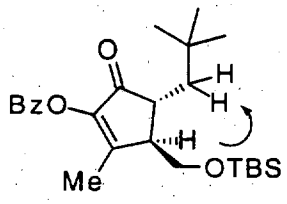
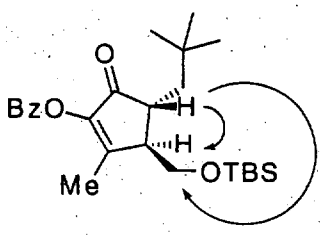
The determination of absolute stereochemistry was made by correlating **11** with **4**, whose absolute stereostructure was determined crystallographically (Scheme 1). **(+)-4** and **11** were independently converted to one enantiomer of **31**. Racemic **4** was converted to the benzoate derivative and was selectively hydrogenated under 1 atm of H_2 in the presence of 5% Pd/C catalyst to give racemic **31** (major product) which was purified by HPLC (Cyanopropyl, 5% EtOAc in hexanes). The enantiomers of the pure product had HPLC retention times of 24 min and 36 min (Chiralcel OD, 250 x 10 cm, 2.5% isopropanol in hexanes). The same sample of racemic **4** was resolved by chiral HPLC (Chiralcel OD, 250 x 10 cm, 1% isopropanol in hexanes) to give samples of **(+)-4** ($[\alpha]_D^{24}$ +127°; 98% ee) and **(-)-4** ($[\alpha]_D^{24}$ -110°; 97% ee). The absolute stereochemistry of **(-)-4** is known with certainty from the X-ray crystallographic structure determination of the (*S*)-α-methylbenzylurethan derivative (see reference 1). Consequently, the absolute stereochemistry of **(+)-4** is also known with certainty. Benzoylation and hydrogenation of **(+)-4** gave **31**, which had a retention time of 36 min on the Chiralcel OD column. In a separate series of experiments, **11** (53% ee) was first benzoylated, then treated with the higher-order *tert*-butylcyanocuprate to give **31**. The relative stereochemistry in the two samples of **31** was determined by

