

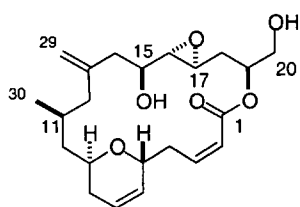
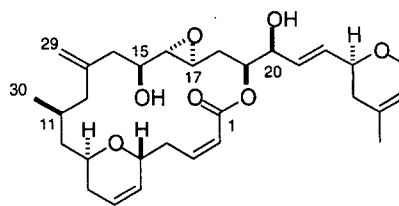
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Synthesis of the Macrocyclic Core of Laulimalide

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Table 1. ^1H NMR data comparison of epoxide **3** (recorded on a Bruker DRX500 in CDCl_3) and laulimalide **1**.^{1c}**3** : laulimalide core**1** : laulimalide

H	δ [ppm], mult., J [Hz] 3	δ [ppm], mult., J [Hz] laulimalide
2	5.90, ddd, 11.5/2.1/1.2	5.91, ddd, 11.6/2.4/1.2
3	6.55, ddd, 11.5/8.8/3.4	6.44, ddd, 11.6/10.1/3.7
4	3.51, dddd, 19.2/11.5/7/1.7 2.43, ddd, 19.2/6.5/4.0	3.72, ddd, 16.8/10.1/1.2 2.22, ddd, 16.8/6.4/4.0
5	4.34, brd, 10.2	4.31, brd, 9.5
6	5.71, brd, 10.2	5.69, brd, 10.3
7	5.84, m	5.83, m
8	1.91, dq, 10.2/2.1 1.80, m	1.93, m 2.02, m
9	3.66, obscured m	3.76, m
10	1.31, obscured m 1.44, m, 14.3	1.33, ddd, 14.3/4.9/3.5 1.45, ddd, 14.3/7.6/7.6
11	1.69, obscured m	1.72, m
12	1.77, obscured m 2.15 obscured m	1.78, dd, 12.8/10.1 2.38, m
14	2.08, m 2.12, obscured brd, 13.9	2.00, m 2.12, brd, 15.7
15	4.10, m	4.07, m
16	2.89, t, 2.6	2.90, t, 2.6
17	3.14, ddd, 9.0/3.8/2.6	3.08, ddd, 9.1/3.7/2.5
18	1.49, m 2.37, dd, 14.1/3.4	1.49, ddd, 14.4/11.3/9.5 2.37, m
19	5.18, ddd, 11.1/5.2/1.6	5.15, ddd, 11.3/5.2/1.5
20	3.74, m 3.65, m	4.22, q, 5.5
29	4.92, brs 4.88, brs	4.86, brs 4.85, brs
30	0.88, d, 6.8	0.82, d, 6.4
$\text{C}_{20}\text{-OH}$	1.69 obscured m	—

Table 2. ^{13}C NMR data comparison with literature data of **3** and laulimalide.^{1c}

