.6 mm), 1:1 MeCN-water, flow 0.5 mL/min, detection at 232 nm. Baseline separation of a racemic sample; retention times 11.9 min and 14.3 min.] showed the enantiomeric ratio to be 94.7:5.3.

4-Nitrobenzoic Acid 3-[(2*R*,3*R*)-4-(Toluene-4-sulfonyloxy)-phenyl]oxiranylmethyl Ester (8b).



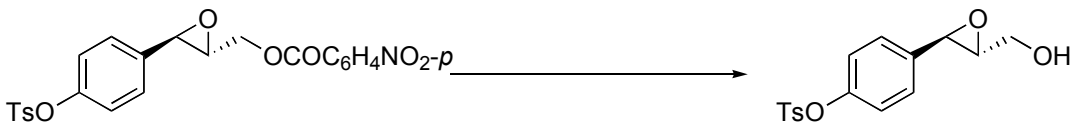
8a **8b**

p-Nitrobenzoyl chloride (43.6 mg, 0.235 mmol) was added in one portion to a stirred solution of **8a** (64.3 mg, 0.201 mmol) and

Et_3N (0.04 mL, 0.3 mmol) in CH_2Cl_2 (3 mL). Stirring was continued for 2 h, and the mixture was then washed once with water, twice with saturated aqueous $NaHCO_3$, and dried ($MgSO_4$). Evaporation of the solvent and crystallization of the residue from MeOH gave **8b** (67.2 mg, 70%) as small white needles: mp 102-104 °C; $[\alpha]^{22}_D$ +20.42 (*c* 0.62, $CHCl_3$); FTIR (CH_2Cl_2, cast) 3112, 3057, 2997, 2955, 2868, 1926, 1728, 1598, 1528, 1373 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.47 (s, 3 H), 3.37 (m, 1 H), 3.88 (d, *J* = 1.9 Hz, 1 H), 4.38 (dd, *J* = 12.4, 6.0 Hz, 1 H), 4.81 (dd, *J* = 12.3, 3.2 Hz, 1 H), 7.01 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.24 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.33 (apparent d as part of AA'BB' system, *J* = 8.1 Hz, 2 H), 7.72 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H), 8.27 (apparent d as part of AA'BB' system, *J* = 8.9 Hz, 2 H), 8.33 (apparent d as part of AA'BB' system, *J* = 8.9 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.7 (q), 55.8 (d), 59.2 (d), 65.3 (t), 122.7 (d), 123.6 (d), 126.9 (d), 128.5 (d), 129.8 (d), 130.9 (d), 132.3 (s), 134.8 (s), 134.9 (s), 145.5 (s), 149.7 (s), 150.8 (s), 164.4 (s); exact mass *m/z* calcd for $C_{23}H_{19}NNaO_8S$ 492.07236, found 492.07249. Anal. Calcd for $C_{23}H_{19}NO_8S$: C 58.84; H 4.08; S 6.83. Found: C 58.82; H 4.14; S 7.07.

A separate sample from a later and larger-scale experiment was crystallized from 7:3 EtOAc-hexane and gave large prisms which had $[\alpha]^{22}_D$ +20.22 (*c* 0.70, $CHCl_3$). This nitrobenzoate was recrystallized again twice from EtOH, and the resulting material (total yield 62%) was used for the conocarpan synthesis.

Toluene-4-sulfonic acid 4-[(2*R*,3*R*)-(3-Hydroxymethyl-oxiranyl)]phenyl Ester (8a').



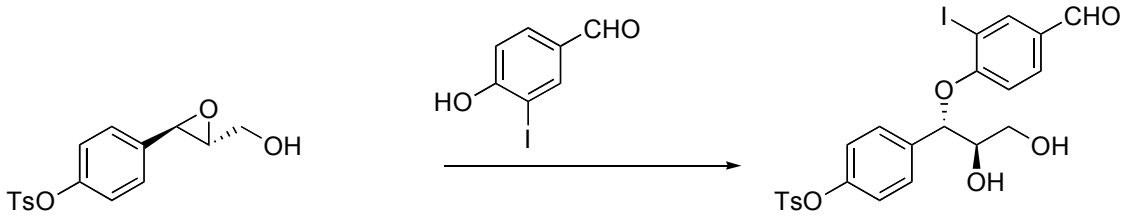
8b **8a'**

K_2CO_3 (1.90 g, 13.7 mmol) was added to a stirred solution of

8b (5.46 g, 11.6 mmol) in 80% MeOH (100 mL). The mixture was stirred until a clear solution was obtained (ca 2.5 h). The MeOH was then evaporated, the residue was dissolved in EtOAc and the solution was washed three times with saturated aqueous $NaHCO_3$ and once with brine, and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography of the residue over silica gel (2.5 x 40 cm), using first 50% EtOAc-hexane containing Et_3N (ca 3 drops/100 mL) and then 60% EtOAc-hexane containing Et_3N (ca 3 drops/100 mL), gave **8a'** (3.6178 g, 97%).

The hydrolysis was repeated on a small scale, using the same batch of **8b**, and HPLC analysis of the product [Chiralpak AD-RH (150 x 4.6 mm), 1:1 MeCN-water, flow 0.5 mL/min, detection at 232 nm. Baseline separation of a racemic sample] showed the enantiomeric ratio to be 98.9:1.1. The material had: $[\alpha]^{25}_{D}$ 18.35 (*c* 0.75, $CHCl_3$); all other data are identical to those reported above.

Toluene-4-sulfonic Acid 4-[(1*S*,2*R*)-1-(4-formyl-2,3-dihydroxy-2-iodophenoxy)propyl]phenyl Ester (10).[21]



8a' **10**

Epoxy alcohol **8a'** (er = 99.8:1.1) (1.8694 g, 5.8350 mmol) was added in one portion to a stirred and heated (sand bath, 70 °C) solution of 4-hydroxy-3-iodobenzaldehyde[19] (2.6359 g, 10.628 mmol) in a mixture of aqueous NaOH (1 M, 5.8 mL, 5.8 mmol) and water (6 mL). Stirring at 70 °C was continued for 2.5 h. The mixture was allowed to cool and was then poured into aqueous NaOH (1 M, 10 mL). The aqueous phase was extracted with Et_2O and the combined organic extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography of

the residue over silica gel (2.5 x 35 cm), using 50-80% EtOAc-hexane containing Et_3N (ca 3 drops/100 mL) (gradient elution), gave **10** [2.1124 g, 64%, or 83% based on recovered **8a'** (436.8 mg, 23%)] as a white, crystalline solid: mp 55-58 °C; $[\alpha]^{22}_D$ -39.52 (*c* 5.69, $CHCl_3$); FTIR ($CDCl_3$ cast) 3417, 3067, 2927, 2883, 2731, 1694, 1587, 1502, 1480, 1371, 1255, 1198, 1177, 1155, 1093, 1038, 869 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.33 (br s, 1 H), 2.45 (s, 3 H), 2.75 (br s, 1 H), 3.82 (dd, *J* = 3.7, 11.5 Hz, 1 H), 3.94 (dd, *J* = 5.2, 11.5 Hz, 1 H), 4.03-4.06 (m, 1 H), 5.40 (d, *J* = 5.8 Hz, 1 H), 6.64 (d, *J* = 8.6 Hz, 1 H), 7.03 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.30 (apparent dd as part of AA'BB' system, *J* = 0.6, 8.6 Hz, 2 H), 7.33 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.60 (dd, *J* = 2.0, 8.6 Hz, 1 H), 7.69 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H), 8.27 (d, *J* = 2.0 Hz, 1 H), 9.76 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.7 (q), 62.3 (t), 74.4 (d) 81.4 (d), 87.4 (s), 113.3 (d), 122.9 (d), 128.2 (d), 128.3 (d), 129.8 (d), 131.7 (d), 131.8 (s), 132.3 (s), 135.2 (s), 140.9 (d), 145.6 (s), 149.6 (s), 160.1 (s), 189.2 (d); exact mass *m/z* calcd for $C_{23}H_{21}INaO_7S$ 590.99450, found 590.99454.

Toluene-4-sulfonic Acid 4-[(1*S*,2*R*)-1-(4-formyl-2-iodo-phenoxy)-2,3-bismethanesulfonyloxypropyl]phenyl Ester (11).

10 **11**

Et_3N (0.022 mL, 0.16 mmol) and then $MeSO_2Cl$ (0.012 mL, 0.16 mmol) were added to a stirred and cooled (0 °C) solution of **10** (37.4 mg, 0.0659 mmol) in CH_2Cl_2 (2 mL). After the addition stirring was continued for 10 min, the cooling bath was removed and stirring was continued overnight. The mixture was washed

twice with water and dried ($MgSO_4$). Evaporation of the solvent gave an oil which was kept under oil pump vacuum for 12 h to give **11** (48.8 mg, 100%) as a white, crystalline solid: mp 60-64 °C; $[\alpha]^{22}_D$ -31.92 (*c* 4.10, $CHCl_3$); FTIR ($CDCl_3$ cast) 3031, 2939, 2849, 1694, 1588, 1503, 1480, 1412, 1365, 1251, 1199, 1178, 1156, 1041, 1017, 866 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.50 (s, 3 H), 2.89 (s, 3 H), 3.11 (s, 3 H), 4.68 (dd, *J* = 2.5, 11.9 Hz, 1 H), 4.92 (dd, *J* = 5.9, 11.9 Hz, 1 H), 5.12 (ddd, *J* = 2.5, 5.8, 5.8 Hz, 1 H), 5.69 (d, *J* = 5.8 Hz, 1 H), 6.70 (d, *J* = 8.6 Hz, 1 H), 7.13 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.36 (apparent dd as part of AA'BB' system, *J* = 0.6, 8.6 Hz, 2 H), 7.44 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.73 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H), 7.73 (dd, *J* = 2.0, 8.5 Hz, 1 H), 8.35 (d, *J* = 2.0 Hz, 1 H), 9.84 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.0 (q), 38.0 (q), 38.7 (q), 67.0 (t), 78.9 (d), 80.4 (d), 87.4 (s), 113.4 (d), 123.8 (d), 128.4 (d), 128.7 (d), 130.2 (d), 132.0 (d), 132.3 (s), 132.6 (s), 133.3 (s), 141.3 (d), 146.0 (s), 150.6 (s), 159.5 (s), 189.3 (d); exact mass *m/z* calcd for $C_{25}H_{25}INaO_{11}S_3$ 746.94960, found 746.94935.

Toluene-4-sulfonic Acid 4-[(*R*)-1-(4-formyl-2-iodophenoxy)-allyl]phenyl Ester (12).

11 **12**

NaI (91.7 mg, 0.612 mmol) was added to a stirred solution of **11** (29.5 mg, 0.0408 mmol) in 2-butanone (2 mL), and the mixture was refluxed for 4 h, and then allowed to cool. The solvent was evaporated and the residue was partitioned between EtOAc and saturated aqueous $Na_2S_2O_3$. The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash

chromatography of the residue over silica gel (0.5 x 20 cm), using 30% EtOAc-hexane, gave **12** (15.7 mg, 71%) as an amber oil: $[\alpha]^{22}_{D}$ -8.88 (*c* 13.43, CH_2Cl_2); FTIR (CH_2Cl_2 cast) 3065, 2922, 2834, 2727, 1695, 1587, 1501, 1479, 1371, 1252, 1197, 1177, 1154, 1093, 866 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.48 (s, 3 H), 5.36 (dd, *J* = 0.8, 10.4 Hz, 1 H), 5.50 (dd, *J* = 0.8, 17.1 Hz, 1 H), 5.83 (d, *J* = 5.9 Hz, 1 H), 6.05 (ddd, *J* = 5.9, 10.4, 17.0 Hz, 1 H), 6.88 (d, *J* = 8.5 Hz, 1 H), 7.06 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.33 (apparent d as part of AA'BB' system, *J* = 8.5 Hz, 2 H), 7.45 (apparent d as part of AA'BB' system, *J* = 8.8 Hz, 2 H), 7.73 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H), 7.76 (dd, *J* = 2.0, 8.5 Hz, 1 H), 8.34 (d, *J* = 1.9 Hz, 1 H), 9.83 (s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.7 (q), 81.4 (d), 87.8 (s), 113.6 (d), 117.8 (t), 122.8 (d), 127.8 (d), 128.4 (d), 129.8 (d), 131.5 (d), 131.6 (s), 132.4 (s), 136.2 (d), 137.6 (s), 141.2 (d), 145.5 (s), 149.3 (s), 160.6 (s), 189.2 (d); exact mass *m/z* calcd for $C_{23}H_{19}INaO_5S$ 556.98902, found 556.98890. Anal. Calcd for $C_{23}H_{19}IO_5S$: C 51.69; H 3.58; S 6.00. Found: C 51.41; H 3.65; S 5.92.

When the experiment was repeated on a larger scale with the dimesylate (2.1255 g, 2.94 mmol), the yield was 65% [or 80% based on recovered **11** (398.1 mg, 19%)].

Toluene-4-sulfonic Acid 4-[(2*S*,3*R*)-2,3-Dihydro-5-formyl-3-methylbenzofuran-2-yl]phenyl Ester (13).

12 **13**

A solution of Bu_3SnH (0.62 mL, 2.3 mmol) and AIBN (48.1 mg, 0.293 mmol) in PhMe (18 mL) was added over 4 h (syringe pump) to a stirred and heated (80 °C) solution of **12** (910.4 mg, 1.704

mmol) in PhMe (18 mL) (N_2 atmosphere). After the addition the mixture was heated for a further 2 h and then allowed to cool. Evaporation of the solvent and flash chromatography of the residue over KF-silica gel[31] (10%$^w/_w$, 2.5 x 30 cm), using 25% EtOAc-hexane, gave **13** (482.6 mg, 69%) as a light yellowish oil: $[\alpha]^{22}_D$ -50.54 (*c* 0.77, $CHCl_3$); FTIR ($CHCl_3$ cast) 2964, 2928, 1690, 1605, 1504, 1483, 1373, 1247, 1198, 1177, 1154, 1093, 867 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.40 (d, *J* = 6.9 Hz, 3 H), 2.38 (s, 3 H), 3.31-3.38 (m, 1 H), 5.19 (d, *J* = 8.4 Hz, 1 H), 6.88 (d, *J* = 8.1 Hz, 1 H), 6.96 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.24-7.27 (m, 4 H), 7.64-7.67 (m, 4 H), 9.80 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) (the spectrum shows minor aromatic impurities) δ 18.3 (q), 21.7 (q), 44.8 (d), 92.7 (d), 109.8 (d), 122.8 (d), 124.7 (d), 127.1 (d) 128.5 (d), 129.8 (d), 131.0 (s), 132.4 (s), 133.1 (s), 133.4 (d), 138.9 (s), 145.5 (s), 149.6 (s), 164.3 (s), 190.5 (d); exact mass *m/z* calcd for $C_{23}H_{20}NaO_5S$ 431.09237, found 431.09242.

Toluene-4-sulfonic Acid 4-[(2*R*,3*S*)-2,3-Dihydro-(3-methyl-5-(1*E*)-1-propenylbenzofuran-2-yl)phenyl Ester (*E*-14) and Toluene-4-sulfonic Acid 4-[(2*R*,3*S*)-2,3-Dihydro-3-methyl-5-(1*Z*)-1-propenylbenzofuran-2-yl]phenyl Ester (*Z*-14).