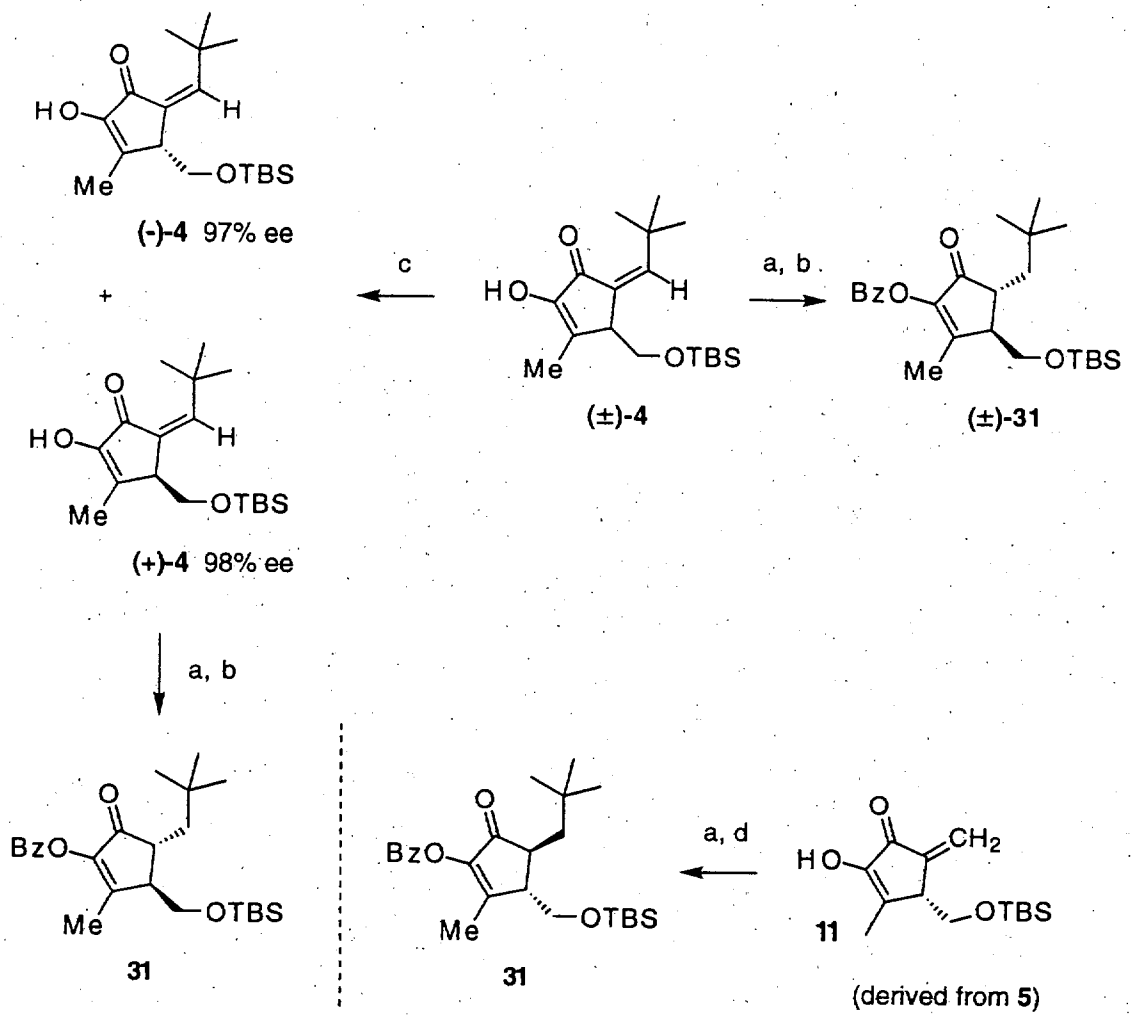




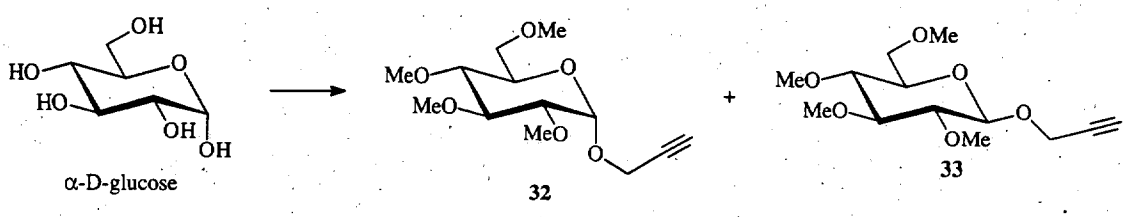
nOe. Irradiation of the allylic methine hydrogen at 2.67 ppm (br t, J = 3.9 Hz) gave a strong enhancement of one of the methylene hydrogens adjacent to the *tert*-butyl group (1.34 ppm, dd, J = 14.2, 8.8 Hz). Only a very weak nOe was observed to the methine α to the carbonyl group. Irradiation of the methine proton α to the carbonyl group (2.32 ppm, br d, J = 8.8 Hz) led to enhancement of *both* the allylic methine, and to the methylene protons adjacent to the OTBS group. The enhancements were of approximately the same magnitude. The HPLC retention times of major and minor peaks of the sample of **31** which was derived from **11** were 24 min and 36 min, respectively. The retention times were the same as for the racemate, and since the *minor* component of the mixture from **11** is identical with **31** derived from **(+)-4**, the *major* component must be its enantiomer. Hence, the cyclization of **10** with **5** led to (*S*)-**11** as the major product.

It is, of course, possible that amides other than **10** may have cyclized following the opposite stereochemical course.

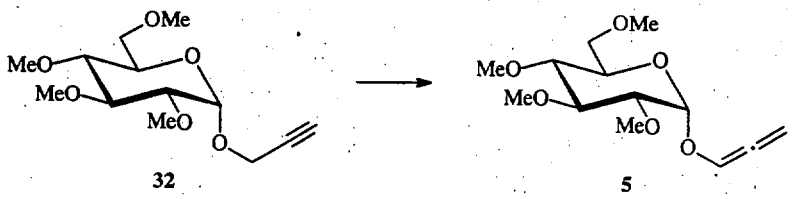
Scheme 1



(a) Bz_2O, pyridine; (b) H_2, Pd/C; (c) Chiralcel OD, 1% isopropanol in hexanes; (d) (*tert*-Bu)$_2$Cu(CN)Li$_2$, Et_2O.