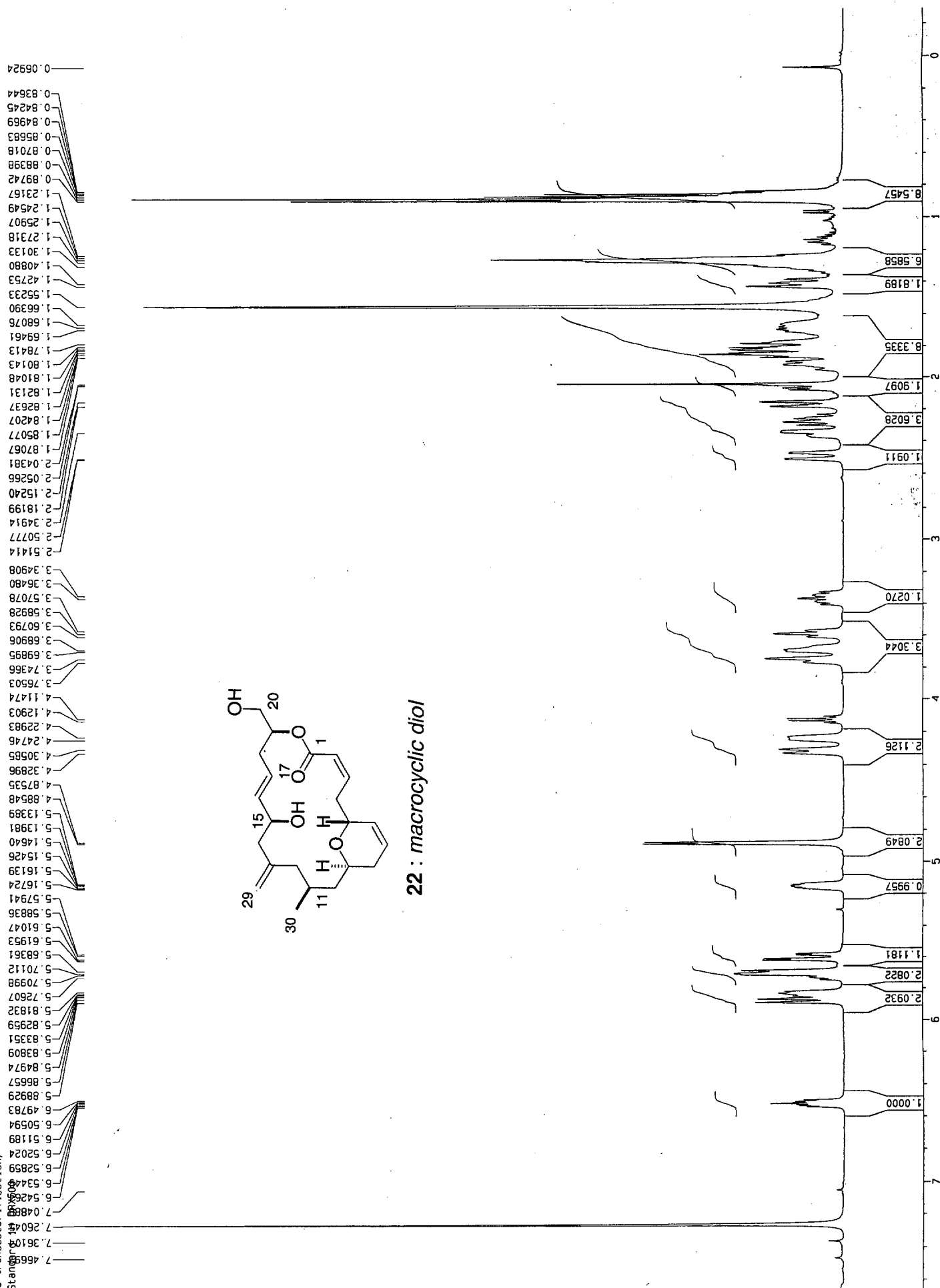
C	δ [ppm] 3 125 MHz, CDCl_3	δ [ppm] laulimalide CDCl_3
1	166.1	166.0
2	119.7	120.5
3	151.1	150.3
4	33.5	33.8
5	72.8	73.1
6	128.6	128.5
7	125.3	125.2
8	31.5	31.6
9	65.8	67.9
10	44.6	43.4
11	27.0	29.5
12	46.6	45.5
13	144.4	144.9
14	37.5	37.1
15	66.1	66.5
16	60.6	60.7
17	51.3	52.1
18	33.5	33.3
19	70.6	72.3
20	65.2	73.2
29	112.9	112.5
30	21.6	20.7