13 **14**

(a) Use of *t*-BuOK

t-BuOK (33.0 mg, 0.294 mmol) was added to a stirred suspension of $Ph_3PEt^+I^-$ (129.6 mg, 0.3098 mmol) in Et_2O (2 mL), and the mixture was stirred for 0.5 h. A solution of **13** (54.2 mg, 0.133 mmol) in Et_2O (1 mL) was added by syringe. The mixture was stirred for 15 min and then Et_2O (5 mL) was added, and the

mixture was washed twice with water, and once with brine and dried ($MgSO_4$). Evaporation of the solvent and flash chromatograph of the residue over silica gel (1.5 x 30 cm), using 5-10% EtOAc-hexane (gradient elution), gave **14** (33.9 mg, 62%) as a yellowish oil. Integration of the allylic methyl peaks in the ^1H NMR spectrum showed the *E*:*Z* ratio to be 1:3; apart from this ratio difference, all spectral data corresponded to those reported below for the 97:3 mixture of the same compounds.

(b) Use of BuLi

BuLi (1.6 M in hexanes, 0.06 mL, 0.096 mmol) was added to a stirred and cooled (0 °C) suspension of $Ph_3PEt^+I^-$ (39.5 mg, 0.0944 mmol) in THF (2 mL). Stirring was continued for 15 min and **13** (35.7 mg, 0.0796 mmol) in THF (1.3 mL plus 0.3 mL as a rinse) was added dropwise by syringe. Stirring was continued for 2 h and the mixture was then quenched by addition of saturated aqueous $NaHCO_3$ (0.5 mL), and partitioned between water (5 mL) and Et_2O (10 mL). The organic extract was dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (0.5 x 30 cm), using 20% EtOAc-hexane containing ca 1% Et_3N, gave **14** (23.2 mg, 69%) as a yellowish oil, which was a mixture of *Z* and *E* isomers.

Toluene-4-sulfonic Acid 4-[(2*R*,3*S*)-2,3-Dihydro-3-methyl-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl Ester (15)

14 **15**

(a) Short reaction time

$PdCl_2(PhCN)_2$ (9.4 mg, 0.025 mmol) was added to a stirred solution of **14** (102.3 mg, 0.2433 mmol) in CH_2Cl_2 (2 mL, and

stirring was continued for 23 h. Et_2O (3 mL) was added and the solution was filtered through a pad of Florisil (3 x 2 cm) using Et_2O (25 mL). Evaporation of the solvent and flash chromatography of the residue over silica gel (1 x 30 cm) using 8% EtOAc-hexane containing Et_3N (ca 3 drops/100 mL), gave **15** (100.9 mg, 99%) as a colorless oil which contained 3.1% of the *Z* isomer (^{1}H NMR): $[\alpha]^{22}_D$ -59.93 (*c* 2.24, CH_2Cl_2); FTIR (CH_2Cl_2 cast) 3021, 2962, 2928, 1598, 1503, 1486, 1375, 1243, 1199, 1177, 1154, 1094, 968, 868 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.42 (d, *J* = 6.9 Hz, 3 H), 1.86 (dd, *J* = 1.7, 6.6 Hz, 3 H), 2.45 (s, 3 H), 3.34 (m, 1 H), 5.12 (d, *J* = 8.4 Hz, 1 H), 6.09 (dq, *J* = 6.7, 15.7 Hz, 1 H), 6.36 (dd, *J* = 1.7, 15.7 Hz, 1 H), 6.77 (d, *J* = 8.8 Hz, 1 H), 6.99 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.12 (s, 1 H), 7.12-7.13 (m, 1 H), 7.32 (apparent dd as part of AA'BB' system, *J* = 0.7, 7.9 Hz, 2 H), 7.33 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H), 7.72 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.3 (q), 18.4 (q), 21.7 (q), 45.6 (d), 91.7 (d), 109.3 (d), 120.8 (d), 122.6 (d), 123.3 (d), 126.4 (d), 127.2 (d), 128.5 (d), 129.8 (d), 130.6 (d), 131.6 (s), 131.8 (s), 132.4 (s), 140.0 (s), 145.4 (s), 149.3 (s), 158.1 (s); exact mass *m/z* calcd for $C_{25}H_{24}NaO_4S$ 443.12875, found 443.12864.

(b) Long reaction time

$PdCl_2(PhCN)_2$ (5.3 mg, 0.0138 mmol) was added to a stirred solution of **14** (36.0 mg, 0.0856 mmol) in CH_2Cl_2 (2 mL, and stirring was continued for 10 days. The solution was filtered through a pad of Florisil (1 x 1 cm), using CH_2Cl_2 as a rinse. Evaporation of the solvent and flash chromatography of the residue over silica gel (0.5 x 30 cm), using 13% EtOAc-hexane containing Et_3N (ca 3 drops/100 mL), gave **15** (30.5 mg, 85%) as a colorless oil with spectral data identical to those reported above, except that the *Z* isomer could not be detected in the ^{1}H NMR spectrum (400 MHz).

4-[(2*R*,3*R*)-2,3-Dihydro-3-methyl-5-(1*E*)-1-propenylbenzo-

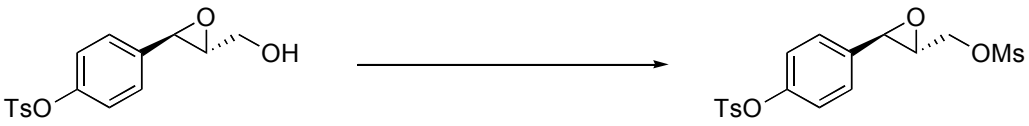
furan-2-yl]phenol [(+)-Conocarpan] (1).

15 **1**

Na(Hg) (Aldrich, 10% Na, 868.9 mg, 3.779 mmol Na) were added in one portion to a stirred solution of **15** (197.0 mg, 0.4685 mmol) in 80% MeOH (8 mL), and stirring was continued overnight. The solution was then decanted from the Hg, and diluted with water (10 mL). The mixture was extracted with Et_2O (3 x 10 mL), by which stage the aqueous layer was free of product (TLC control, silica, 30% EtOAc-hexane). The combined organic extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography of the residue over silica gel (1.5 x 25 cm), using 0-15% EtOAc-hexane, gave **1** (119.0 mg, 95%) as a white, crystalline solid: mp 120-123 °C [lit.[4a] 133-135 °C; lit.[4g] 124-126 °C]; $[\alpha]^{22}_D$ -82.24 (*c* 1.04, MeOH), Lit.[4a] $[\alpha]^{21}_D$ +122 (*c* 1.03, MeOH); FTIR (microscope, CH_2Cl_2) 3395, 3022, 2962, 2928, 2882, 1614, 1517, 1487, 1240, 1202, 1171, 964, 831; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.40 (d, *J* = 6.8 Hz, 3 H), 1.86 (dd, *J* = 1.6, 6.6 Hz, 3 H), 3.37-3.43 (m, 1 H), 5.00 (s, 1 H), 5.08 (d, *J* = 8.9 Hz, 1 H), 6.09 (dq, *J* = 6.6, 15.6 Hz, 1 H), 6.37 (d, *J* = 15.6 Hz, 1 H), 6.76 (d, *J* = 8.1 Hz, 1 H), 6.83 (apparent d as part of AA'BB' system, *J* = 8.5 Hz, 2 H), 7.12-7.14 (m, 2 H), 7.30 (apparent d as part of AA'BB' system, *J* = 8.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.9 (q), 18.4 (q), 45.3 (d), 92.7 (d), 109.3 (d), 115.5 (d), 120.8 (d), 123.1 (d), 126.3 (d), 127.9 (d), 130.8 (d), 131.3 (s), 132.4 (s), 132.9 (s), 155.7 (s), 158.3 (s); exact mass *m/z* calcd for $C_{19}H_{22}O_2$ 282.16199, found 282.16095. HPLC analysis [Chiralcel OD column (0.46 x 15.0 cm); 90:10 heptane-isopropanol; flow rate 0.6 mL/min; 40 °C; detection at 210 nm] of our synthetic conocarpan showed that it had ee of 88%

(i.e. enantiomeric ratio = 94:6)

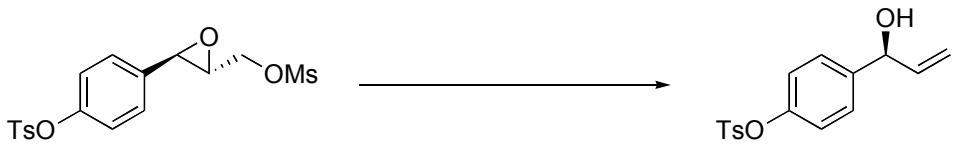
Toluene-4-sulfonic Acid 4-[(2*R*,3*R*)-3-(methanesulfonyloxy-methyl)oxiranyl]phenyl Ester (16).



8a' **16**

$MeSO_2Cl$ (0.14 mL, 1.8 mmol) was added dropwise by syringe to a stirred and cooled (0 °C) solution of **8a'** (514.6 mg, 1.606 mmol) and Et_3N (0.30 mL, 2.2 mmol) in CH_2Cl_2 (Ar atmosphere). The mixture was stirred for 1 h, diluted with CH_2Cl_2 (10 mL), washed once with water (6 mL) and dried ($MgSO_4$). Evaporation of the solvent gave **16** as a colorless oil that was used without further purification: $[\alpha]^{22}_D$ +16.33 (*c* 1.56, $CHCl_3$); FTIR ($CHCl_3$ cast) 3032, 1598, 1506, 1359, 1199, 1177, 1155, 1093, 868 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.48 (s, 3 H), 3.12 (s, 3 H), 3.30 (ddd, *J* = 2.0, 3.2, 5.5 Hz, 1 H), 3.87 (d, *J* = 2.0 Hz, 1 H), 4.31 (dd, *J* = 5.6, 12.1 Hz, 1 H), 4.58 (dd, *J* = 3.2, 12.1 Hz, 1 H), 7.01 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.22 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.34 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H), 7.72 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.0 (q), 38.2 (q), 56.0 (d), 59.1 (d), 68.8 (t), 123.0 (d), 127.2 (d), 128.8 (d), 130.1 (d), 132.5 (s), 134.7 (s), 145.8 (s), 150.1 (s); exact mass *m/z* calcd for $C_{17}H_{18}NaO_7S_2$ 421.03862, found 421.03835.

Toluene-4-sulfonic Acid 4-[(*S*)-1-Hydroxyallyl]phenyl Ester (17).

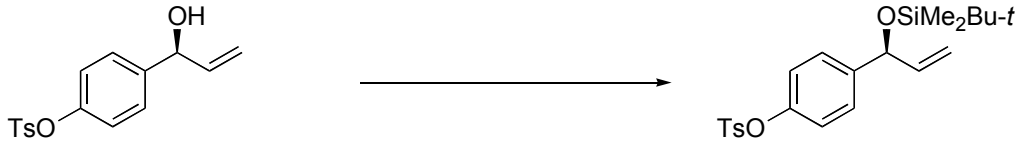


16 **17**

NaI (2.42 g, 16.1 mmol) was added to a stirred solution of **16** (total product from previous experiment, ca 1.6 mmol) in glyme (8 mL). The vessel was flushed with Ar and the mixture was refluxed for 12 h, and then allowed to cool. The mixture was diluted with EtOAc (10 mL), washed with saturated aqueous $Na_2S_2O_3$ (8 mL), water (8 mL) and brine (5 mL), dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 30 cm), using 27% EtOAc-hexanes containing a trace (0.4-1% v/v) of Et_3N, gave **17** (279.8 mg, 57% over 2 steps from the hydroxy epoxide) as a colorless oil: $[\alpha]^{22}_D$ +4.63 (*c* 0.57, $CHCl_3$); FTIR ($CHCl_3$ cast) 3533, 3400, 3068, 2981, 2924, 2872, 1597, 1500, 1402, 1371, 1197, 1175, 1154, 1093, 867 cm^{-1}; ^1H NMR (C_6D_6, 300 MHz) δ 1.10 (d, *J* = 3.7 Hz, 1 H), 1.74 (s, 3 H), 4.62-4.65 (m, 1 H), 4.86 (dt, *J* = 1.5, 10.3 Hz, 1 H), 5.03 (dt, *J* = 1.5, 17.1 Hz, 1 H), 5.64 (ddd, *J* = 5.9, 10.3, 17.1 Hz, 1 H), 6.57 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H), 6.92-9.98 (m, 4 H), 7.63 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H); ^{13}C NMR (C_6D_6, 100 MHz) (two signals coincident) δ 21.2 (q), 74.4 (d), 114.7 (t), 122.6 (d), 128.7 (d), 129.8 (d), 133.4 (s), 140.5 (d), 142.3 (s), 144.9 (s), 149.5 (s); exact mass *m/z* calcd for $C_{16}H_{16}NaO_4S$ 327.06615, found 327.06657.

Attempts to prepare the Mosher ester by a literature method[32] gave material that had clearly undergone extensive epimerization during the derivatization, as the ratio of diastereoisomers was 2.3:0.95 (^1H NMR), while the parent epoxide had an er of 98.9:1.1. We were unable to separate the corresponding racemic alcohol by chiral HPLC.

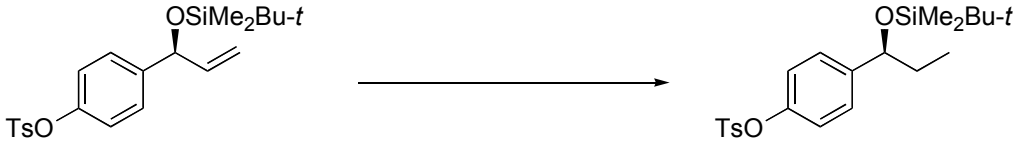
Toluene-4-sulfonic Acid 4-[(*S*)-1-(*tert*-Butyldimethyl-silanyloxy)allyl]phenyl Ester (18).



17 **18**

t-$BuMe_2SiOSO_2CF_3$ (0.25 mL, 1.1 mmol) was added dropwise by syringe to a stirred and cooled (-78 °C) solution of **17** (269.8 mg, 0.8865 mmol) and *sym*-collidine (0.26 mL, 2.0 mmol) in CH_2Cl_2 (3 mL) (Ar atmosphere). Stirring at -78 °C was continued for 15 min and then saturated aqueous $NaHCO_3$ (0.5 mL) was added and the cooling bath was removed. After ca 15 min, CH_2Cl_2 (10 mL) was added and the mixture was washed with water (8 mL), dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 25 cm), using 13% EtOAc-hexanes containing a trace (0.5-1%v/v) of Et_3N, gave **18** (370.6 mg, 100%) as a colorless oil: $[\alpha]^{22}_D$ -6.46 (*c* 1.21, $CHCl_3$); FTIR ($CHCl_3$ cast) 2954, 2928, 2885, 2856, 1598, 1499, 1472, 1376, 1294, 1197, 1175, 1154, 1093, 865 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) δ 0.00 (s, 3 H), 0.11 (s, 3 H), 1.02 (s, 9 H), 1.84 (s, 3 H), 4.98 (dt, *J* = 1.5, 10.3 Hz, 1 H), 5.02 (d, *J* = 6.0 Hz, 1 H), 5.23 (dt, *J* = 1.5, 17.0 Hz, 1 H), 5.80 (ddd, *J* = 5.9, 10.2, 17.0 Hz, 1 H), 6.67 (apparent dd as part of AA'BB' system, *J* = 0.7, 8.6 Hz, 2 H), 7.06 (apparent d as part of AA'BB' system, *J* = 8.8 Hz, 2 H), 7.17 (apparent dd as part of AA'BB' system, *J* = 0.6, 8.9 Hz, 2 H), 7.71 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H); ^{13}C NMR (C_6D_6, 100 MHz) δ -4.8 (q), 18.4 (s), 21.1 (q), 26.0 (q), 75.6 (d), 113.8 (t), 122.6 (d), 127.4 (d), 128.8 (d), 129.6 (d), 133.6 (s), 141.4 (d), 142.7 (s), 144.7 (s), 149.5 (s); exact mass *m/z* calcd for $C_{22}H_{30}NaO_4SSi$ 441.15263, found 441.15262.