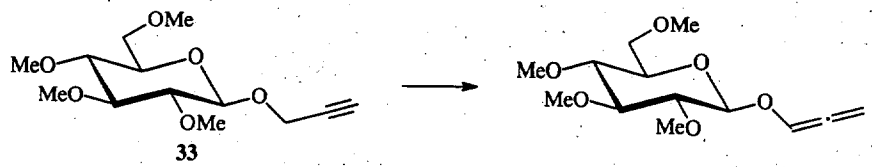


A suspension of α-D-glucose (4.015 g, 22.29 mmol) in propargyl alcohol (30 mL) containing DOWEX-50H$^+$ (1.019 g) was heated to 80°C for 12 h, cooled to room temperature, filtered through cotton, and concentrated to give the crude alkyne. The crude alkyne was dissolved in THF (30 mL), 18-crown-6 (ca. 500 mg) was added and the solution was transferred via cannula to a suspension of potassium hydroxide (11.032 g, 197 mmol) in THF (10 mL) at 0°C. Methyl iodide (10 mL, 22.8 g, 161 mmol) was added and the reaction mixture was warmed to room temperature. After 21 h, the reaction mixture was diluted with brine, water, and EtOAc. The aqueous phase was extracted with EtOAc (5 x) and the combined organic extracts were washed with brine (1 x) and dried over $MgSO_4$. Purification by flash column chromatography on silica (30% to 40% EtOAc in hexanes) gave a mixture of alkynes **32** and **33** (4.172 g combined, 68% yield; 2:1, **32**:**33**) as a colorless oil. Data for **32**: R_f = 0.19 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.16 (d, *J* = 3.7 Hz, 1H), 4.25 (d, *J* = 2.4 Hz, 2H), 3.61-3.35 (m, 4H), 3.59 (s, 3H), 3.50 (s, 3H), 3.47 (s, 3H), 3.37 (s, 3H), 3.22 (dd, *J* = 3.7 Hz, 1H), 3.18 (t br, *J* = 9.6 Hz, 1H), 2.39 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 94.5, 83.1, 81.2, 79.1, 78.7, 74.7, 70.8, 70.5, 60.8, 60.4, 59.2, 58.4, 54.3; IR (neat) 3265, 2940, 2840, 2130, 1455, 1380, 1165, 1105, 1050, 1000 cm^{-1}; mass spectrum m/z 102 (14), 101 (100), 99 (78), 89 (23), 88 (100), 83 (11), 75 (32), 74 (10), 73 (48), 71 (40); exact mass calcd for $C_{10}H_{19}O_5$ (M^+ - $OCH_2C{\equiv}CH$) 219.1232, found 219.1230; optical rotation $[\alpha]^{27}_D$ +185° (*c* 0.018, $CHCl_3$).



