$Yb(OTf)_3$-Catalyzed Oxymercuration of Homoallylic Alcohol-Derived Hemiacetals and Hemiketals

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Supporting Information

General Information. All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring unless otherwise indicated. Flash chromatography was performed as described by Still[1] on EM silica gel 60 (230-240 mesh). Acetone was dried over $CaSO_4$ and then distilled from fresh $CaSO_4$. Benzaldehyde was distilled prior to use. All other commercially obtained reagents were used as received. HgCl(OAc) was prepared as described previously.[2] Melting points were obtained on a Büchi melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker DRX-400 (400 MHz) or a Bruker DPX-300 (300 MHz) spectrometer and are reported in ppm from internal tetramethylsilane. Data are reported as follows: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad; integration; coupling constant(s) in Hz). Proton decoupled ^{13}C NMR spectra were recorded on a Bruker DRX-400 (100 MHz) or a Bruker DPX-300 (75 MHz) spectrometer using $CDCl_3$ (77.0 ppm) as internal standard. Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrometer. High resolution mass spectra were obtained on a JEOL HX110 mass spectrometer in the Columbia University Mass Spectrometry Laboratory.

General procedure for the oxymercuration with acetone. To a solution of $Yb(OTf)_3$ (31 mg, 0.050 mmol) and HgCl(OAc) (325 mg, 1.1 mmol) in acetone (8 mL) at 0 °C is added the

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(1) Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

(2) Sarraf, S.T.; Leighton, J.L. *Org. Lett.* **2000**, *2*, 403-405.

homoallylic alcohol (1.0 mmol) via cannula. The reaction mixture is allowed to stir 20 min at 0 °C, then 1.5 h at rt. The mixture is then poured into a separatory funnel containing 5 mL of saturated aqueous $NaHCO_3$. The aqueous layer is extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers are dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (EtOAc:hexanes) affords the product organomercury chlorides.

General procedure for the oxymercuration with benzaldehyde. To a solution of $Yb(OTf)_3$ (31 mg, 0.050 mmol) and HgCl(OAc) (325 mg, 1.1 mmol) in benzaldehyde (305 μL, 3.0 mmol) at 0 °C is added the homoallylic alcohol (1.0 mmol). Upon completion of the addition, the reaction is warmed to rt and stirred for 30 min. The mixture is then poured into a separatory funnel containing 5 mL of saturated aqueous $NaHCO_3$. The aqueous layer is extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers are dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (EtOAc:hexanes) affords the product organomercury chlorides.

2,2-Dimethyl-*cis*-4-chloromercurymethyl-6-isobutyl-1,3-dioxane (Table 2, entry 1). White crystalline solid: m.p. 89-91 °C; R_f = 0.33 (20% EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.25 (m, 1H), 3.88 (m, 1H), 2.29 (ABq, 1H, *J* = 5.0, 11.9 Hz), 2.05 (ABq, 1H, *J* = 5.9, 11.9 Hz), 1.76 (m, 1H), 1.62 (dt, 1H, *J* = 2.4, 12.8 Hz), 1.48 (m, 1H), 1.43 (s, 3H), 1.38 (s, 3H), 1.16 (m, 1H), 1.06 (m, 1H, *J* = 11.3, 12.7 Hz), 0.90 (d, 3H, *J* = 5.4 Hz), 0.88 (d, 3H, *J* = 5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.8, 68.0, 66.7, 45.2, 41.6, 39.7, 30.4, 23.8, 23.0, 22.2, 20.0; IR (CCl_4) 2989, 2954, 2873, 1467, 1382, 1270, 1199, 1176, 1118, 1051, 1020, 957, 926, 872 cm^{-1}; HRMS (FAB+) calc'd. for $C_{11}H_{22}ClHgO_2$ $[M+H]^+$ 423.1006, found 423.0998.

2,2-Dimethyl-*cis*-4-chloromercurymethyl-6-(2-benzyloxy)ethyl-1,3-dioxane (Table 2, entry 2). Clear, colorless oil: R_f = 0.21 (20% EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.50 (m, 2H), 4.25 (m, 1H), 4.04 (m, 1H), 3.54 (m, 2H), 2.28 (ABq, 1H, *J* = 5.0,

11.9 Hz), 2.03 (ABq, 1H, *J* = 5.8, 12.0 Hz), 1.75 (m, 2H), 1.63 (m, 1H, *J* = 2.4, 12.8 Hz), 1.42 (s, 3H), 1.36 (s, 3H), 1.09 (m, 1H, *J* = 11.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 128.4, 127.7, 127.6, 99.0, 73.0, 67.9, 66.0, 65.8, 41.1, 39.6, 36.4, 30.3, 20.2; IR (thin film) 2989, 2937, 2864, 1457, 1379, 1259, 1202, 1109, 1021, 953, 870, 741, 699 cm^{-1}; HRMS (FAB+) calc'd. for $C_{16}H_{23}ClHgO_3Na$ $[M+Na]^+$ 519.0901, found 519.0904.

2,2-Dimethyl-*cis*-4-chloromercurymethyl-6-(2-*tert*-butyldimethylsilyloxy)ethyl-1,3-dioxane (Table 2, entry 3). Clear colorless oil: R_f = 0.74 (50% EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (m, 1H), 4.04 (m, 1H), 3.73 (m, 1H), 3.66 (m, 1H), 2.30 (ABq, 1H, *J* = 5.0, 11.9 Hz), 2.05 (ABq, 1H, *J* = 5.9, 11.9 Hz), 1.65 (m, 3H), 1.43 (s, 3H), 1.37 (s, 3H), 1.10 (m, 1H, *J* = 11.4 Hz), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.4, 68.4, 65.7, 59.1, 41.7, 40.1, 39.7, 30.8, 26.4, 20.6, 18.7, -4.9, -4.9; IR (thin film) 2938, 2854, 1471, 1377, 1256, 1204, 1162, 1114, 1093, 1020, 957, 836, 778 cm^{-1}; HRMS (FAB+) calc'd. for $C_{15}H_{32}O_3HgSi$ $[M+H-Cl]^+$ 490.1902, found 490.1888.

2,2-Dimethyl-*cis*-4-chloromercurymethyl-*cis*-5-methyl-6-isopropyl-1,3-dioxane (Table 2, entry 4). The reaction was run for 3 h at RT. White crystalline solid: m.p. 85-87 °C; R_f = 0.41 (20% EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (dt, 1H, *J* = 1.9, 5.9 Hz), 3.28 (dd, 1H, *J* = 9.6 Hz), 2.12 (d, 2H, *J* = 6.0 Hz), 1.68 (m, 1H), 1.54 (m, 1H), 1.39 (s, 3H), 1.39 (s, 3H), 0.94 (d, 3H, *J* = 6.4 Hz), 0.88 (d, 3H, *J* = 6.8 Hz), 0.80 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.2, 79.3, 71.8, 35.7, 35.1, 30.0, 29.2, 19.9, 19.8, 17.4, 4.3; IR (CCl_4) 2968, 2873, 1462, 1382, 1264, 1198, 1103, 1013, 975, 914 cm^{-1}; HRMS (FAB+) calc'd. for $C_{11}H_{22}ClHgO_2$ $[M+H]^+$ 419.0976, found 419.0965.