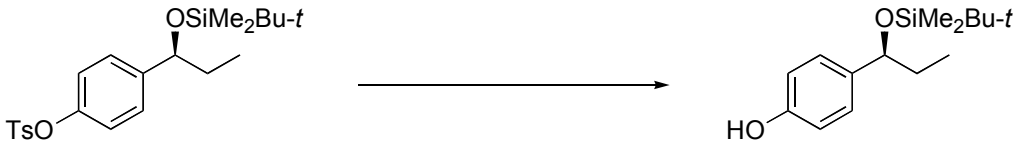
Toluene-4-sulfonic Acid 4-[(*S*)-1-(*tert*-Butyldimethyl-silanyloxy)propyl]phenyl Ester (19).



18 **19**

$Rh\text{-}Al_2O_3$ (5% w/w, 9.7 mg, 0.0047 mmol) was added to a solution of **18** (30.3 mg, 0.0724 mmol) in THF (1.8 mL). The mixture was stirred and degassed by sequentially evacuating the flask (house vacuum) and then admitting H_2, this sequence being repeated twice more. The mixture was stirred overnight under H_2 (balloon) and then filtered through a short pad (0.5 x 1 cm) of silica gel, using CH_2Cl_2 as a rinse. Evaporation of the filtrate gave **19** (30.3 mg, 99%) as a colorless oil: $[\alpha]^{22}_D$ -26.43 (*c* 3.03, $CHCl_3$); FTIR ($CHCl_3$ cast) 3034, 2957, 2929, 2857, 1598, 1501, 1472, 1463, 1378, 1257, 1198, 1175, 1155, 1094, 1060, 1014 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.00 (s, 3 H), 0.18 (s, 3 H), 1.00 (t, *J* = 7.2 Hz, 3 H), 1.03 (s, 9 H), 1.72-1.88 (m, 2 H), 2.61 (s, 3 H), 4.70 (apparent t, *J* = 5.5 Hz, 1 H), 7.08 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.36 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.45 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.84 (apparent d as part of AA'BB' system, *J* = 8.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ -5.0 (q), -4.7 (q), 9.8 (q), 18.2 (s), 21.7 (q), 25.8 (q), 33.5 (t), 75.5 (d), 121.9 (d), 127.0 (d), 128.5 (d), 129.6 (d), 132.3 (s), 144.7 (s), 145.2 (s), 148.3 (s); exact mass *m/z* calcd for $C_{22}H_{32}NaO_4SSi$ 443.16828, found 443.16826.

4-[(*S*)-1-(*tert*-Butyldimethylsilanyloxy)propyl]phenol (20).

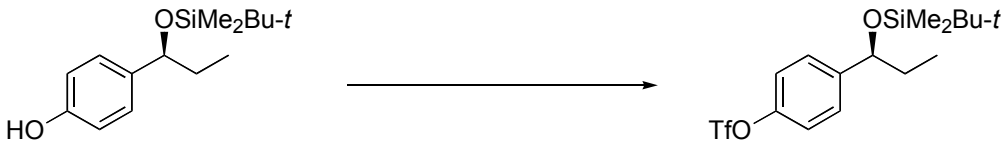


19 **20**

Na(Hg) (815.0 mg, 10% Na, 3.543 mmol) was added to a

stirred, cloudy solution of **19** (316.4 mg, 0.7444 mmol) in 80% MeOH (5.4 mL). The flask was flushed with Ar and stirring was continued for 45 min to give a clear, colorless solution. The mixture was then decanted from the remaining amalgam into a separatory funnel containing phosphate buffer solution (KH_2PO_4-NaOH, pH 7, 8 mL) and Et_2O (8 mL). Saturated aqueous oxalic acid (2 mL) was then added and the biphasic mixture was shaken and separated. The aqueous layer was extracted with Et_2O (2 x 6 mL) and the combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 25 cm), using 0-20% EtOAc-hexanes (gradient elution), gave **20** as a colorless oil (119.3 mg, 60%) and recovered **19** (102.3 mg, 32%). Phenol **20** had: $[\alpha]^{22}_D$ -19.32 (*c* 1.41, $CHCl_3$); FTIR ($CHCl_3$ cast) 3349, 3024, 2958, 2930, 2858, 1614, 1600, 1514, 1472, 1463, 1361, 1252, 1059, 836 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) (phenolic OH not observed) δ -0.09 (s, 3 H), 0.05 (s, 3 H), 0.87 (t, *J* = 6.7 Hz, 3 H), 1.06 (s, 9 H), 1.66-1.88 (m, 2 H), 4.54 (dd, *J* = 5.5, 7.1 Hz, 1 H), 6.62 (apparent d as part of AA'BB' system, *J* = 8.8 Hz, 2 H), 7.19 (apparent dd as part of AA'BB' system, *J* = 0.6, 8.6 Hz, 2 H); ^{13}C NMR (C_6D_6, 100 MHz) δ -4.8 (q), -4.4 (q), 10.3 (q), 18.4 (s), 26.1 (q), 34.1 (t), 76.5 (d), 115.1 (d), 127.4 (d), 137.7 (s), 155.4 (s); exact mass *m/z* calcd for $C_{15}H_{26}NaO_2Si$ 289.15943, found 289.15935.

Trifluoromethanesulfonic Acid 4-[(*S*)-1-(*tert*-butyldimethylsilanyloxy)propyl]phenyl Ester (21).

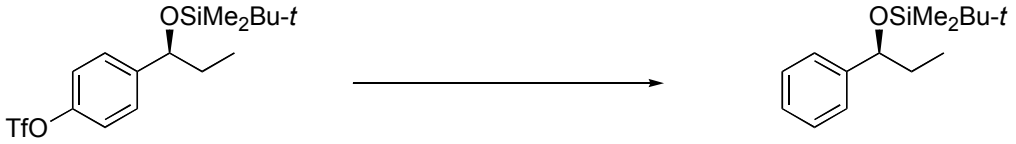


20 **21**

$(CF_3SO_2)_2O$ (0.07 mL, 0.4 mmol) was added dropwise by syringe to a stirred and cooled (-78 °C) solution of **20** (99.9 mg, 0.375 mmol) and Et_3N (0.09 mL, 0.6 mmol) in CH_2Cl_2 (1.8 mL) (Ar

atmosphere). Stirring was continued for 10 min and then saturated aqueous $NaHCO_3$ (0.5 mL) was added. The cooling bath was removed and the mixture was poured into a separatory funnel containing water (5 mL) and CH_2Cl_2 (5 mL). The mixture was shaken and the organic phase was dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 20 cm), using 13% EtOAc-hexanes containing a trace (0.5-1% v/v) of Et_3N, gave **21** (111.6 mg, 75%) as a colorless oil: $[\alpha]^{22}_D$ -21.08 (*c* 0.48, $CHCl_3$); FTIR ($CHCl_3$ cast) 2959, 2932, 2859, 1500, 1427, 1251, 1214, 1143, 890, 861, 837 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) δ 0.00 (s, 3 H), 0.18 (s 3 H), 0.95 (t, *J* = 7.4 Hz, 3 H), 1.12 (s, 9 H), 1.57-1.77 (m, 2 H), 4.54 (dd, *J* = 5.1, 6.9 Hz, 1 H), 7.04 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.18 (apparent dd as part of AA'BB' system, *J* = 0.5, 8.9 Hz, 2 H); ^{13}C NMR (C_6D_6, 100 MHz) δ -5.0 (q), -4.7 (q), 9.7 (q), 18.3 (s), 25.9 (q), 33.6 (t), 75.4 (d), 119.3 (s, CF_3 quartet, *J* = 318.6 Hz), 121.0 (d), 127.7 (d), 146.1 (s), 148.6 (s); exact mass *m/z* calcd for $C_{16}H_{25}F_3NaO_4SSi$ 421.10872, found 421.10906.

(*S*)-*tert*-Butyldimethyl(1-phenylpropoxy)silane (22).

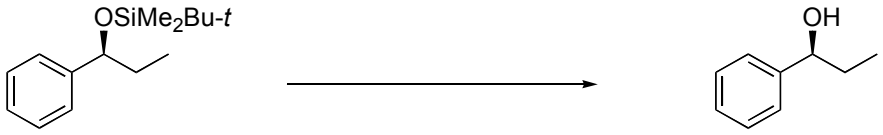


21 **22**

Pd-C (10% w/w, 60.8 mg, 0.0571 mmol) was added to a solution of **21** (99.0 mg, 0.248 mmol) and Et_3N (0.11 mL, 0.79 mmol) in EtOAc (5 mL). The stirred mixture was degassed by sequentially evacuating the flask (house vacuum) and then admitting H_2, the procedure being repeated twice more. A hydrogen-filled balloon was then left in place and stirring was continued for 3 h. The heterogeneous mixture was filtered through a short pad (0.5 x 1.0 cm) of silica gel, using EtOAc as a rinse. Evaporation of the solvent gave **22** (62.6 mg, 100%) as a yellowish oil: $[\alpha]^{22}_D$ -

32.21 (*c* 0.66, $CHCl_3$); FTIR ($CHCl_3$ cast) 3065, 3028, 2958, 2930, 2858, 1493, 1472, 1463, 1453, 1361, 1257, 1104, 1086, 1058, 1013, 860, 837, 775, 699 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) δ -0.10 (s, 3 H), 0.04 (s, 3 H), 0.87 (t, *J* = 7.3 Hz, 3 H), 0.97 (s, 9 H), 1.58-1.79 (m, 2 H), 4.51 (dd, *J* = 5.2, 7.0 Hz, 1 H), 7.07 (tt, *J* = 1.3, 6.7 Hz, 1 H), 7.16-7.19 (m, 2 H), 7.26-7.28 (m, 2 H); ^{13}C NMR (C_6D_6, 100 MHz) δ -4.8 (q), -4.5 (q), 10.2 (q), 18.4 (s), 26.1 (q), 34.0 (t), 76.7 (d), 126.2 (d), 127.2 (d), 128.3 (d), 145.8 (s); exact mass *m/z* calcd for $C_{15}H_{26}NaOSi$ 273.16451, found 273.16448.

(*S*)-1-Phenylpropan-1-ol (23).