Laulimalide core **3**

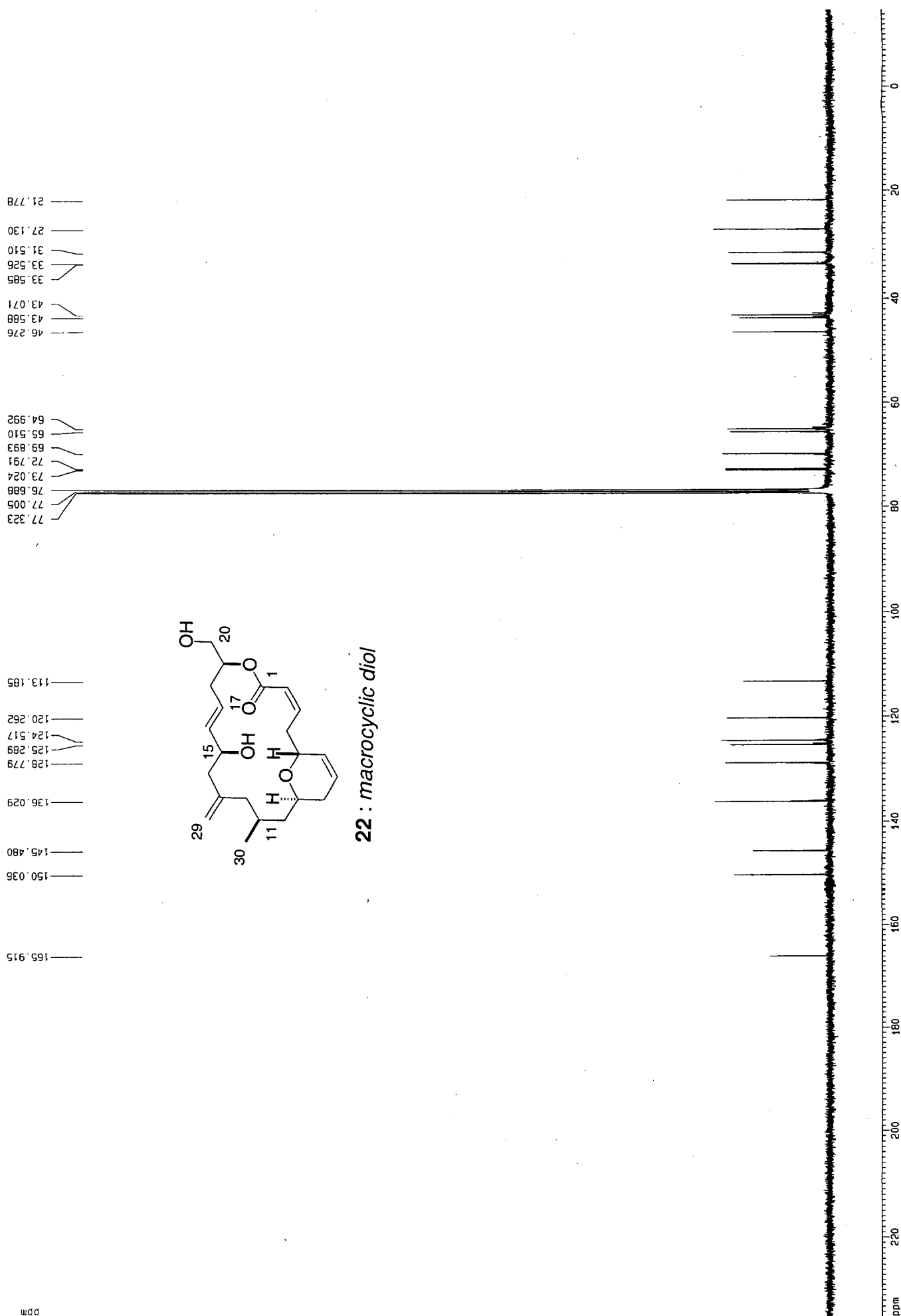
R_f (100% EtOAc/hexane) = 0.28; $[\alpha]_D^{20}$ -42.5 (c = 0.3, CHCl_3); **IR** (FT, liquid film) 3440-3200 (br, OH), 1715 (C=O) cm^{-1} ; **^1H NMR** (500 MHz, CDCl_3) see table; **^{13}C NMR** (125 MHz, CDCl_3) see table; **HRMS** (ES+) $[\text{M}+\text{NH}_4]^+$ found 410.2545, $\text{C}_{22}\text{H}_{36}\text{NO}_6$ requires 410.2543.