2,2-Dimethyl-*cis*-4-chloromercurymethyl-*trans*-5-methyl-6-(2-*tert*-butyldiphenylsilyloxy)ethyl-1,3-dioxane (Table 2, entry 5). The reaction was run from -78 °C to rt instead of 0 °C to RT. Clear tacky oil: R_f = 0.51 (20% EtOAc:hexanes); ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.67 (m, 4H), 7.39 (m, 6H), 3.90 (m, 1H), 3.84 (m, 1H), 3.73 (m, 2H), 2.35 (ABq, 1H, *J* = 4.2, 12.0 Hz), 2.14 (ABq, 1H, *J* = 6.1, 12.0 Hz), 1.93 (m, 1H), 1.48 (m, 1H), 1.41 (s, 3H), 1.34 (s, 3H), 1.12 (m, 1H), 1.04 (s, 9H), 0.83 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 133.9, 129.5, 129.5, 127.6, 127.6, 98.3, 73.6, 70.4, 59.6, 43.8, 38.2, 36.0, 30.3, 26.8, 20.0, 19.2, 12.8; IR (CCl_4) 3067, 2933, 2866, 1468, 1430, 1387, 1263, 1201, 1111, 959, 699, 616, 507 cm^{-1}; HRMS (FAB+) calc'd. for $C_{26}H_{37}ClHgO_3SiNa$ $[M+Na]^+$ 681.1766, found 681.1775.

2,2-Dimethyl-*cis*-4-chloromercurymethyl-6-*E*-isopentenyl-1,3-dioxane (Table 2, entry 6). The reaction was run at 0 °C for 30 min. White crystalline solid: m.p. 82-84 °C; R_f = 0.41 (20% EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67 (dd, 1H, *J* = 6.3, 15.6 Hz), 5.37 (dd, 1H, *J* = 6.4, 15.6 Hz), 4.30 (m, 2H), 2.30 (m, 2H), 2.06 (ABq, 1H, *J* = 5.9, 11.9 Hz), 1.67 (dt, 1H, *J* = 2.3, 12.9 Hz), 1.47 (s, 3H), 1.42 (s, 3H), 1.22 (m, 1H), 0.99 (d, 6H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.9, 127.1, 99.0, 70.0, 67.6, 41.3, 39.5, 30.6, 30.4, 22.0, 22.0, 20.1; IR (CCl_4) 2989, 2968, 2864, 1462, 1379, 1265, 1197, 1026, 969, 927, 876 cm^{-1}; HRMS (FAB+) calc'd. for $C_{12}H_{22}HgO_2$ $[M+H-Cl]^+$ 396.1226, found 396.1200.

Table 2, entry 7. This compound is an intermediate in our total synthesis of *Tolypothrix* pentaether. Experimental details and spectral data will be disclosed elsewhere.[3]

***cis*-2-Phenyl-*cis*-4-chloromercurymethyl-6-octyl-1,3-dioxane (Table 2, entry 8).** Off-white, crystalline solid: m.p. 76-78 °C; R_f = 0.44 (20% EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.50 (m, 5H), 5.55 (s, 1H), 4.22 (m, 1H), 3.79 (m, 1H), 2.36 (ABq, 1H, *J* = 5.0, 12.0 Hz), 2.16 (ABq, 1H, *J* = 6.6, 12.0 Hz), 1.27-1.79 (m, 16H), 0.88 (t, 3H, *J* = 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 128.3, 126.1, 100.6, 76.7, 75.4, 40.9, 38.4, 35.8, 31.8, 29.5, 29.5, 29.2, 25.0, 22.6, 14.1; IR ($CDCl_3$) 2926, 2843, 1457, 1376, 1338, 1213, 1121, 1060, 1020,

(3) Sarraf, S.T.; Leighton, J.L. *Org. Lett.* Accepted for publication.

904, 836, 747, 699 cm^{-1}; HRMS (FAB+) calc'd. for $C_{19}H_{29}ClHgO_2Na$ $[M+Na]^+$ 545.1421, found 545.1403.

***cis*-2-Phenyl-*cis*-4-chloromercurymethyl-6-*E*-isopentenyl-1,3-dioxane (Table 2, entry 9).** The reaction was run for 15 min from -78 °C to rt instead of 0 °C to rt. Off-white crystalline solid: m.p. 91-93 °C; R_f = 0.41 (20% EtOAc:hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.50 (m, 5H), 5.71-5.77 (dd, 1H, *J* = 6.4, 15.6 Hz), 5.6 (s, 1H), 5.50-5.61 (ddd, 1H, *J* = 1.1, 6.2, 15.6 Hz), 4.28 (m, 2H), 2.35 (ABq, 1H, *J* = 5.1, 12.1 Hz), 2.30 (m, 1H), 2.18 (ABq, 1H, *J* = 6.4, 12.1 Hz), 1.83 (dt, 1H, *J* = 2.4, 13.1 Hz), 1.50 (m, 1H), 1.00 (d, 6H, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0, 137.9, 128.9, 128.3, 126.3, 100.8, 77.2, 75.3, 41.1, 38.3, 30.7, 22.0; IR (liquid film) 3035, 2957, 2865, 2720, 1671, 1458, 1394, 1330, 1261, 1215, 1010, 907, 839, 752, 702 cm^{-1}; HRMS (FAB+) calc'd. for $C_{16}H_{21}ClHgO_2Na$ $[M+Na]^+$ 501.0795, found 501.0790.

Stereochemical proofs. The stereochemistry of the acetonides were demonstrated to be *cis* by employing the ^{13}C NMR method of Rychnovsky.[4] The stereochemistry of the benzylidene acetals were determined to be all-*syn* by the illustrated selective 1D NOESY experiments (Figure 1).

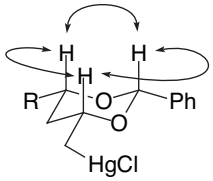


Figure 1. Observed selective 1D NOESY enhancements to establish the all *cis* stereochemistry of the benzylidene acetals.

(4) (a) Rychnovsky, S.D.; Skalitzky, D.J. *Tetrahedron Lett.* **1990**, *31*, 945-948. (b) Rychnovsky, S.D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511-3515.

^{1}H NMR Spectra.