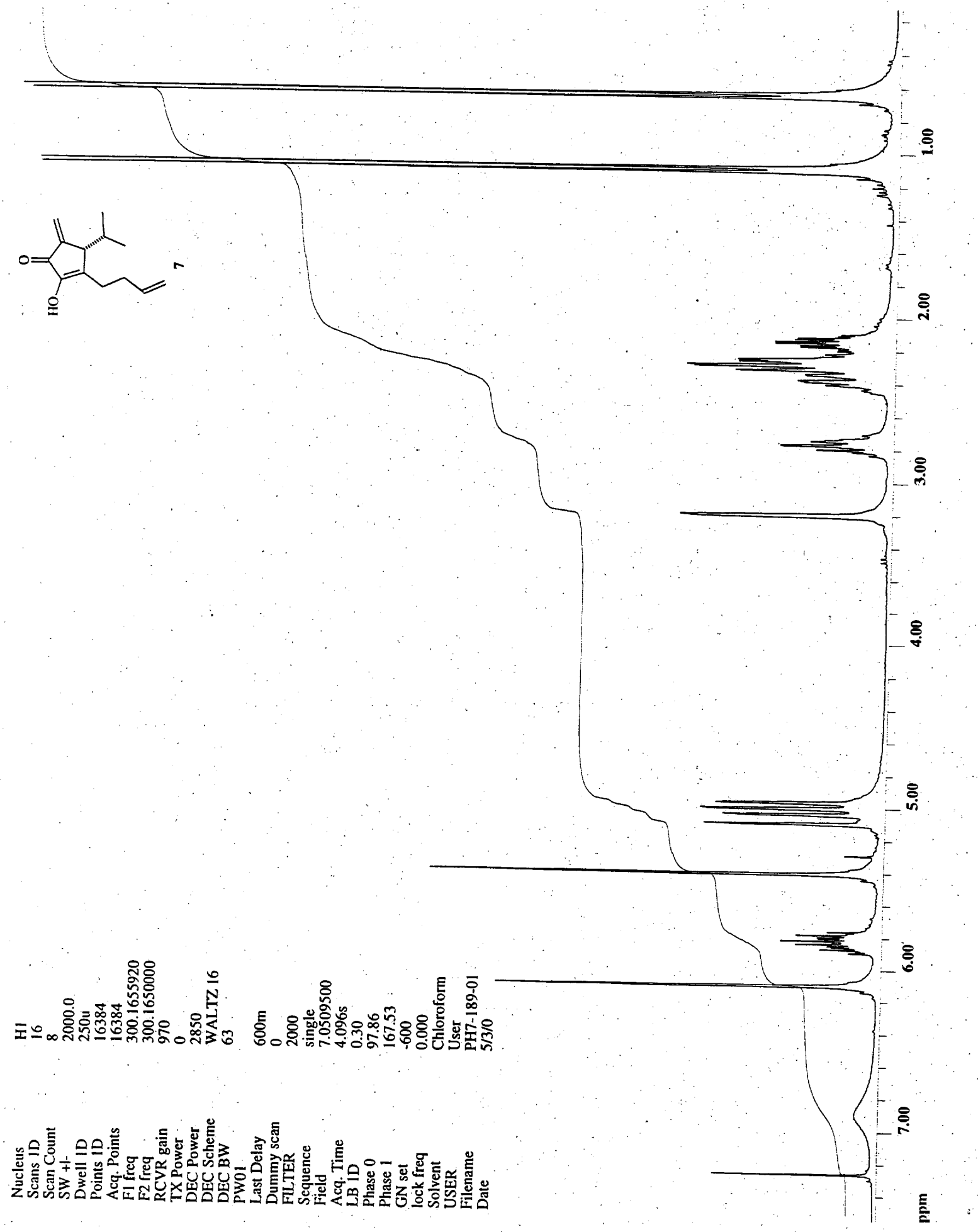
A mixture of alkyne **32** (1.624 g, 5.92 mmol) and potassium *tert*-butoxide (63 mg, 0.56 mmol) was heated to 60°C for 1 h, cooled to room temperature, and diluted with saturated $NaHCO_3$, brine, and EtOAc. The aqueous phase was extracted with EtOAc (3 x) and the

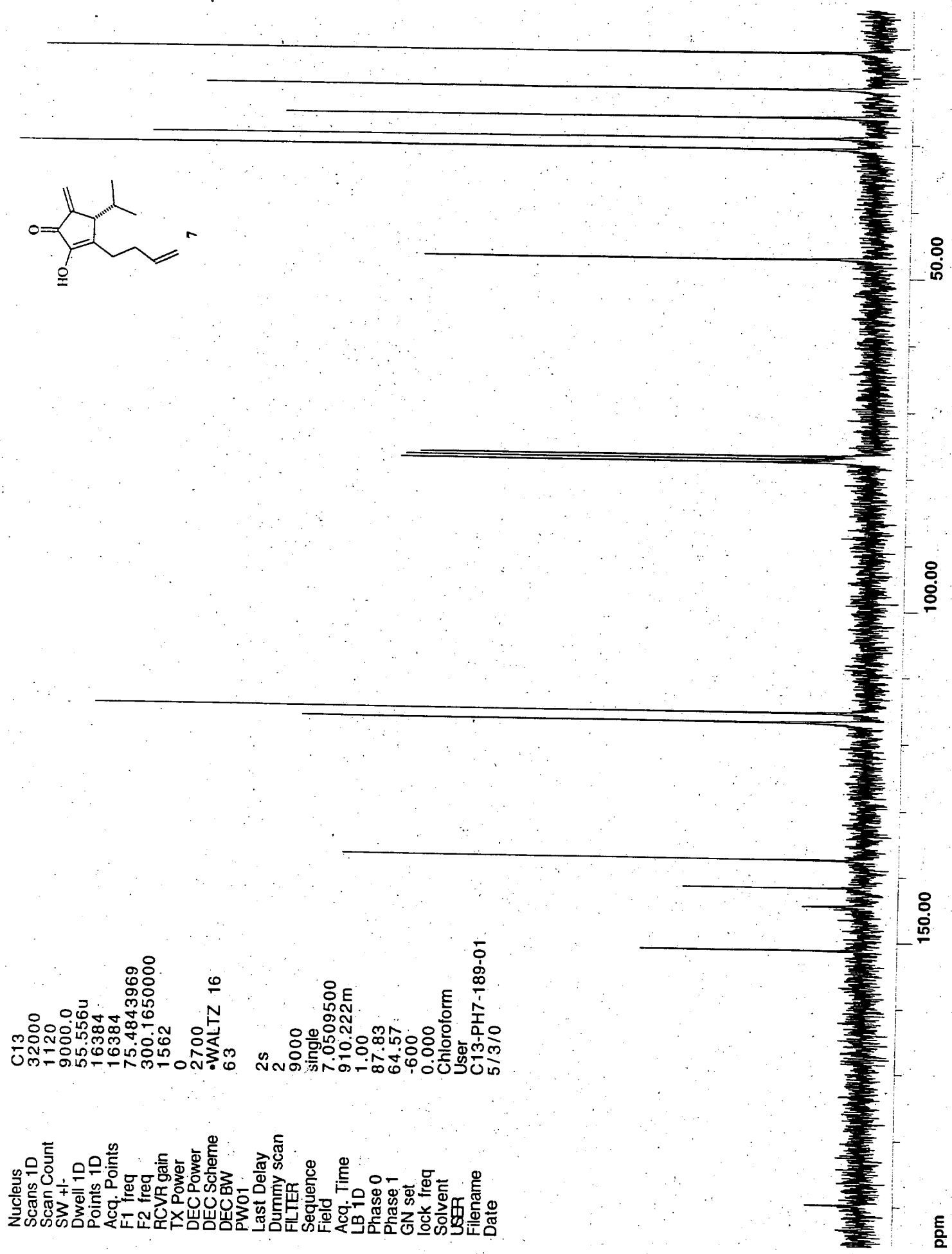
combined organic extracts were washed with brine (1 x) and dried over K_2CO_3. Purification by flash column chromatography on silica (5% to 10% EtOAc in hexanes) gave allene **5** (1.265 g, 78% yield) as a colorless oil: R_f = 0.18 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.62 (t, *J* = 6.1 Hz, 1H), 5.42 (dd, *J* = 9.0, 6.1 Hz, 1H), 5.35 (dd, *J* = 8.8, 5.9 Hz, 1H), 5.19 (d, *J* = 3.4 Hz, 1H), 3.66-3.36 (m, 4H), 3.62 (s, 3H), 3.53 (s, 3H), 3.49 (s, 3H), 3.39 (s, 3H), 3.28-3.22 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.0, 117.7, 95.3, 90.1, 83.3, 81.3, 79.0, 70.7, 70.5, 60.9, 60.5, 59.1, 59.0; IR (neat) 2950, 2845, 1970, 1450, 1170, 1105, 1025 cm^{-1}; mass spectrum m/z 187 (67), 155 (20), 127 (19), 111 (79), 101 (100), 99 (18), 95 (12), 89 (33), 88 (35), 75 (44), 74 (16), 73 (37), 71 (60); exact mass calcd for $C_{13}H_{22}O_6$ 274.1416, found 274.1430; optical rotation $[\alpha]^{27}_D$ +158° (*c* 0.015, $CHCl_3$).