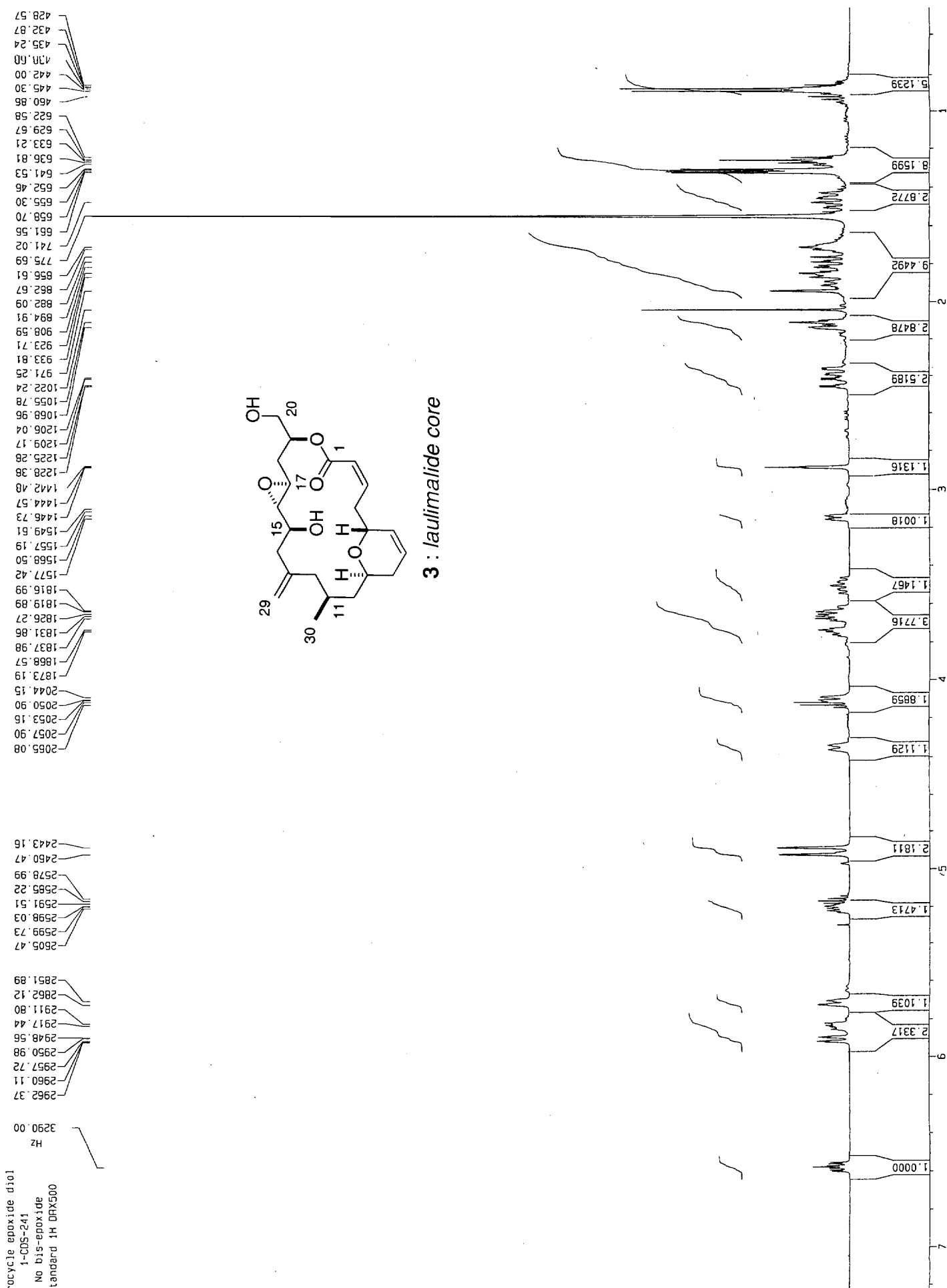
Macrocyclic diol **22**

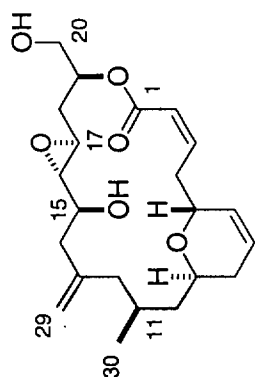
R_f (50% EtOAc/hexane) = 0.12; $[\alpha]_D^{20}$ -72.4 (c = 0.9, CHCl_3); **IR** (FT, liquid film) 3414-3200 (br, OH), 1717 (C=O) cm^{-1} ; **^1H NMR** (500 MHz, CDCl_3) δ 6.53 (ddd, J = 11.5, 7.3, 4.2 Hz, 1H), 5.87 (ddd, J = 11.5, 2.1, 1.2 Hz, 1H), 5.83 (m, 1H), 5.71 (m, 1H), 5.70 (m, 1H), 5.59 (dd, J = 15.8, 4.7 Hz, 1H), 5.16 (m, 1H), 4.89 (brs, 1H), 4.88 (brs, 1H), 4.31 (brd, J = 11.0 Hz, 1H), 4.23 (m, 1H), 3.75 (m, 1H), 3.69 (m, 1H), 3.59 (m, 1H), 3.36 (ddd, J = 19.2, 7.2, 2.1 Hz, 1H), 2.51 (dq, J = 19.2, 2.6 Hz, 1H), 2.35 (m, 1H), 2.28 (m, 1H), 2.15 (brd, J = 14.1 Hz, 1H), 2.00-1.69 (complex m, 6H), 1.41 (m, 1H), 1.25 (obscured m, 1H), 0.88 (d, J = 6.8 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 165.9, 150.0, 145.5, 136.0, 128.8, 125.3, 124.5, 120.3, 113.2, 73.0, 72.8, 69.9, 65.5, 64.9, 46.3, 43.6, 43.1, 33.6, 33.5, 31.5, 27.1, 21.8; **HRMS** (ES+) $[\text{M}+\text{NH}_4]^+$ found 394.2600, $\text{C}_{22}\text{H}_{36}\text{NO}_5$ requires 394.2593.



Standard 13C DRX400







3 : laulimalide core