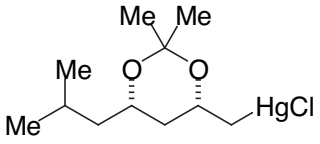
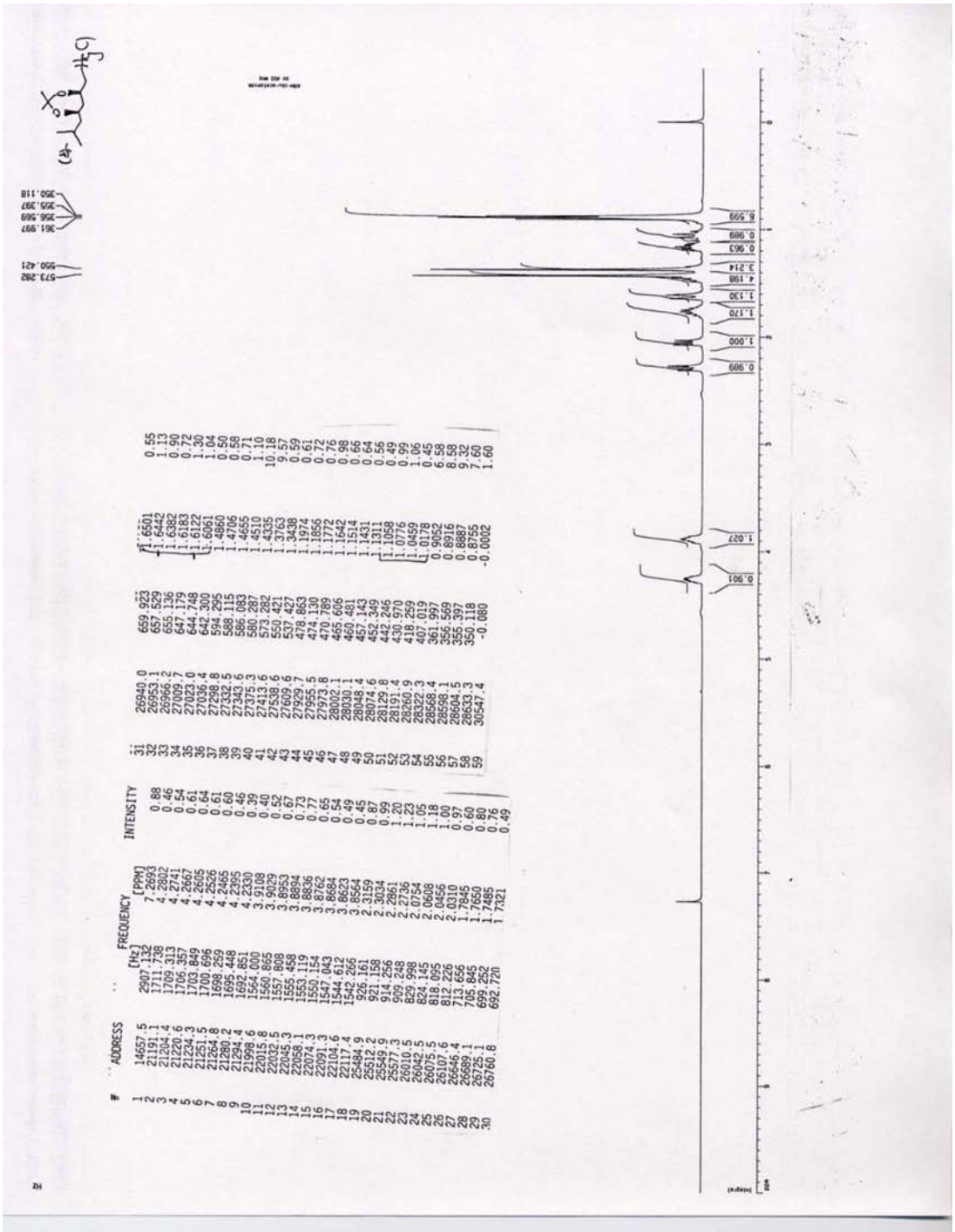


Table 2, Entry 1



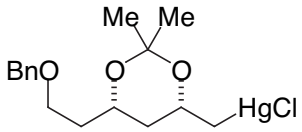
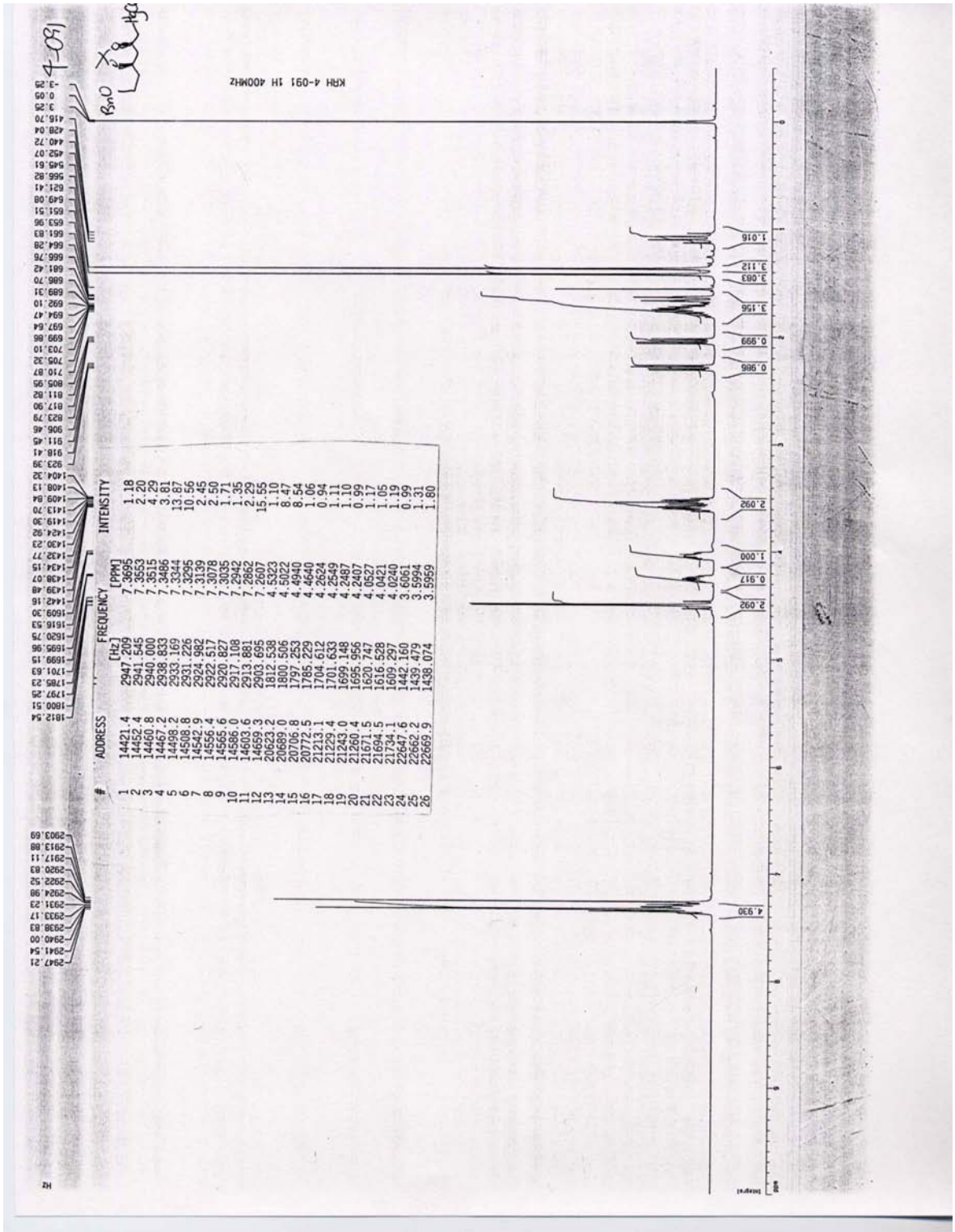