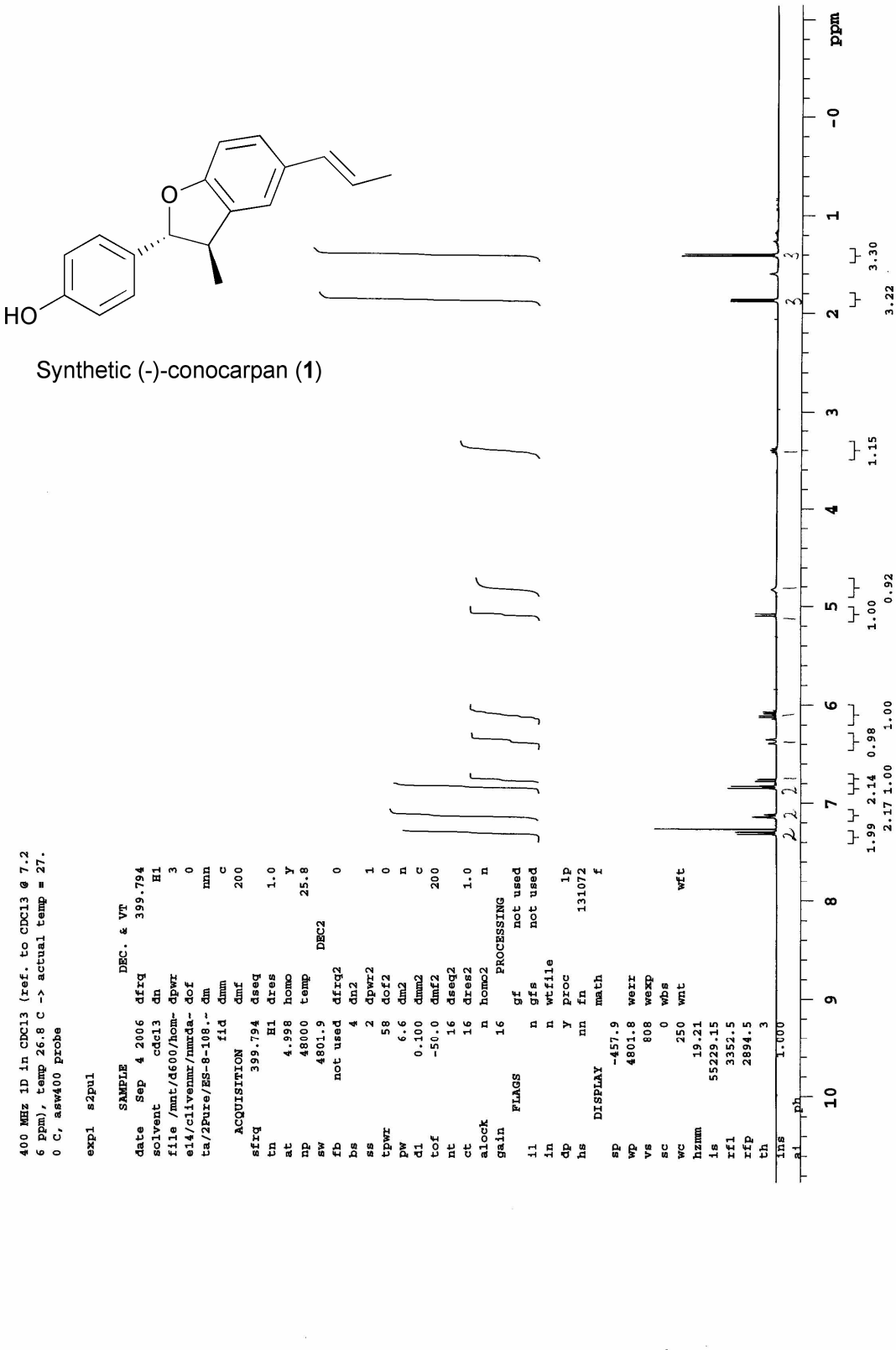
22 **23**

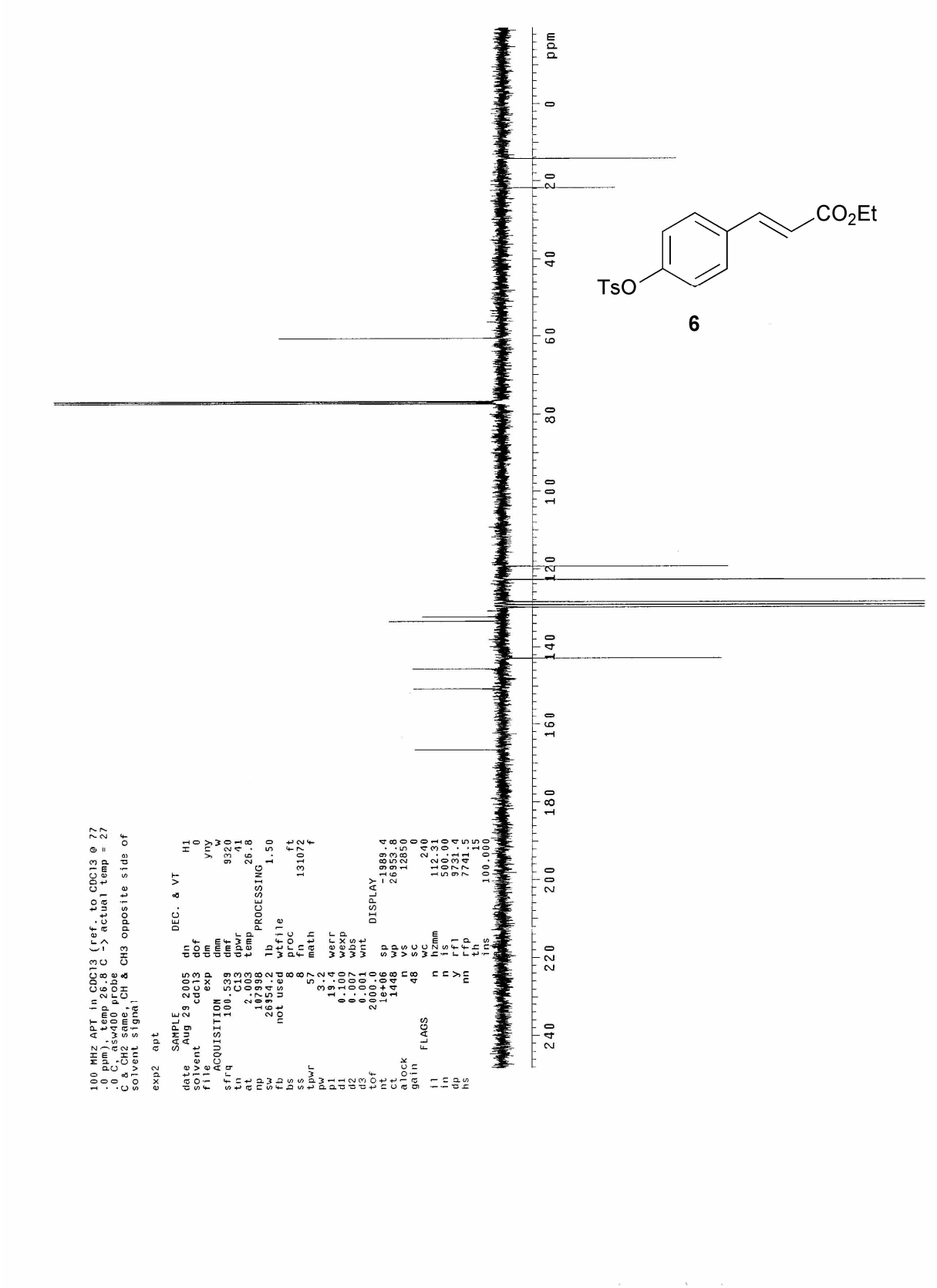
Bu_4NF (1M in THF, 0.3 mL, 0.3 mmol) was added to a stirred solution of **22** (56.0 mg, 0.224 mmol) in THF (3.6 mL) (Ar atmosphere). The mixture was stirred for 12 h, diluted with Et_2O (8 mL) and washed with water (2 x 4 mL) and once with brine (4 mL), dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (0.5 x 30 cm), using 20% Et_2O-pentane containing a trace (0.5-1% v/v) of Et_3N, gave an impure product. Further purification by Kugelrohr distillation and flash chromatography over silica gel (0.5 x 30 cm), using 20% EtOAc-hexanes containing a trace (0.5-1% v/v) of Et_3N, gave **23** (21.5 mg, 71%) as a colorless liquid whose ^1H NMR spectrum was identical to that reported.[28] The material had: $[\alpha]^{22}_D$ -29.26 (*c* 1.23, $CHCl_3$) [Lit.[28,29] $[\alpha]^{22}_D$ -45.6 (*c* 1.3, $CHCl_3$)] indicating an er = 88:12.

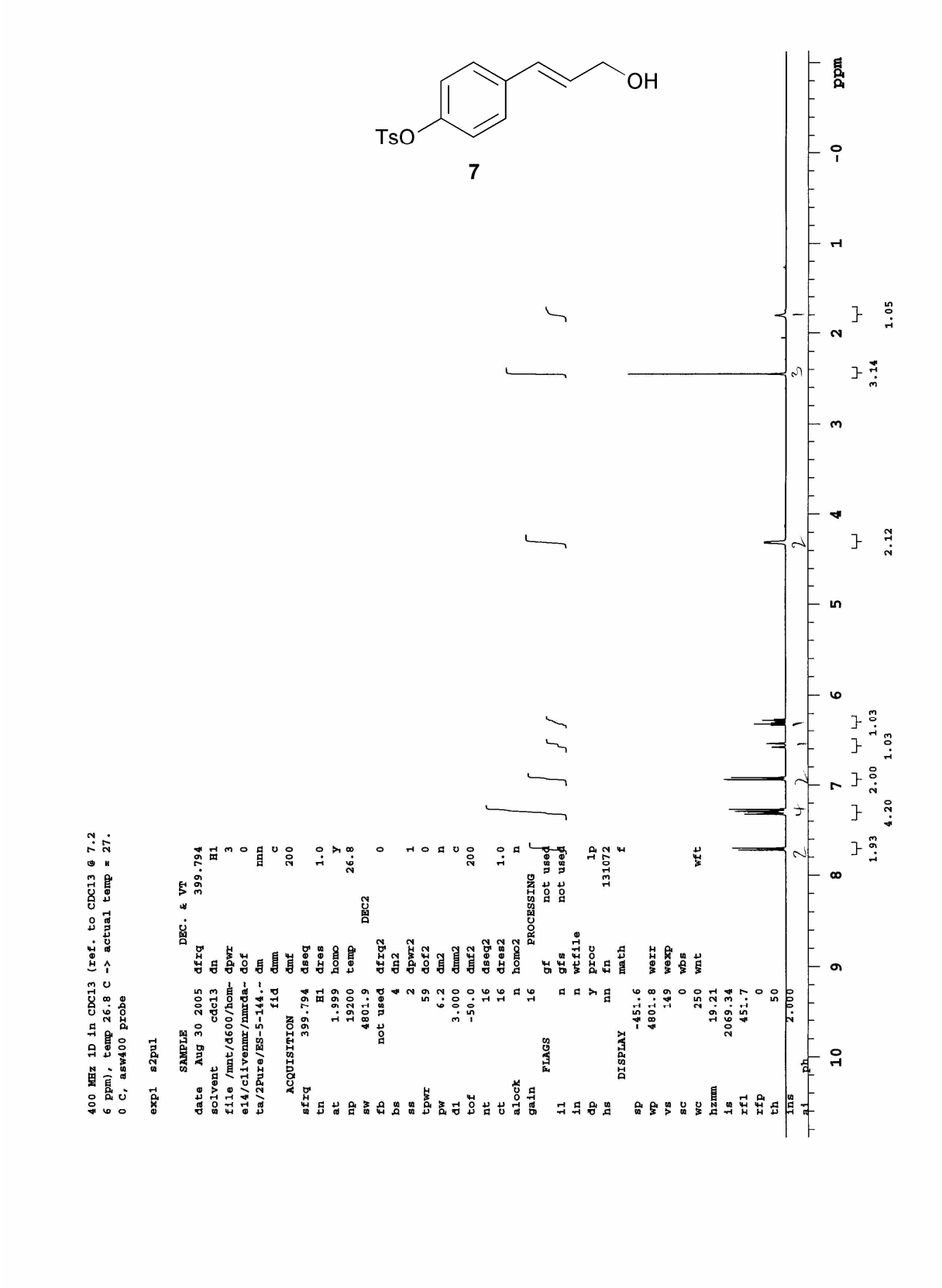
References

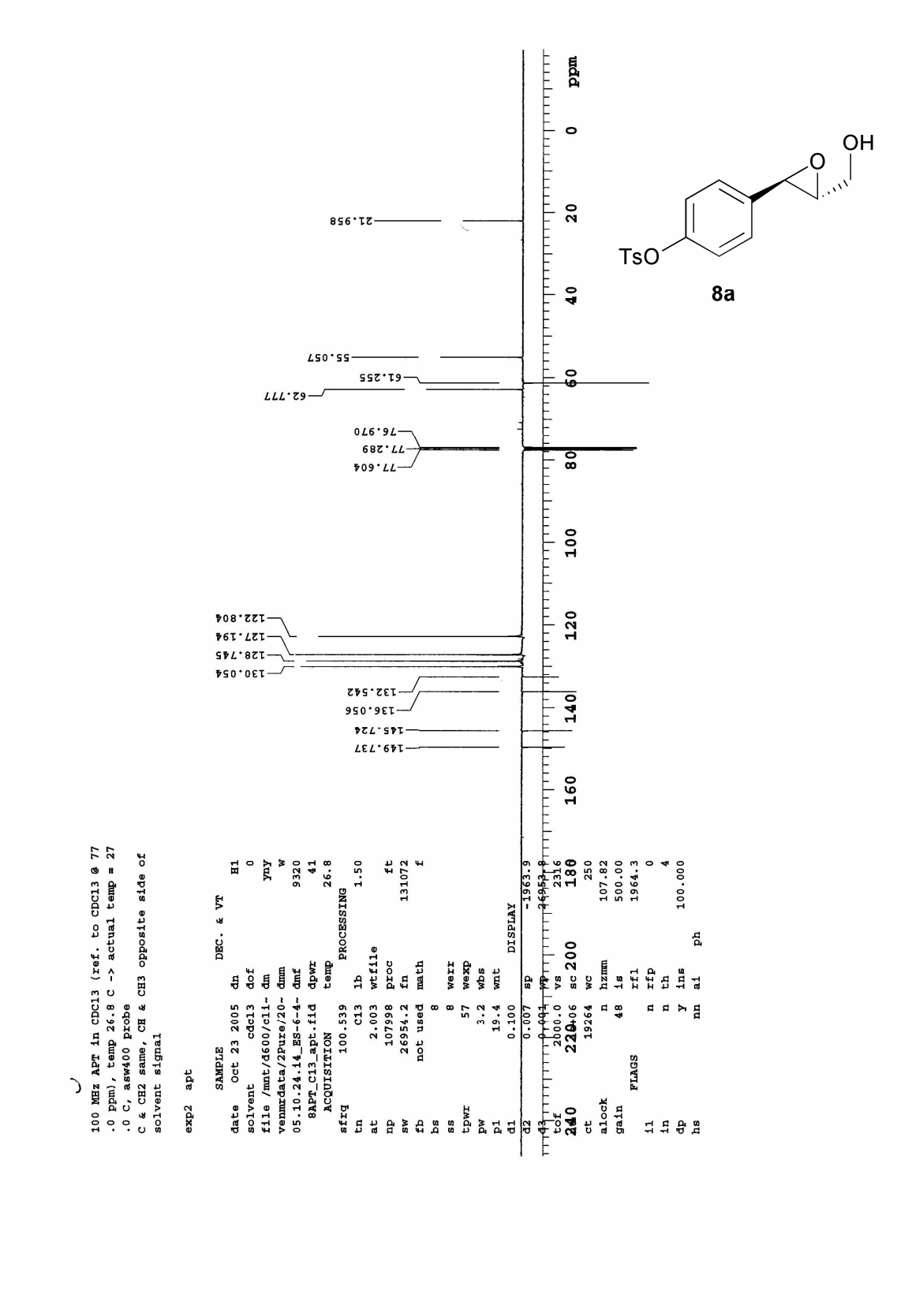
31 D. C. Harrowven and I. L. Guy, *Chem. Comm*. 2004, 1968-1969.
32 A. J. M. Janssen, A. J. H. Klunder and B. Zwanenburg,

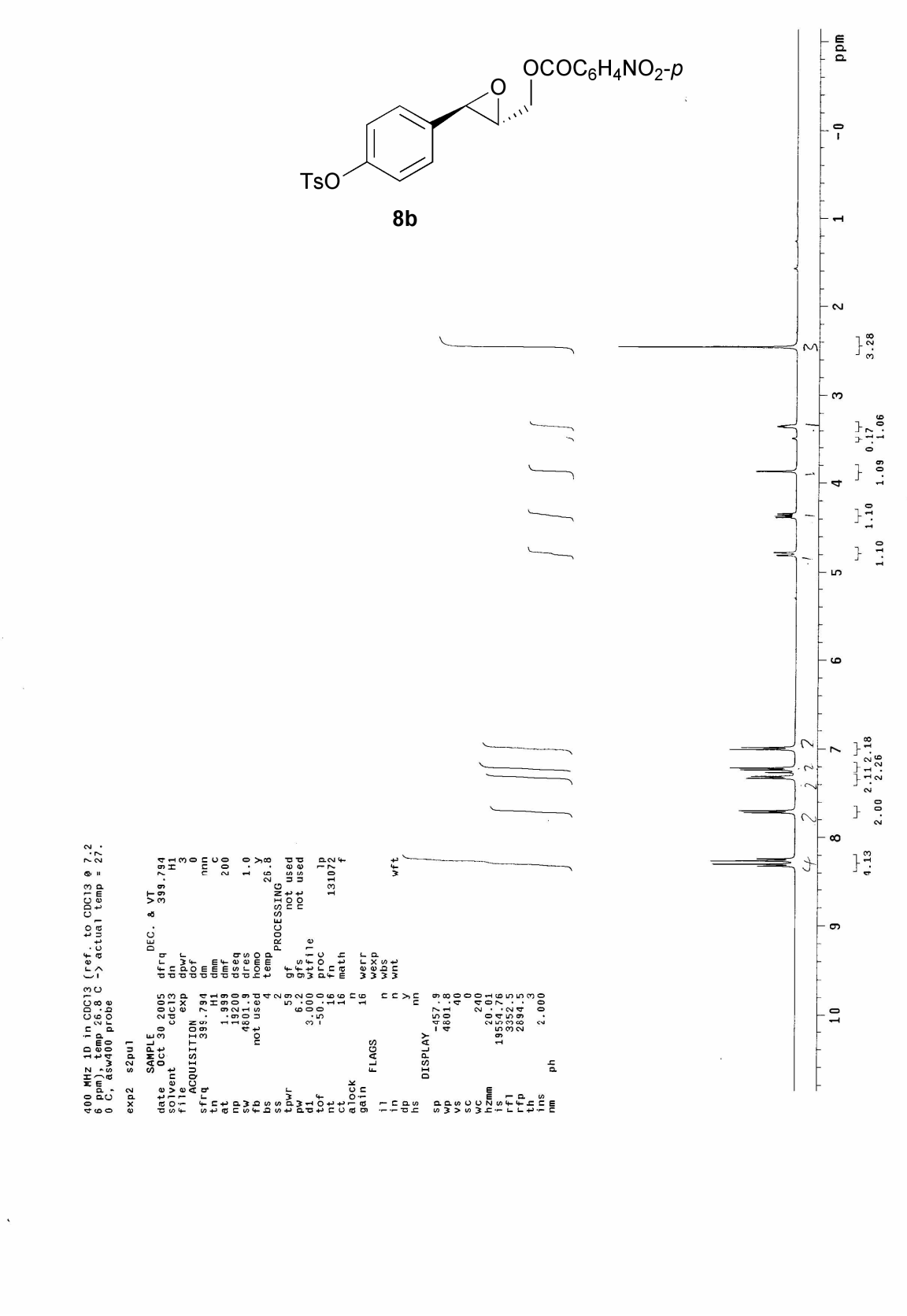
Tetrahedron 1991, **47**, 7645-7662.