Table 2, Entry 2



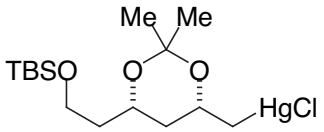
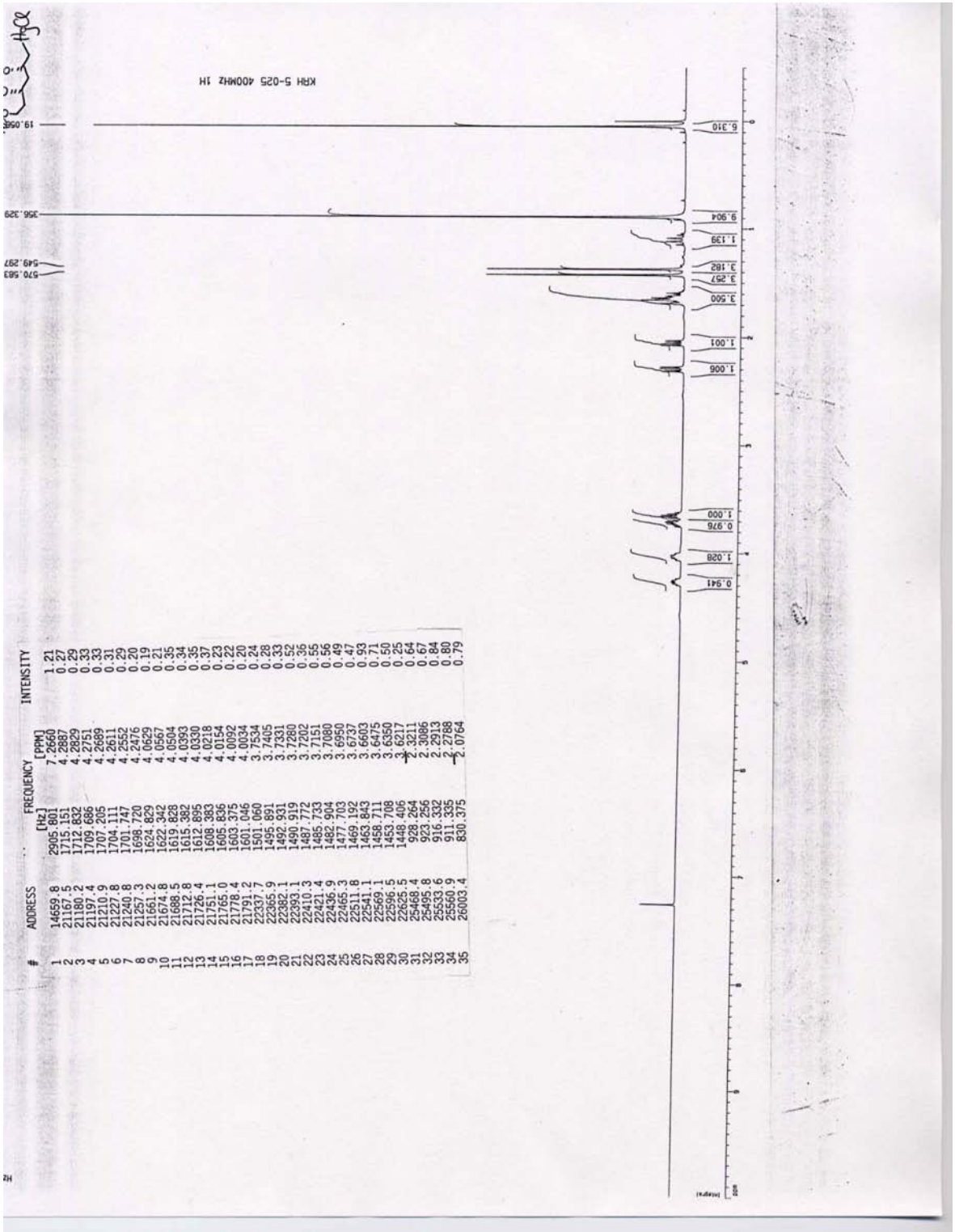
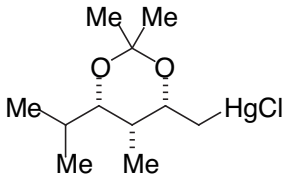


Table 2, Entry 3





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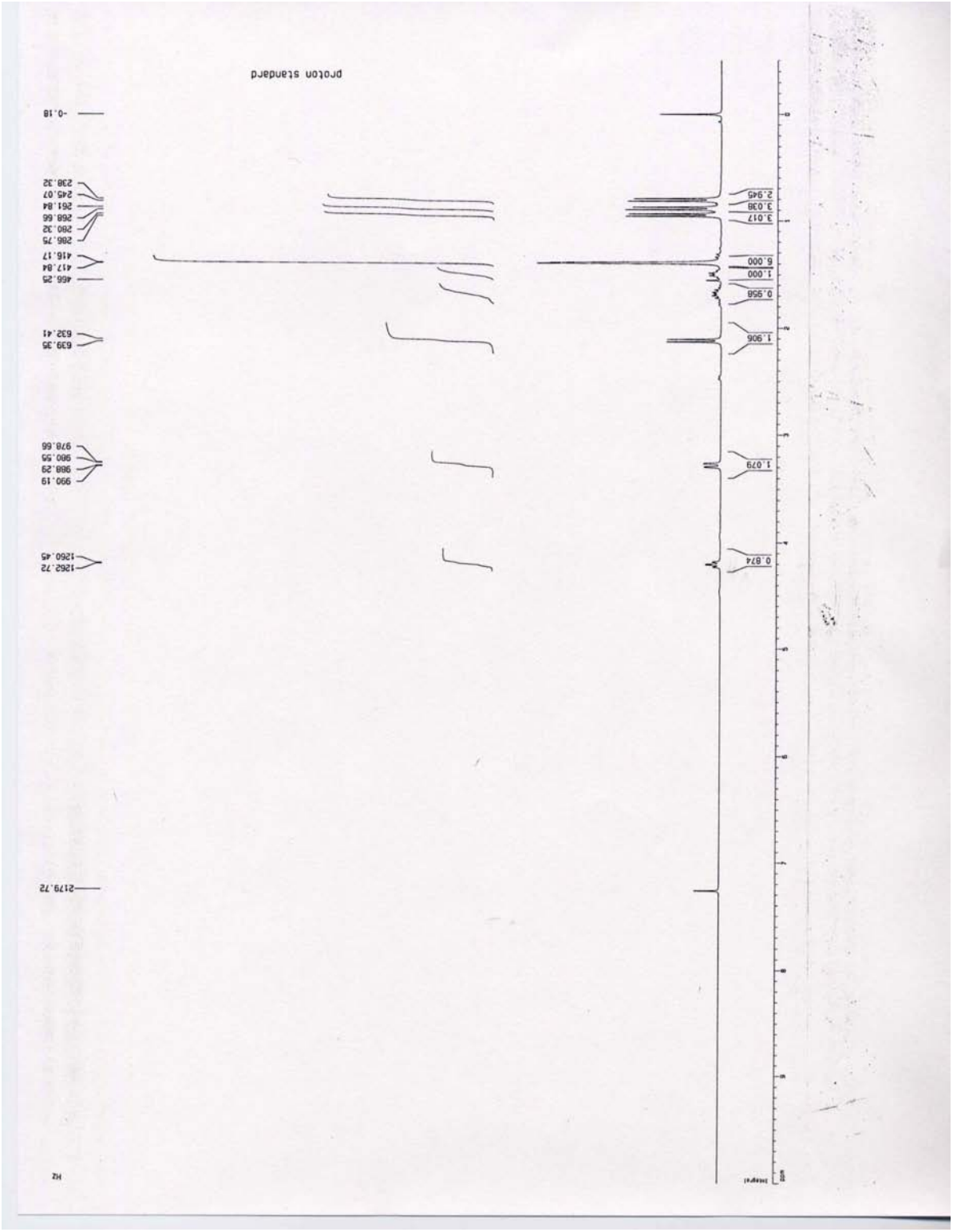

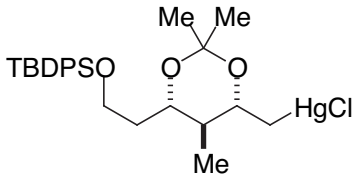

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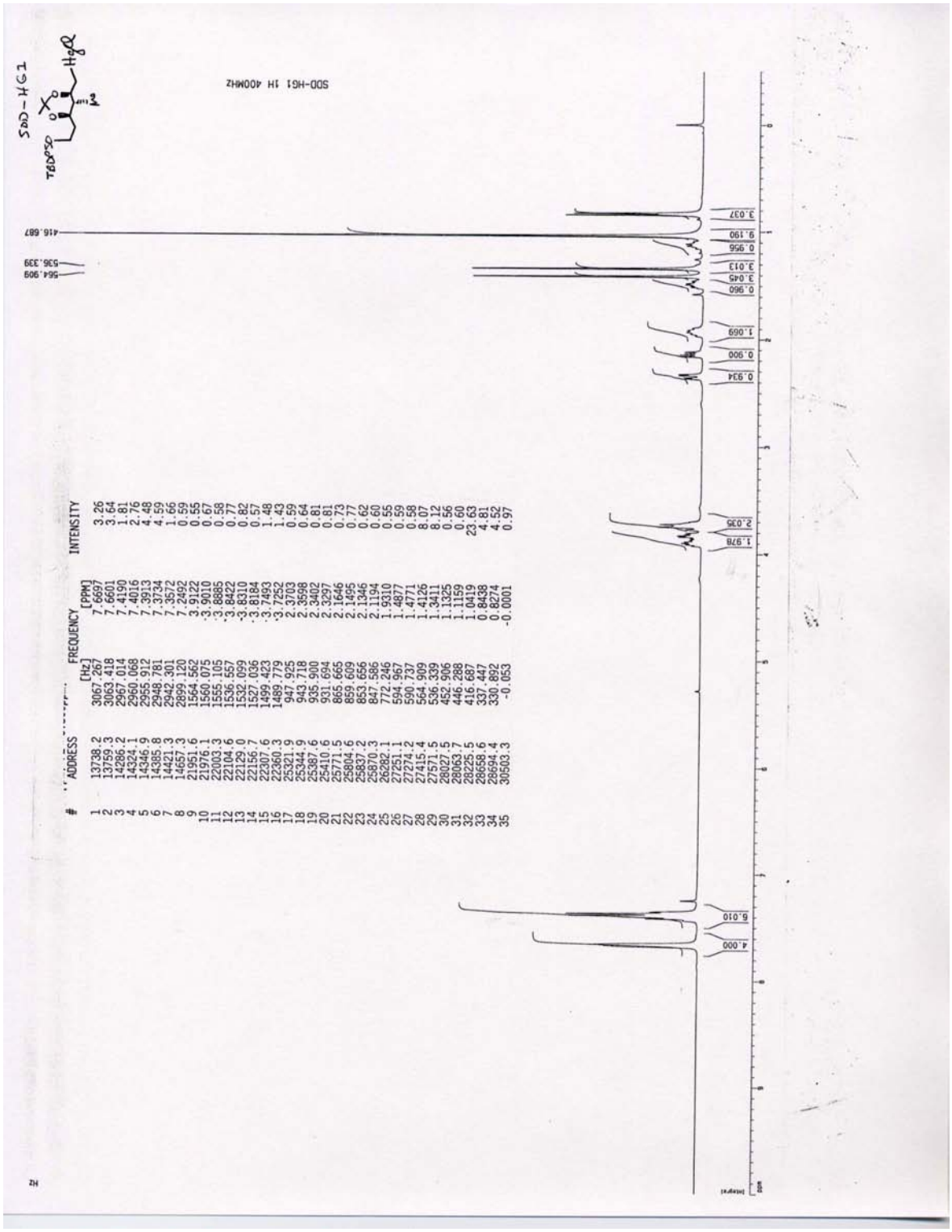

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2	13759.3	3063.418	7.6601	3.64
3	14286.2	2967.014	7.4190	1.81
4	14324.1	2960.068	7.4016	2.76
5	14346.9	2955.912	7.3913	4.48
6	14385.8	2948.781	7.3734	4.59
7	14421.3	2942.301	7.3672	1.66
8	14657.3	2899.120	7.2492	0.59
9	21951.6	1564.562	3.9122	0.55
10	21976.1	1560.075	3.9010	0.67
11	22003.3	1555.105	3.8885	0.58
12	22104.6	1536.557	3.8422	0.77
13	22129.0	1532.099	3.8310	0.82
14	22156.7	1527.036	3.8184	0.57
15	22307.6	1499.423	3.7493	1.48
16	22360.3	1489.779	3.7252	1.43
17	25321.9	947.925	2.3703	0.59
18	25344.9	943.718	2.3598	0.64
19	25387.6	935.900	2.3402	0.81
20	25410.6	931.694	2.3297	0.81
21	25771.5	865.665	2.1646	0.73
22	25804.6	859.609	2.1495	0.77
23	25837.2	853.656	2.1346	0.62
24	25870.3	847.586	2.1194	0.60
25	26282.1	772.246	1.9310	0.55
26	27251.1	594.967	1.4877	0.59
27	27274.2	590.737	1.4771	0.58
28	27415.4	564.909	1.4126	8.07
29	27571.5	536.339	1.3411	8.12
30	28027.5	452.906	1.1325	0.56
31	28063.7	446.288	1.1159	0.60
32	28225.5	416.687	1.0419	23.63
33	28658.6	337.447	0.8438	4.81
34	28694.4	330.892	0.8274	4.52
35	30503.3	-0.053	-0.0001	0.97