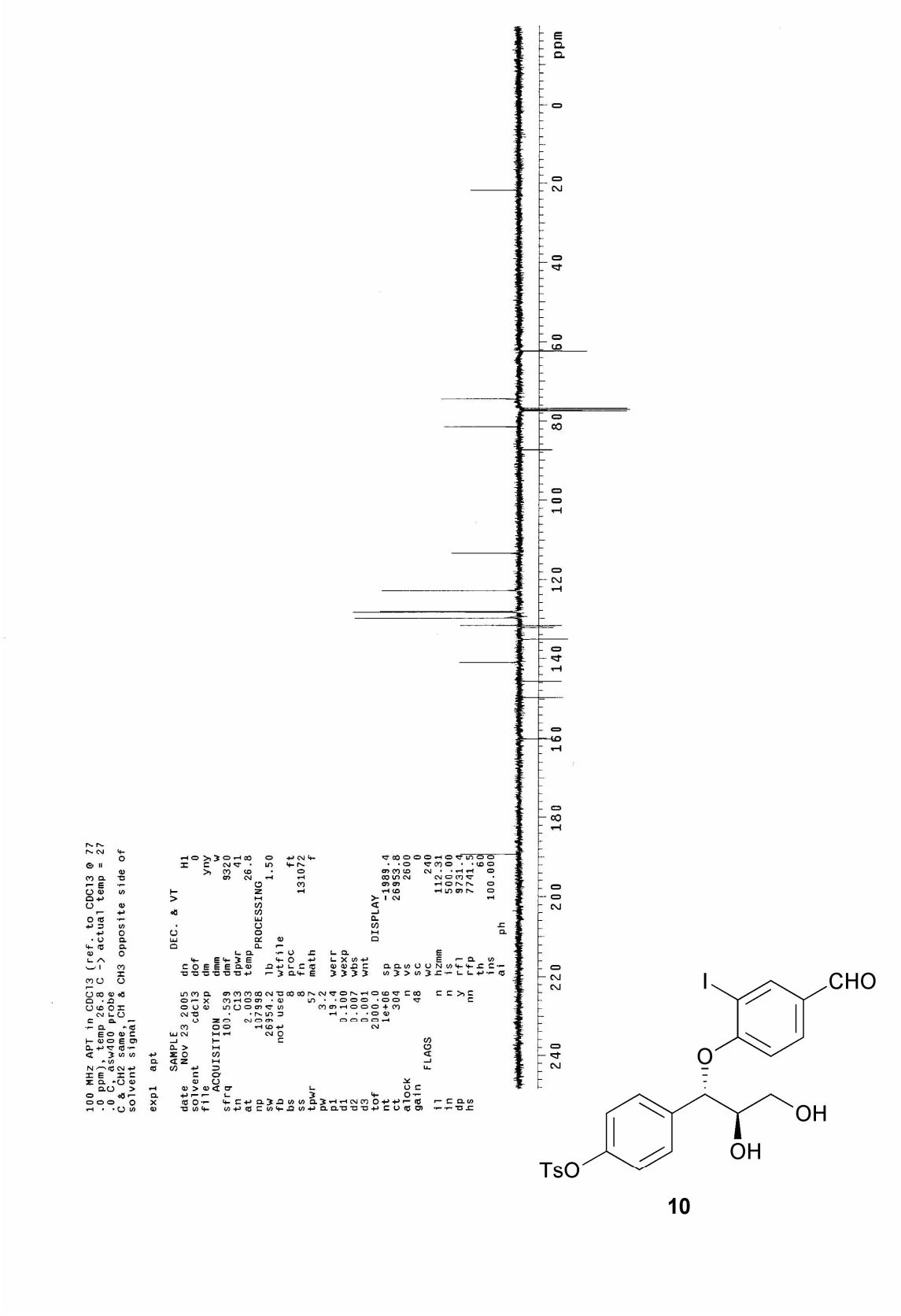

HO
O
Synthetic (-)-conocarpan (1)
400 MHz 1D in CDCl3 (ref. to CDCl3 @ 7.2
6 ppm), temp 26.8 C -> actual temp = 27.
0 C, asw400 probe
expl s2pul
SAMPLE
date Sep 4 2006
solvent cdcl3
file /mnt/d600/hom-
e14/clivenmr/nmrda-
ta/2Pure/ES-8-108.-
fid
ACQUISITION
sfrq 399.794
tn H1
at 4.998
np 48000
sw 4801.9
fb not used
bs 4
ss 2
tpwr 58
pw 6.6
d1 0.100
tof -50.0
nt 16
ct 16
alock n
gain 16
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -457.9
wp 4801.8
vs 808
sc 0
wc 250
hzmm 19.21
is 55229.15
rfl 3352.5
rfp 2894.5
th 3
ins 1.000
DEC. & VT
dfrq 399.794
dn H1
dpwr 3
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo y
temp 25.8
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
PROCESSING
gf not used
gfs not used
wtfile
proc lp
fn 131072
math f
werr
wexp
wbs
wnt wft
ppm
10 9 8 7 6 5 4 3 2 1 -0
1.99 2.14 0.98 1.00 1.00 0.92 1.15 3.30
2.17 1.00 3.22


100 MHz APT in CDCl3 (ref. to CDCl3 @ 77
.0 ppm), temp 26.8 C -> actual temp = 27
.0 C, asw400 probe
C & CH2 same, CH & CH3 opposite side of
solvent signal
exp2 apt
SAMPLE
date Aug 29 2005
solvent cdcl3
file
ACQUISITION
sfrq 100.539
tn C13
at 2.003
np 107398
sw 26954.2
fb not used
bs 8
ss 8
sw 57
pw 19.4
p1 0.100
d1 0.007
d2 0.001
d3 2000.0
tof 1e+06
nt 1448
ct
alock n
gain 48
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm yny
dmm w
dmf 9320
dpwr 41
temp 26.8
PROCESSING
lb 1.50
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
DISPLAY
sp -1989.4
wp 26953.8
vs 12850
sc 0
wc 240
hzmm
is 112.31
rfl 500.00
rfp 9731.4
th 7741.5
ins 15
100.000
ppm
240
220
200
180
160
140
120
100
80
60
40
20
0
TsO
CO2Et
6

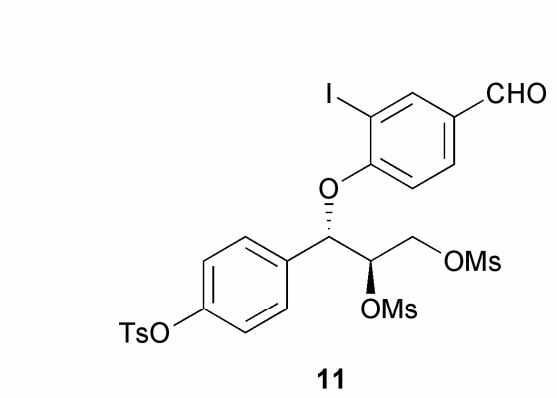

400 MHz 1D in CDCl3 (ref. to CDCl3 @ 7.2
6 ppm), temp 26.8 C -> actual temp = 27.
0 C, asw400 probe
expl s2pul
SAMPLE
date Aug 30 2005
solvent cdcl3
file /mnt/d600/hom-
e14/cllvenmr/nmrda-
ta/2Pure/ES-5-144.-
fid
ACQUISITION
sfrq 399.794
tn H1
at 1.999
np 19200
sw 4801.9
fb not used
bs 4
ss 2
tpwr 59
pw 6.2
d1 3.000
tof -50.0
nt 16
ct 16
alock n
gain 16
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -451.6
wp 4801.8
vs 149
sc 0
wc 250
hzmm 19.21
is 2069.34
rf1 451.7
rfp 0
th 50
ins 2.000
a1 ph
DEC. & VT
dfrq 399.794
dn H1
dpwr 3
dof 0
nnn
dmm c
dmf 200
dseq
dres 1.0
homo y
temp 26.8
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
PROCESSING
gf not used
gfs not used
wtfile
proc lp
fn 131072
math f
warr
wexp
wbs
wnt wft
OH
TsO
7
ppm
1.93
2.00
1.03
4.20
1.03
3.14
2.12
1.05


100 MHz APT in CDCl3 (ref. to CDCl3 @ 77
.0 ppm), temp 26.8 C -> actual temp = 27
.0 C, asw400 probe
C & CH2 same, CH & CH3 opposite side of
solvent signal
exp2 apt
SAMPLE
date Oct 23 2005
solvent cdcl3
file /mnt/d600/cil-
venmrdata/2Pure/20-
05.10.24.14_ES-6-4-
8APT_C13_apt.fid
ACQUISITION
sfrq 100.539
tn C13
at 2.003
np 107998
sw 26954.2
fb not used
bs 8
ss 8
tpwr 57
pw 3.2
p1 19.4
d1 0.100
d2 0.007
tof 2000.0
ct 19264
alock n
gain 48
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm ynn
dmm w
dmf 9320
dpwr 41
temp 26.8
PROCESSING
lb 1.50
wtfile
proc ft
fn 131072
math f
wexp
wbs
wnt
DISPLAY
sp -1963.9
wp 24957.8
vs 2316
sc 107
wc 250
hzmm 107.82
is 500.00
rf1 1964.3
rfp 0
th 4
ins 100.000
ai ph
21.958
55.057
61.255
62.777
76.970
77.289
77.604
122.804
127.194
128.745
130.054
132.542
136.056
145.724
149.737
ppm
OH
O
TsO
8a


OCOC6H4NO2-p
O
TsO
8b
ppm
10
9
8
7
6
5
4
3
2
1
-0
4.13
2.00
2.11
2.18
2.26
1.10
1.10
1.09
0.17
1.06
3.28
400 MHz 1D in CDCl3 (ref. to CDCl3 @ 7.2
6 ppm), temp 26.8 C -> actual temp = 27.
0 C, dsw400 probe
exp2 s2pul
SAMPLE
date Oct 30 2005
solvent cdcl3
file exp
ACQUISITION
sfrq 399.794
tn H1
at 1.999
np 19200
sw 4601.9
fb not used
bs 4
ss 2
tpwr 59
pw 6.2
d1 3.000
tof -50.0
nt 16
ct 16
alock n
gain 16
FLAGS
il n
in y
dp nn
hs
DISPLAY
sp -457.9
wp 4601.8
vs 40
sc 0
wc 240
hzmm 20.01
is 19554.76
rfl 3352.5
rfp 2894.5
th 3
ins 2.000
nm ph
DEC. & VT
dfrq 399.784
dn H1
dpwr 3
dof 0
nnn
dmm c
dmf 200
dseq
dres 1.0
homo y
temp 26.8
PROCESSING
not used
gf not used
gfs
wtfile
proc lp
fn 131072
math f
werr
wexp
wbs
wnt
wft

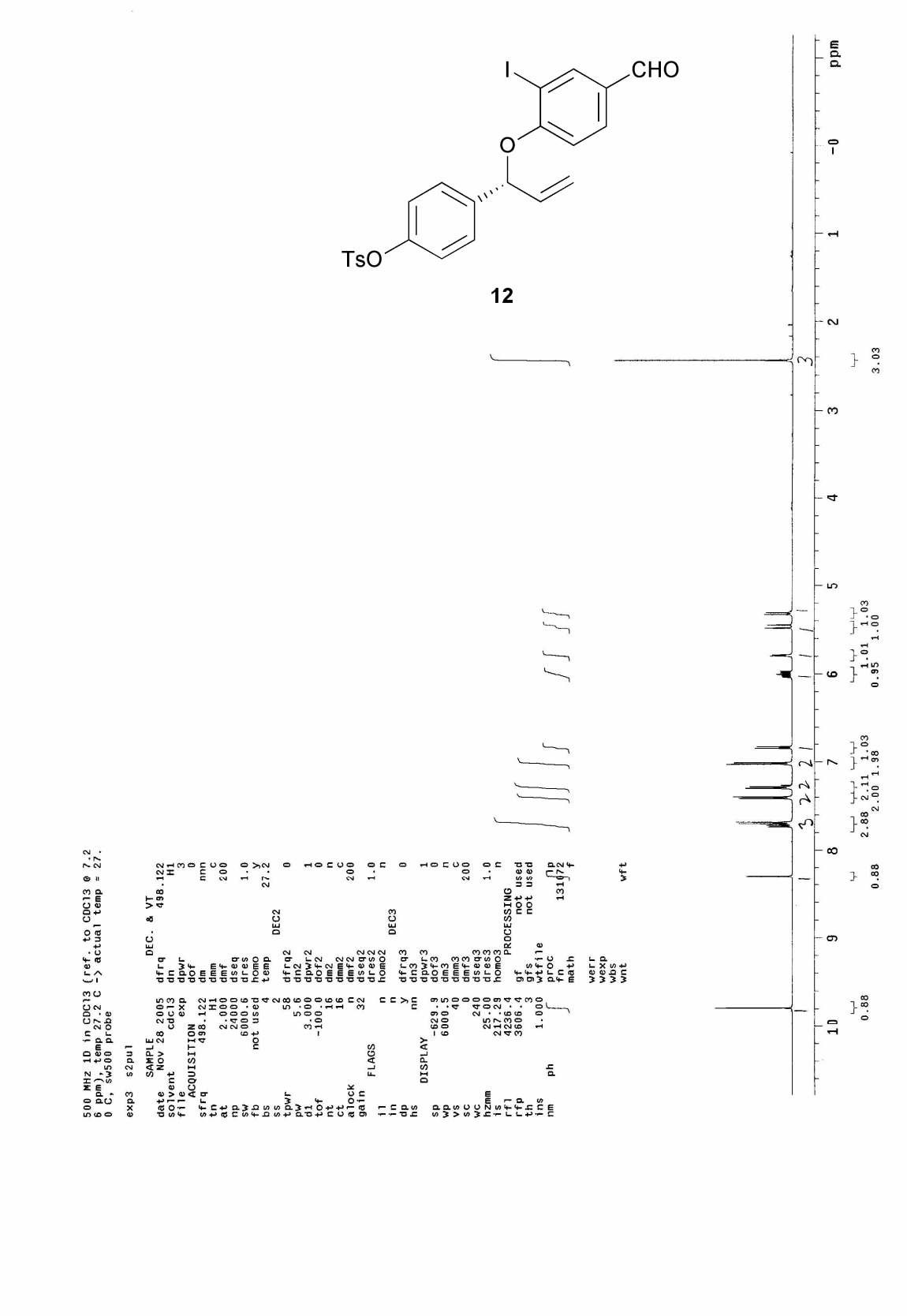

100 MHz APT in CDCl3 (ref. to CDCl3 @ 77
.0 ppm), temp 26.8 C -> actual temp = 27
.0 C, asw400 probe
C & CH2 same, CH & CH3 opposite side of
solvent signal
expl apt
SAMPLE
date Nov 23 2005
solvent cdcl3
file exp
ACQUISITION
sfrq 100.539
tn C13
at 2.003
np 107998
sw 26954.2
fb not used
bs 8
ss 8
tpwr 57
pw 3.2
p1 19.4
d1 0.100
d2 0.007
d3 0.001
tof 2100.0
nt 1e+06
ct 304
alock n
gain 48
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm yny
dmm y
dmf 9320
dpwr 41
temp 26.8
PROCESSING
lb 1.50
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
DISPLAY
sp -1989.4
wp 26953.8
vs 2600
sc 0
wc 240
hzmm 112.31
is 500.00
rfl 9731.4
rfp 7741.5
th 60
ins 100.000
ai
ph
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240
I
CHO
O
OH
OH
TsO

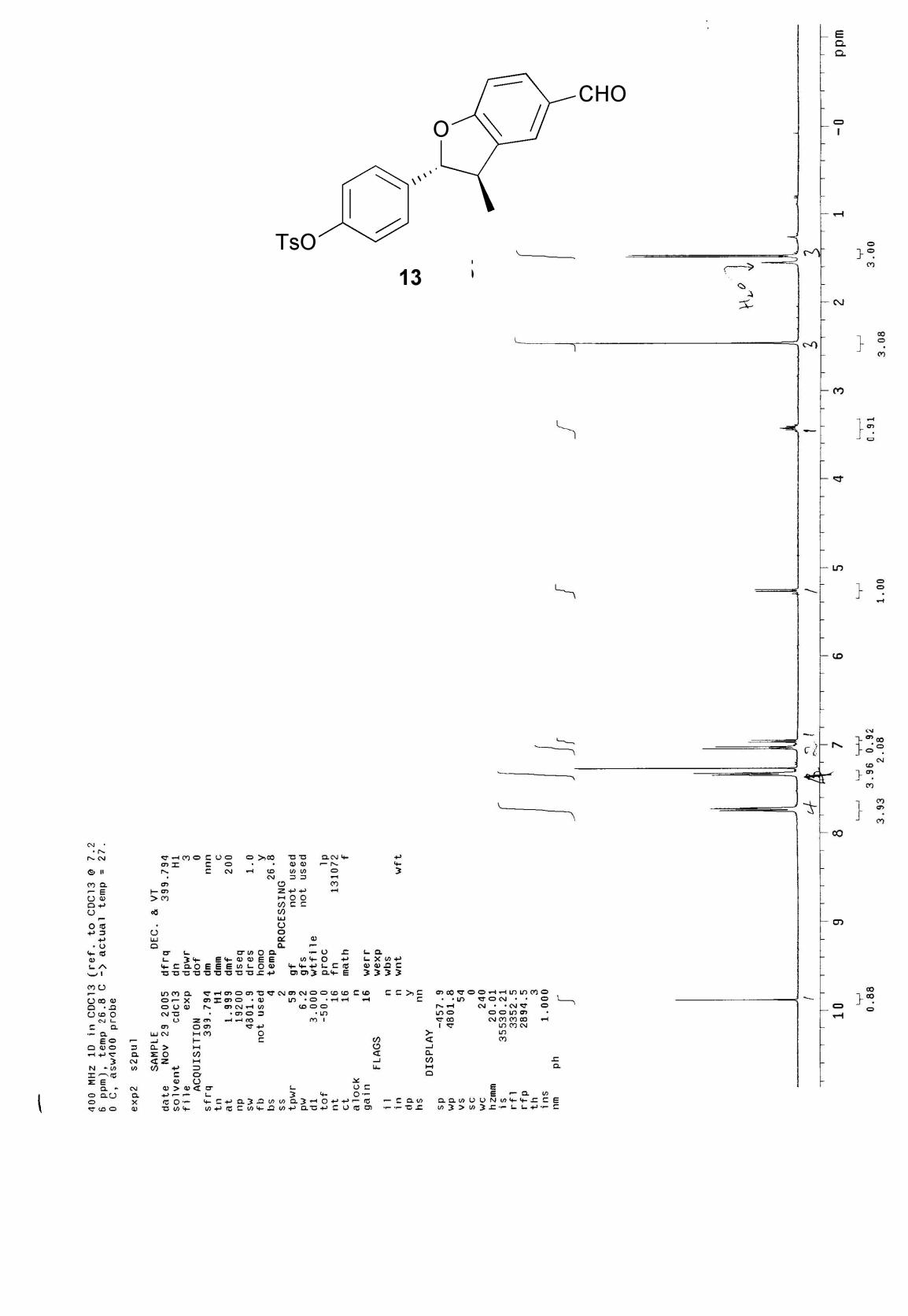
10


I
CHO
O
OMs
OMs
TsO

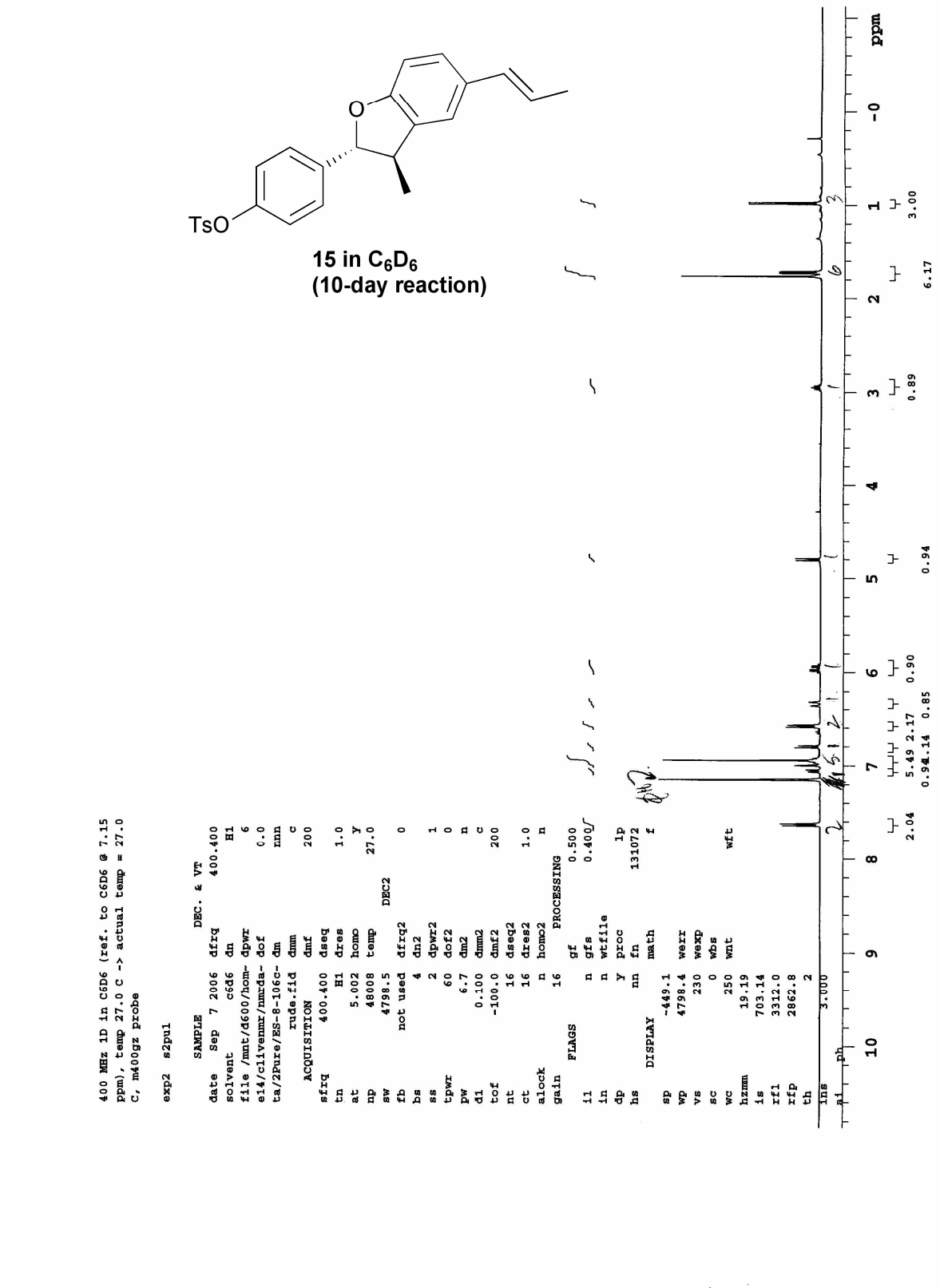
11

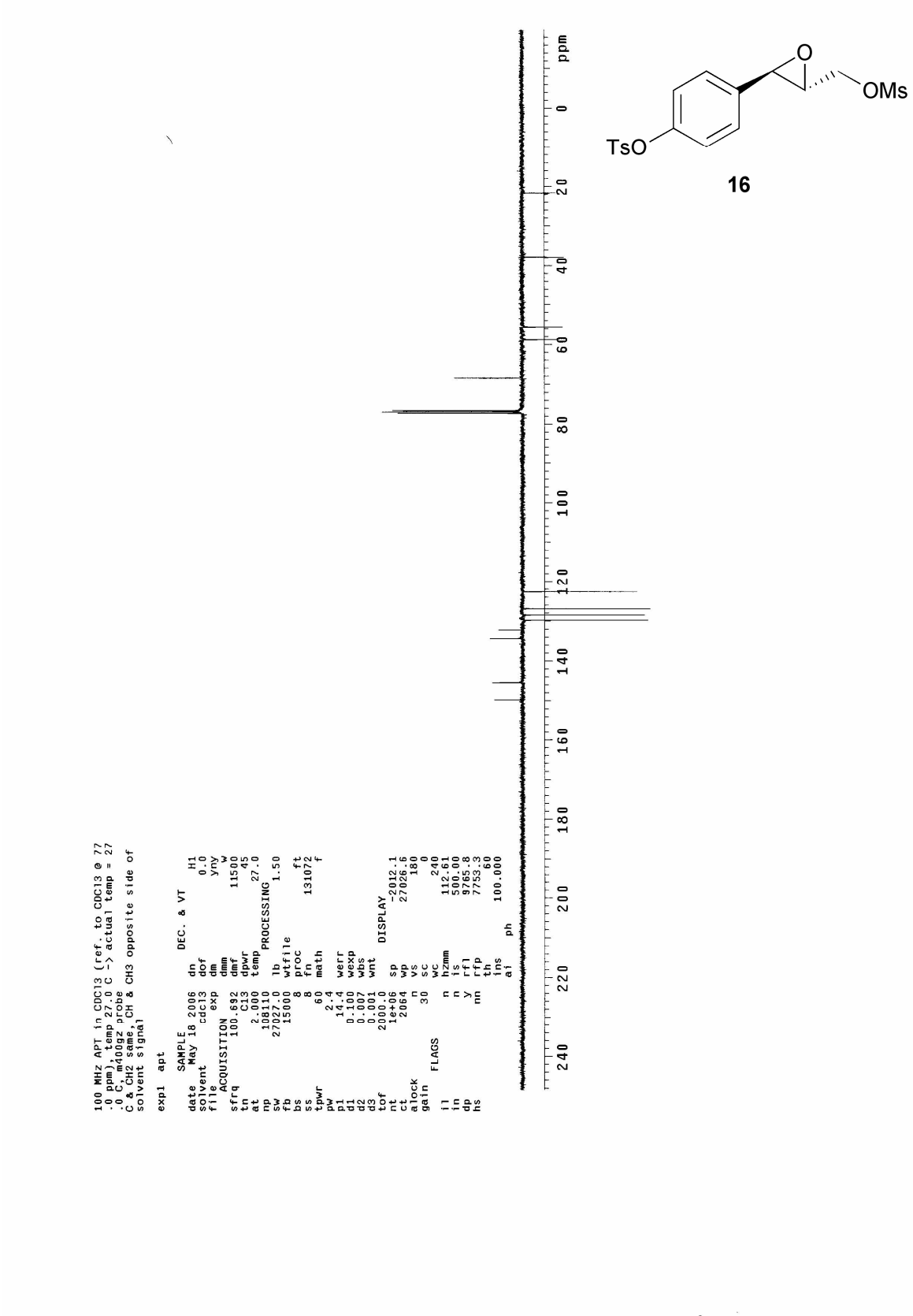
100 MHz APT in CDCl3 (ref. to CDCl3 @ 77
.0 ppm), temp 26.8 C -> actual temp = 27
.0 C, asw400 probe
C & CH2 same, CH & CH3 opposite side of
solvent signal
exp1 apt
SAMPLE DEC. & VT
date Nov 23 2005 dn H1
solvent cdcl3 dof 0
file /mnt/d600/cil- dm yyy
vennmrdata/2Pure/ES- dmm w
-6-102APT.fid dmf 9320
ACQUISITION dpwr 41
sfrq 100.539 temp 26.8
tn C13 PROCESSING
at 2.003 lb 1.50
np 107998 wtfile
sw 26954.2 proc ft
fb not used fn 131072
bs 8 math f
ss 8
tpwr 57 werr
pw 3.2 wexp
p1 19.4 wbs
d1 0.100 wnt
d2 0.007 DISPLAY
d3 0.001 sp -1989.4
tof 2000.0 wp 24453.8
nt 1e+06 vs 2295
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
alock n wc 250
gain 48 hzmm 112.31
FLAGS ls 500.00
il n rfl 9731.4
in n rfp 7741.5
dp y th 60
hs nn ins 100.000
ai ph