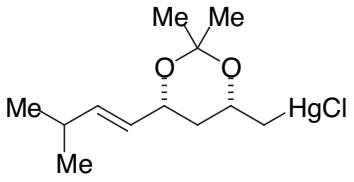
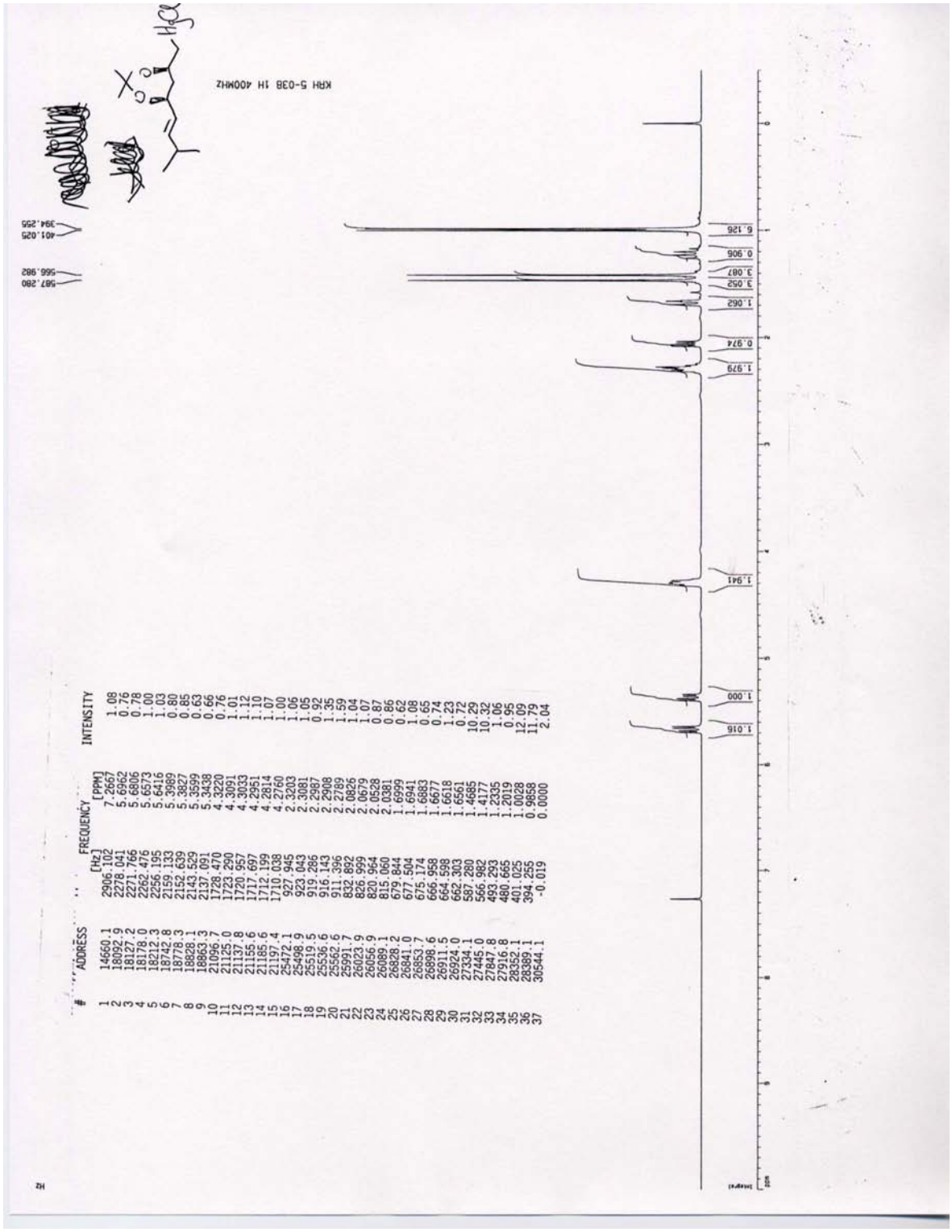


Table 2, Entry 6



#	ADDRESS	FREQUENCY [Hz]	[PPM]	INTENSITY
1	14660.1	2906.102	7.2667	1.08
2	18092.9	2278.041	5.6962	0.76
3	18127.2	2271.766	5.6806	0.78
4	18178.0	2262.476	5.6573	1.00
5	18212.3	2256.195	5.6416	1.03
6	18742.8	2159.133	5.3989	0.80
7	18778.3	2152.639	5.3827	0.85
8	18828.1	2143.529	5.3599	0.63
9	18863.3	2137.091	5.3438	0.66
10	21096.7	1728.470	4.3220	0.76
11	21125.0	1723.290	4.3091	1.01
12	21137.8	1720.957	4.3033	1.12
13	21156.6	1717.697	4.2951	1.10
14	21185.6	1712.199	4.2814	1.07
15	21197.4	1710.038	4.2760	1.00
16	25472.1	927.945	2.3203	1.06
17	25498.9	923.043	2.3081	1.05
18	25519.5	919.286	2.2987	0.92
19	25536.6	916.143	2.2908	1.35
20	25562.6	911.396	2.2789	1.59
21	25991.7	832.892	2.0826	1.04
22	26023.9	826.999	2.0679	1.07
23	26056.9	820.964	2.0528	0.87
24	26089.1	815.060	2.0381	0.86
25	26828.2	679.844	1.6999	0.62
26	26841.6	677.504	1.6941	1.08
27	26853.7	675.174	1.6883	0.65
28	26898.6	666.958	1.6677	0.74
29	26911.5	664.598	1.6618	1.23
30	26924.0	662.303	1.6561	0.72
31	27334.1	587.280	1.4685	10.29
32	27445.0	566.982	1.4177	10.32
33	27847.8	493.293	1.2335	1.06
34	27916.8	480.665	1.2019	0.95
35	28352.1	401.025	1.0028	12.09
36	28389.1	394.255	0.9858	11.79
37	30544.1	-0.019	0.0000	2.04