I
CHO
O
TsO
12
ppm

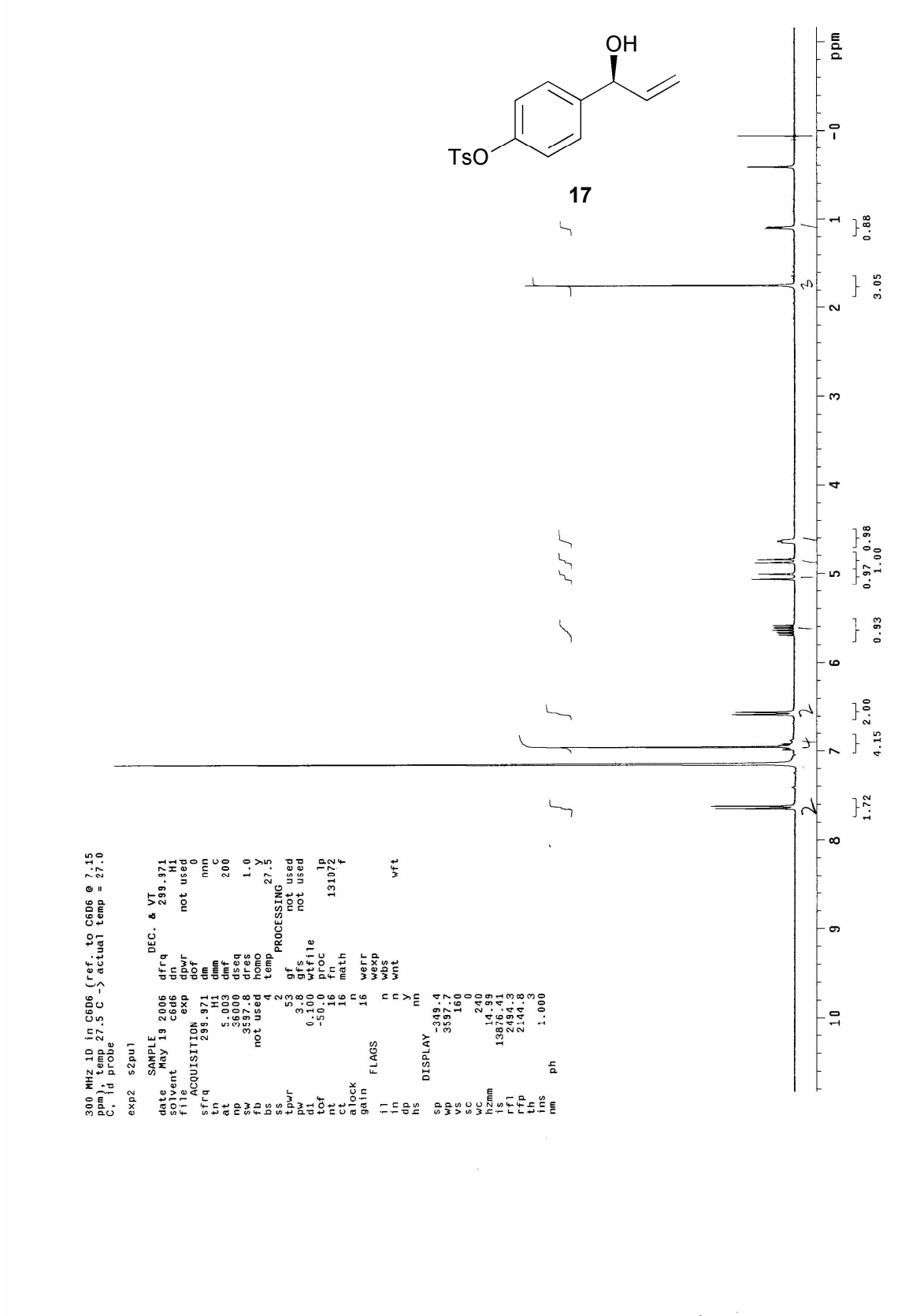

CHO
O
TsO
13
ppm
0
1
2
3
4
5
6
7
8
9
10
3.00
3.08
0.91
1.00
3.96
0.92
2.08
3.93
0.88
400 MHz 1D in CDCl3 (ref. to CDCl3 @ 7.2
6 ppm), temp 26.8 C -> actual temp = 27.
0 C, asw400 probe
exp2 s2pul
SAMPLE
date Nov 29 2005
solvent cdcl3
file exp
ACQUISITION
sfrq 399.794
tn H1
dm nnn
dmm c
dmf 200
dseq
dres
homo y
temp 26.8
PROCESSING
gf not used
gfs not used
wtfile
proc lp
fn 131072
math f
werr
wexp
wbs
wnt wft
DISPLAY
sp -457.9
wp 4801.8
vs 54
sc 0
wc 240
hzmm 20.01
is 35530.21
rfl 3352.5
rfp 2894.5
th 3
ins 1.000
nm ph

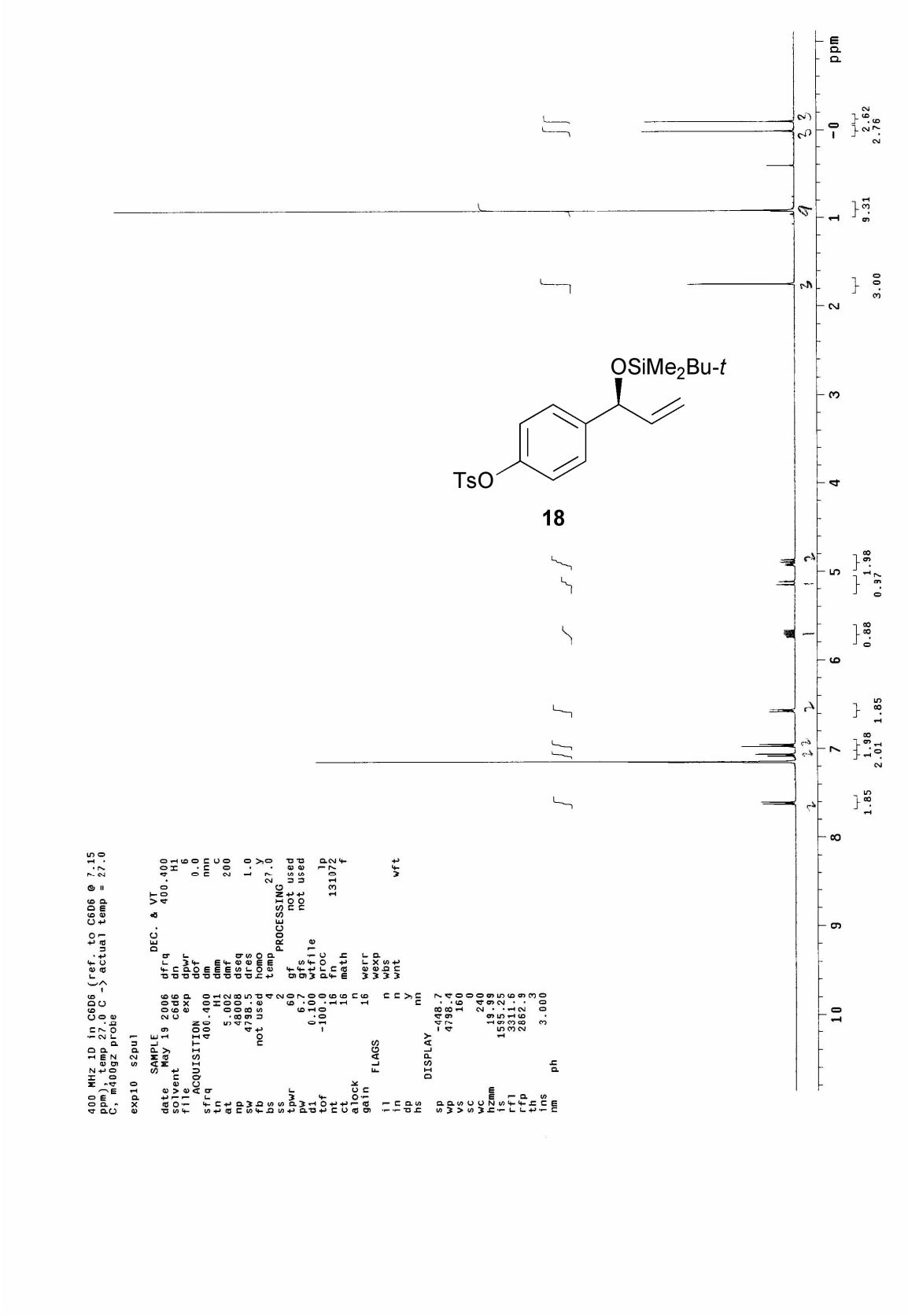

TsO
O
14
ppm

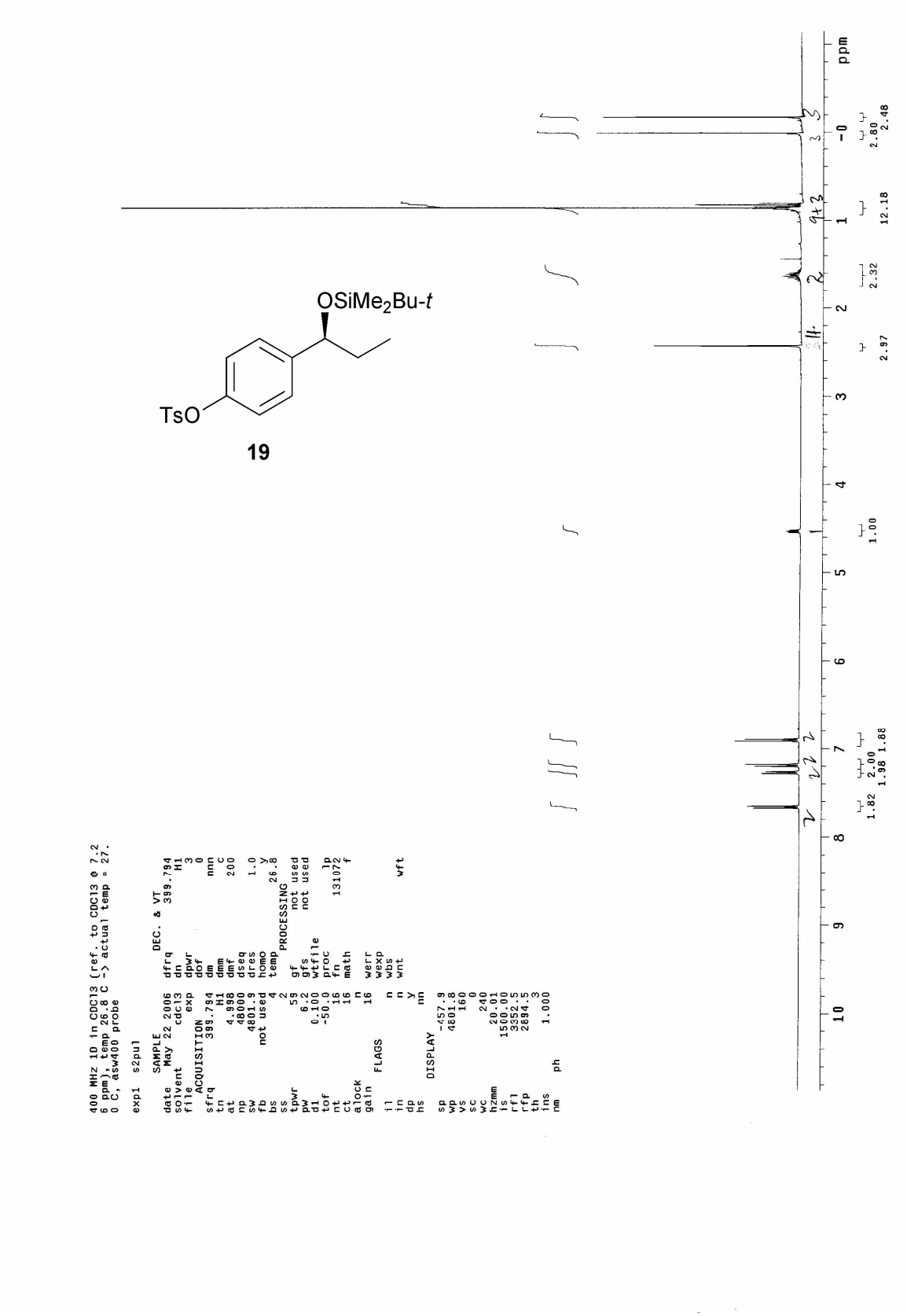

TsO
O
15 in C6D6
(10-day reaction)
ppm

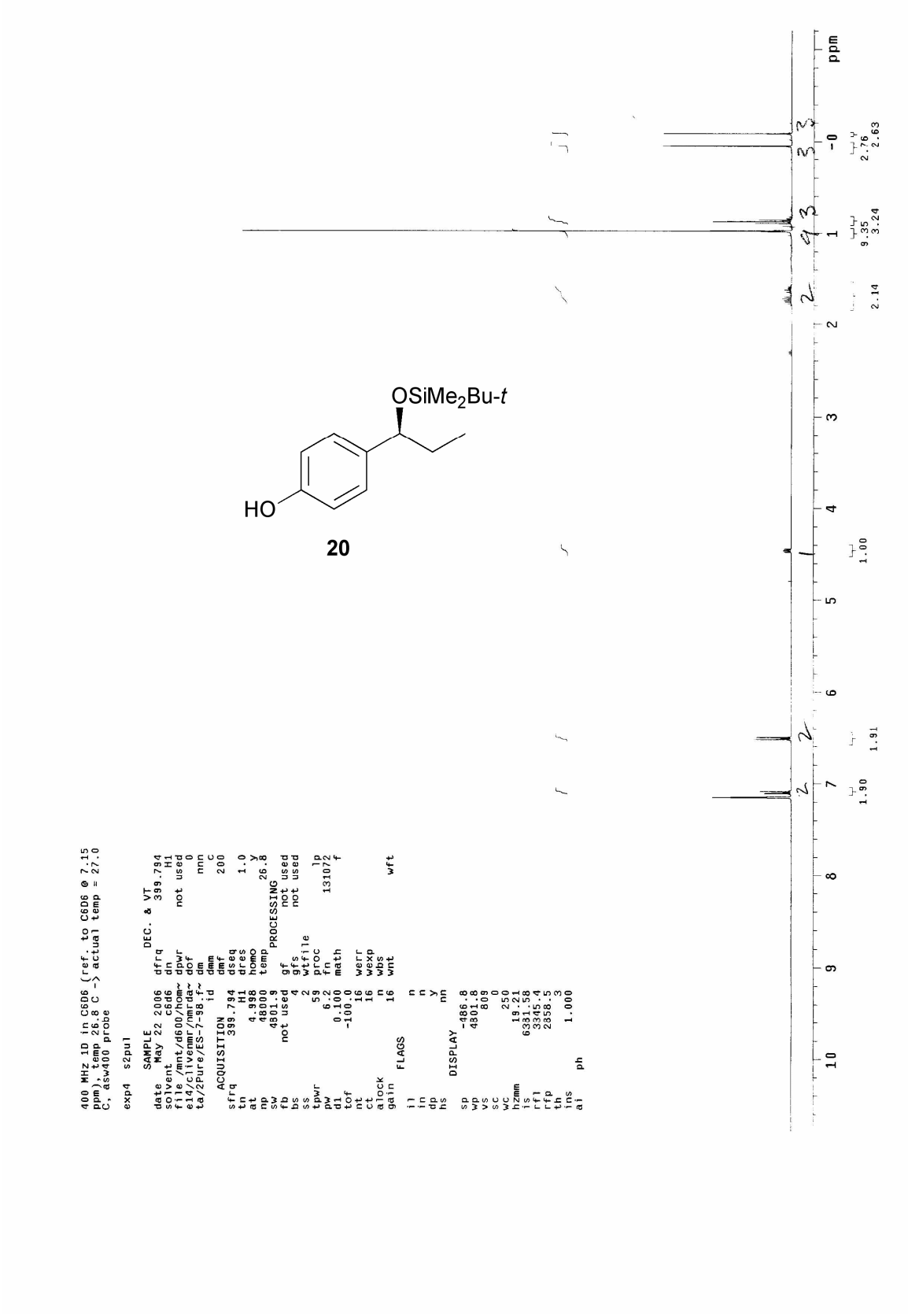

100 MHz APT in CDCl3 (ref. to CDCl3 @ 77
.0 ppm), temp 27.0 C -> actual temp = 27
.0 C, 5mm dual probe
C & CH2 same, CH & CH3 opposite side of
solvent signal
exp1 apt
SAMPLE
date May 18 2006
solvent cdcl3
file exp
ACQUISITION
sfrq 100.692
tn C13
at 2.000
np 108110
sw 27027.0
fb 15000
bs 8
ss 8
tpwr 60
pw 2.4
p1 14.4
d1 0.100
d2 0.007
d3 0.001
tof 2000.0
nt 1e+06
ct 2064
alock n
gain 30
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0.0
dm yny
dmm w
dmf 11500
dpwr 45
temp 27.0
PROCESSING
lb 1.50
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
DISPLAY
sp -2012.1
wp 27026.6
vs 180
sc 0
wc 240
hzmm 112.61
is 500.00
rfl 9765.8
rfp 7753.3
th 60
ins 100.000
ai
ph
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240
O
OMs
TsO

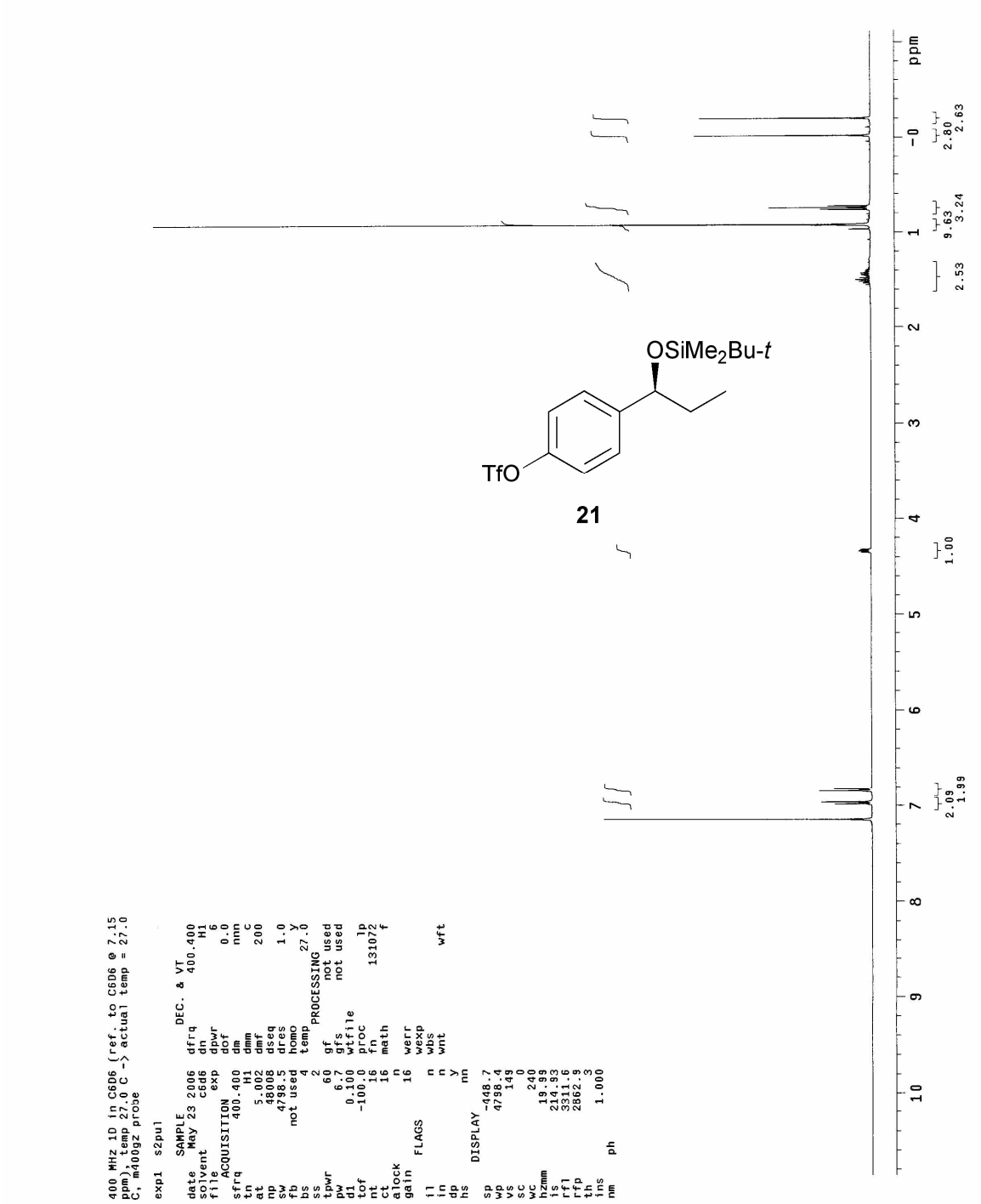
16


OH
TsO
17
ppm


OSiMe2Bu-t
TsO
18
ppm


OSiMe2Bu-t
TsO
19
ppm

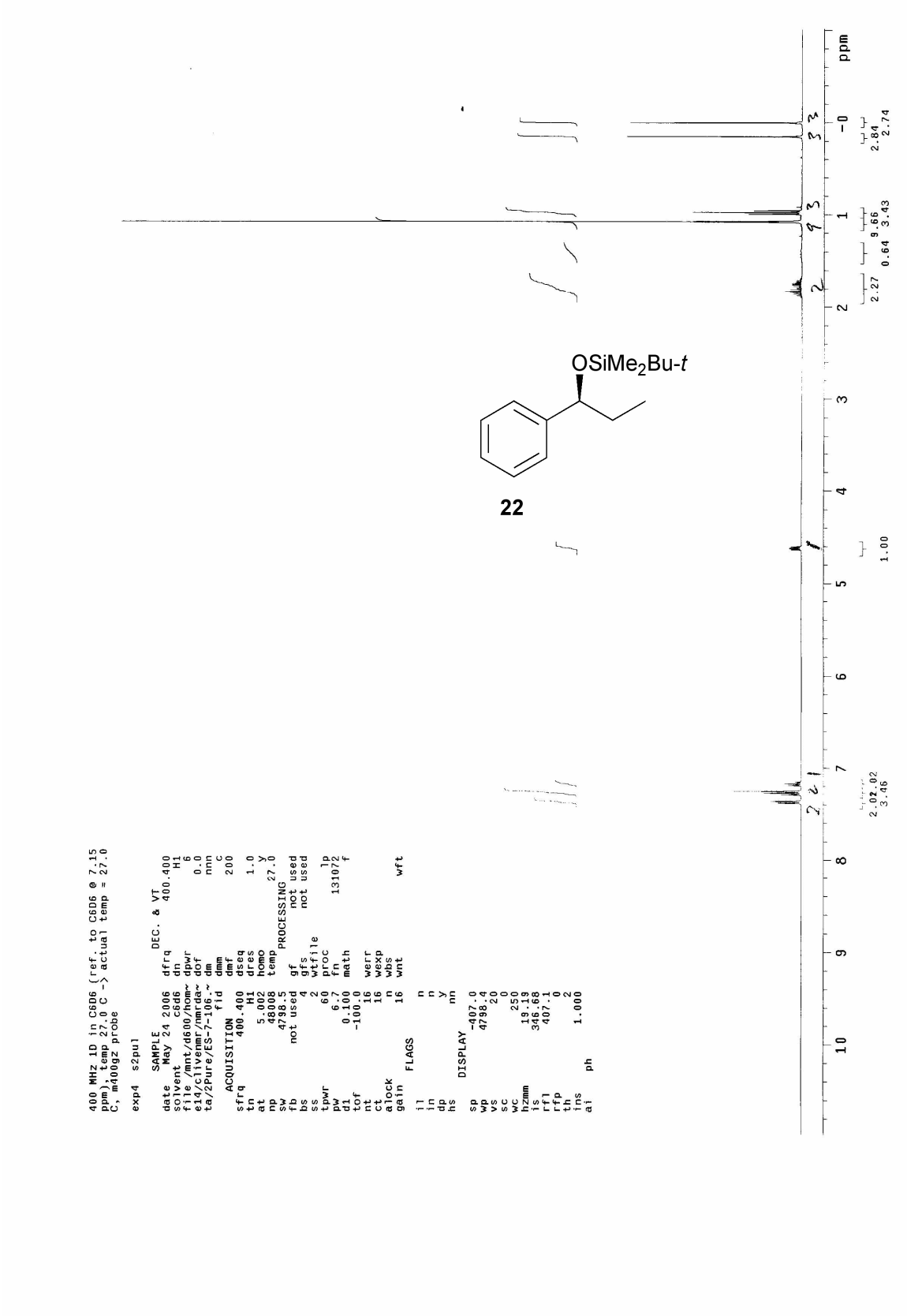

OSiMe2Bu-t
HO
20
ppm

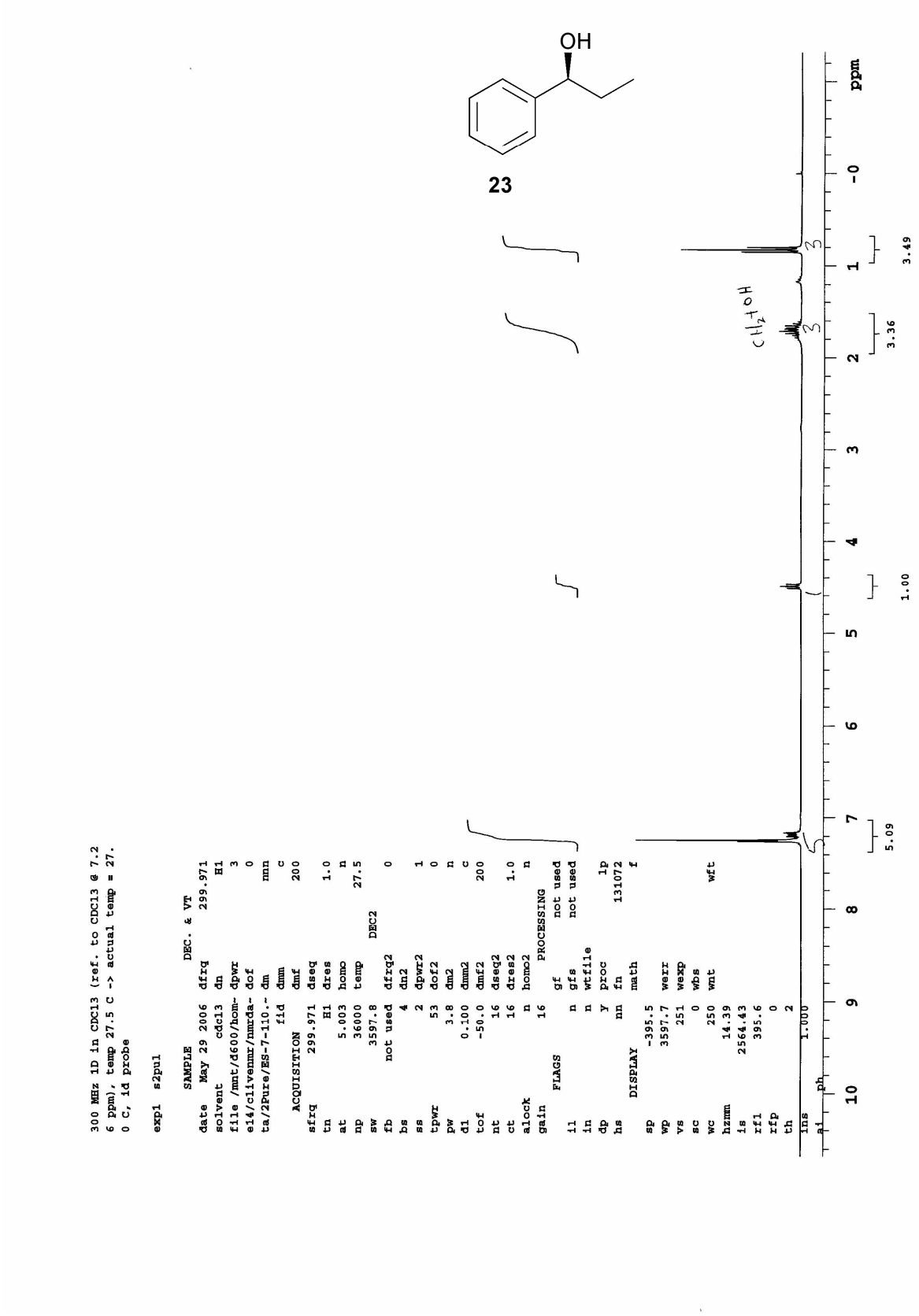



```
400 MHz 1D in C6D6 (ref. to C6D6 @ 7.15
ppm), temp 27.0 C -> actual temp = 27.0
C, m400gz probe

exp1   s2pul

                    DEC. & VT
date      SAMPLE    dfrq     400.400
solvent   May 23 2006 dn          H1
file      c6d6      dpwr          6
          exp       dof         0.0
ACQUISITION         dm          nnn
sfrq      400.400   dmm           C
tn          H1      dmf         200
at        5.002     dres
np        48008     homo
sw        4798.5    temp         1.0
fb      not used    PROCESSING    y
bs            4     not used     27.0
ss            2     gf             y
tpwr         60     gfs          6.7
pw          6.7     wtfile     not used
d1        0.100     proc
tof      -100.0     fn           131072
nt            16    math           lp
ct            16    werr           f
alock         n     wexp
gain         16     wbs
                    wnt
FLAGS               wft
il            n
in            n
dp            y
hs           nn
DISPLAY
sp        -448.7
wp        4798.4
vs         149
sc           0
wc         240
hzmm      19.99
is        214.83
rfl       3311.6
rfp       2862.9
th           3
ins      1.000
nm   ph
```


OSiMe2Bu-t
22
ppm


300 MHz 1D in CDCl3 (ref. to CDCl3 @ 7.2
6 ppm), temp 27.5 C -> actual temp = 27.
0 C, id probe
exp1 s2pul
SAMPLE DEC. & VT
date May 29 2006 dfrq 299.971
solvent cdcl3 dn H1
file /mnt/d600/hom- dpwr 3
e14/cliveenmr/nmrda- dof 0
ta/2Pure/ES-7-110.- dm nnn
fid dmm c
ACQUISITION dmf 200
sfrq 299.971 dseq
tn H1 dres 1.0
at 5.003 homo n
np 36000 temp 27.5
sw 3597.8 DEC2
fb not used dfrq2 0
bs 4 dn2
ss 2 dpwr2 1
tpwr 53 dof2 0
pw 3.8 dm2 n
d1 0.100 dmm2 c
tof -50.0 dmf2 200
nt 16 dseq2
ct 16 dres2 1.0
alock n homo2 n
gain 16 PROCESSING
FLAGS gf not used
il n gfs not used
in n wtfile
dp y proc 1p
hs nn fn 131072
DISPLAY math f
sp -395.5
wp 3597.7 werr
vs 251 wexp
sc 0 wbs
wc 250 wnt wft
hzmm 14.39
is 2564.43
rf1 395.6
rfp 0
th 2
ins 1.000
al ph
OH
23
CH2OH
5.09
1.00
3.36
3.49
10 9 8 7 6 5 4 3 2 1 -0 ppm