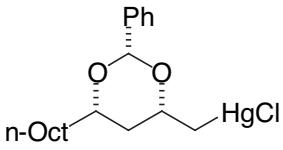
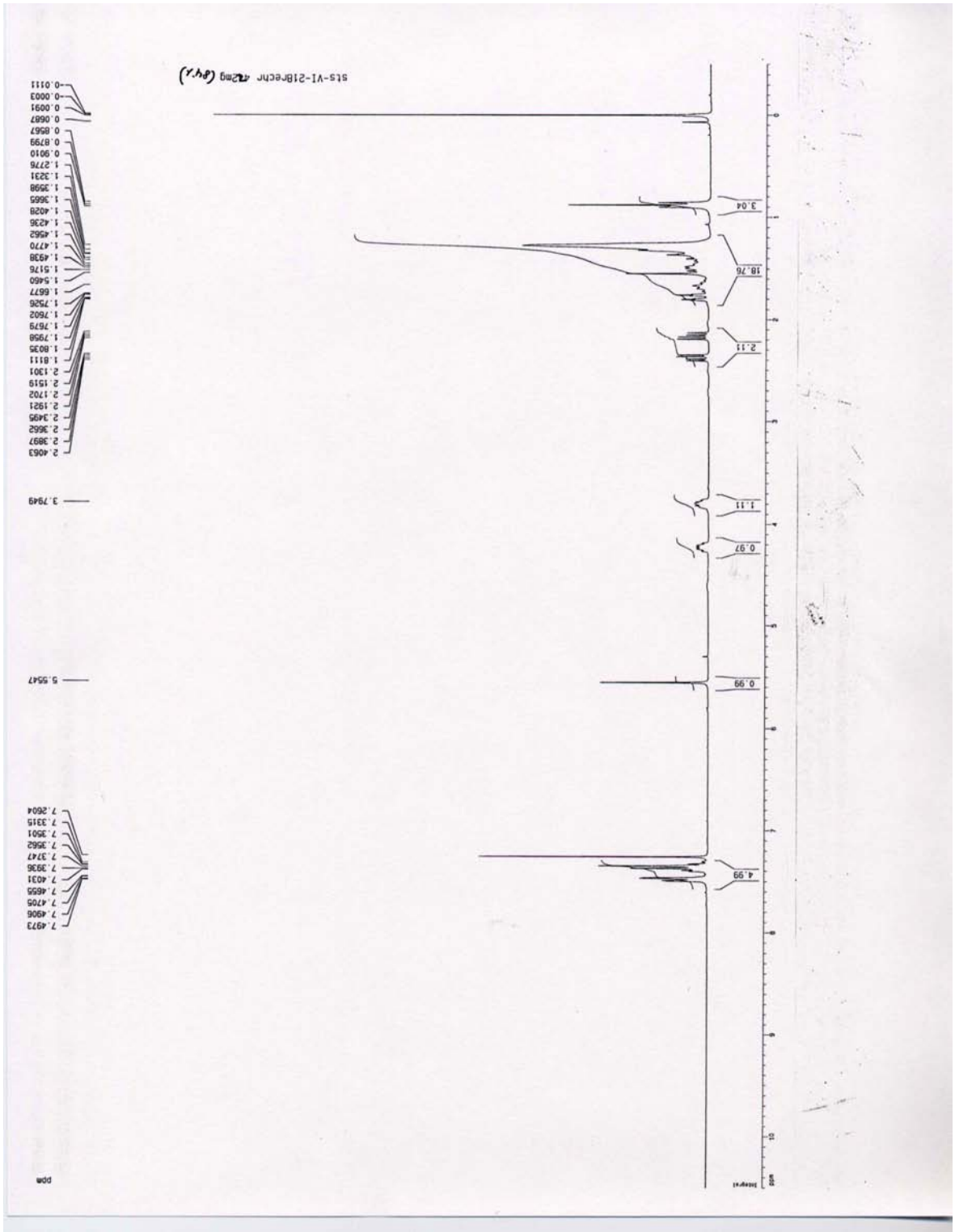


Table 2, Entry 8



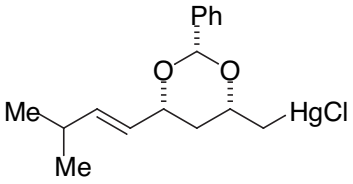
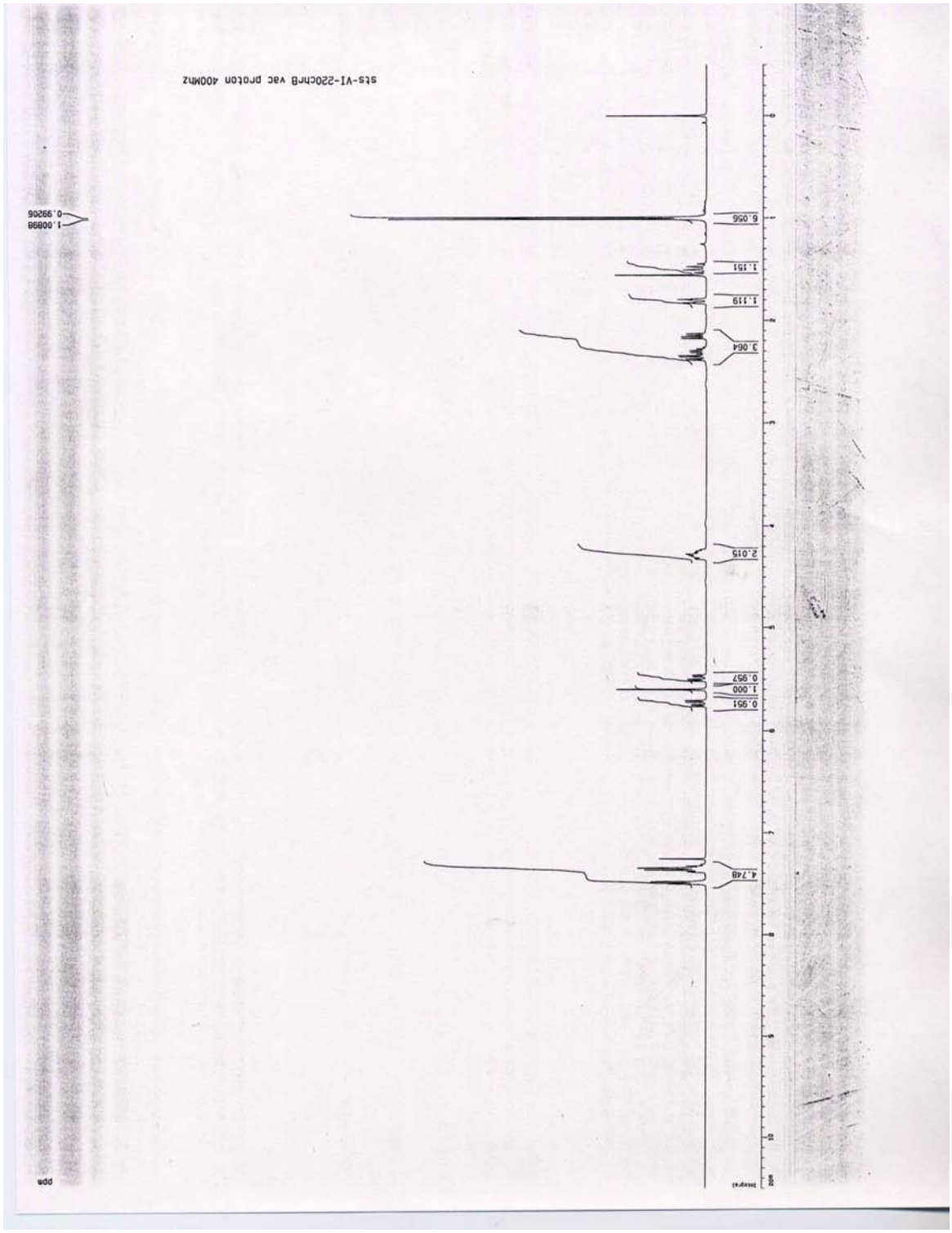


Table 2, Entry 9

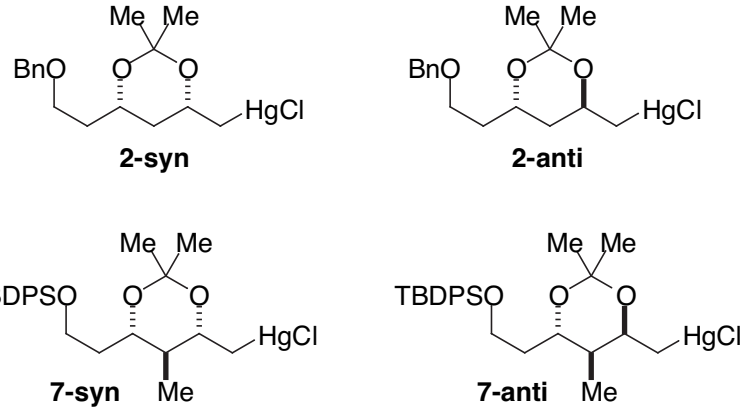


Determination of diastereoselectivity. By stopping the reactions at early reaction times, mixtures of the *syn* and *anti* diastereomers could be obtained. Comparison of these reactions to the reactions run under the optimized conditions allowed an assessment of the diastereoselectivity by ^{1}H NMR analysis. This is demonstrated for entries 2 and 5 in Table 2:

In Figure 2, a detail from the ^{1}H NMR spectrum of a 1:1.5 mixture of **2-*syn*:2-*anti*** is shown. Two sets of singlets for the acetonide methyl groups are clearly visible. In Figure 3, a detail from the ^{1}H NMR spectrum of the unpurified reaction mixture of entry 2, Table 2 is shown. Integration reveals a 54:1 ratio of **2-*syn*:2-*anti***. Since there is clearly a large error associated with this measurement, we simply claim a conservative lower limit of >20:1.

In Figure 4, a detail from the ^{1}H NMR spectrum of a 6:1 mixture of **7-*syn*:7-*anti*** is shown. Two sets of singlets for the acetonide methyl groups are clearly visible as well as two doublets for the C(5) methyl group. In Figure 5, a detail from the ^{1}H NMR spectrum of the unpurified reaction mixture of entry 5, Table 2 is shown. Integration of the methyl doublets reveals a 62:1 ratio of **7-*syn*:7-*anti***. Since there is clearly a large error associated with this measurement, we simply claim a conservative lower limit of >20:1.

For all other reactions in Table 2, similar analyses of the ^{1}H NMR spectra of the unpurified reaction mixtures revealed no peaks attributable to the *anti* diastereomer in any quantity approaching 5%. We therefore conclude that all reactions in Table 2 proceed with >20:1 diastereoselectivity except entry 4 as noted in the text.



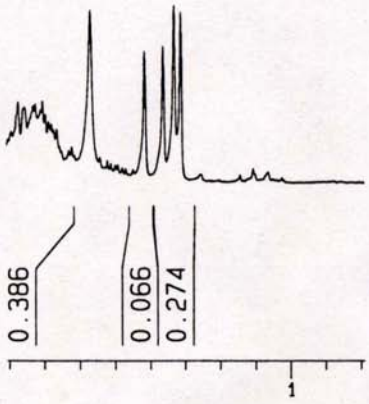


Figure 2. Detail of the ^{1}H NMR spectrum of a 1:1.5 mixture of **2-*syn*:2-*anti***.

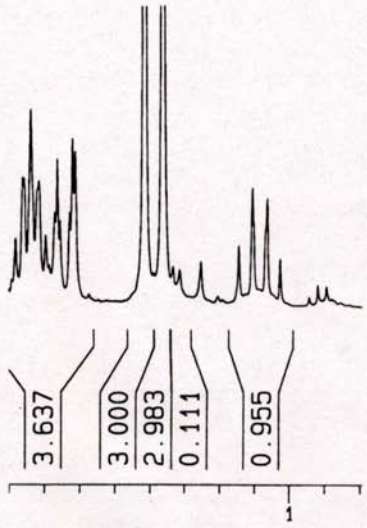


Figure 3. Detail of the ^{1}H NMR spectrum of the unpurified reaction in entry 2, Table 2.

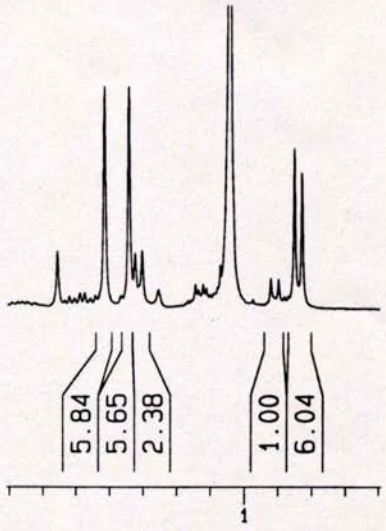


Figure 4. Detail of the ^{1}H NMR spectrum of a 6:1 mixture of **7-*syn*:7-*anti***.

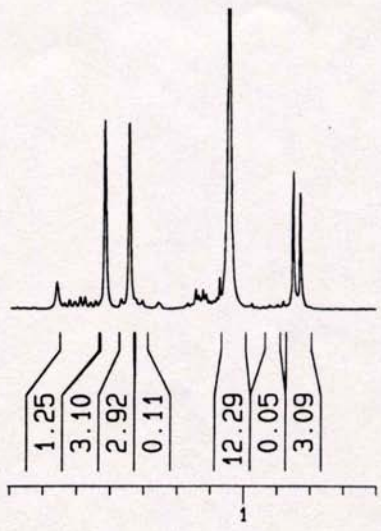


Figure 5. Detail of the ^{1}H NMR spectrum of the unpurified reaction in entry 5, Table 2.