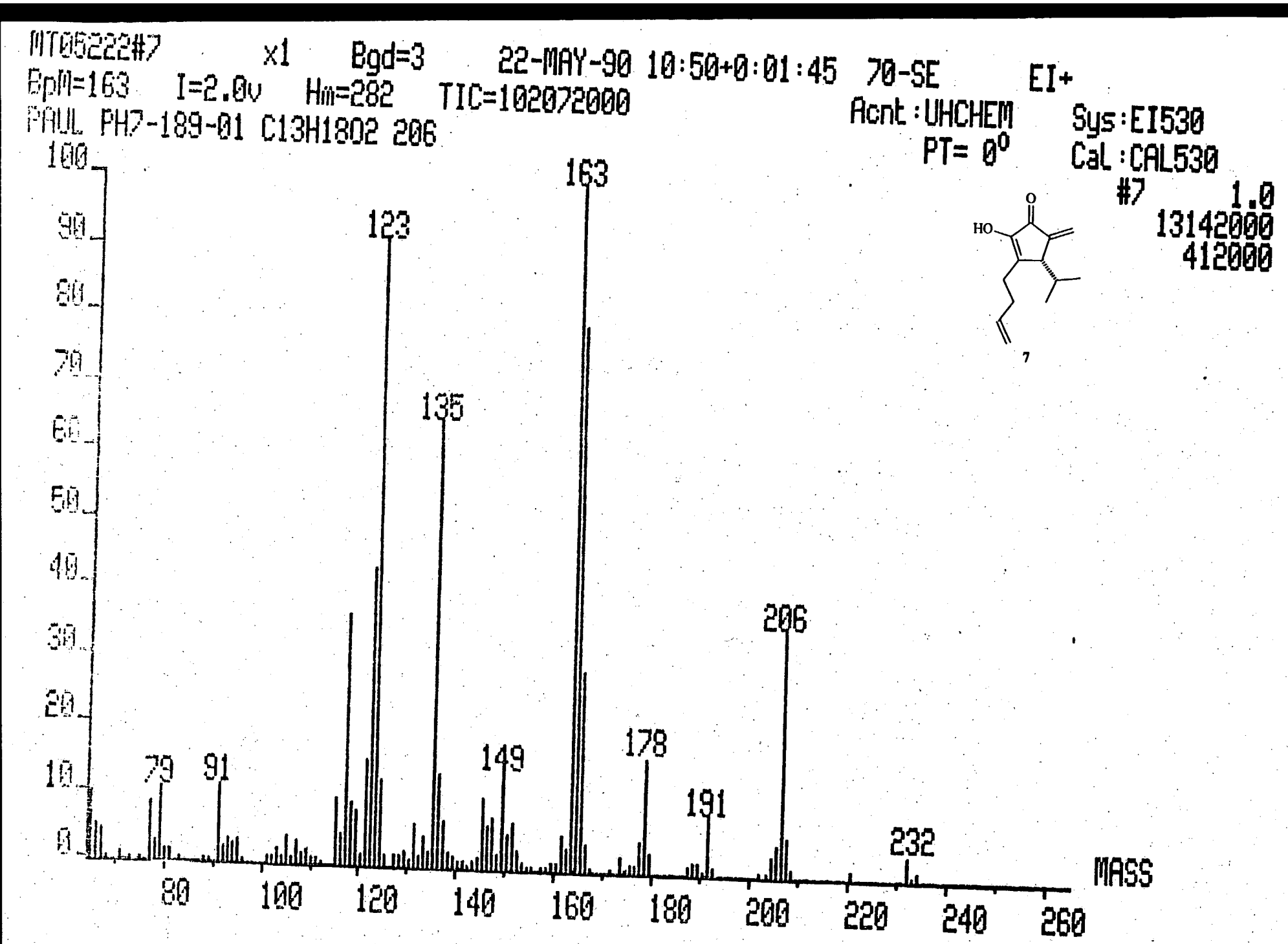


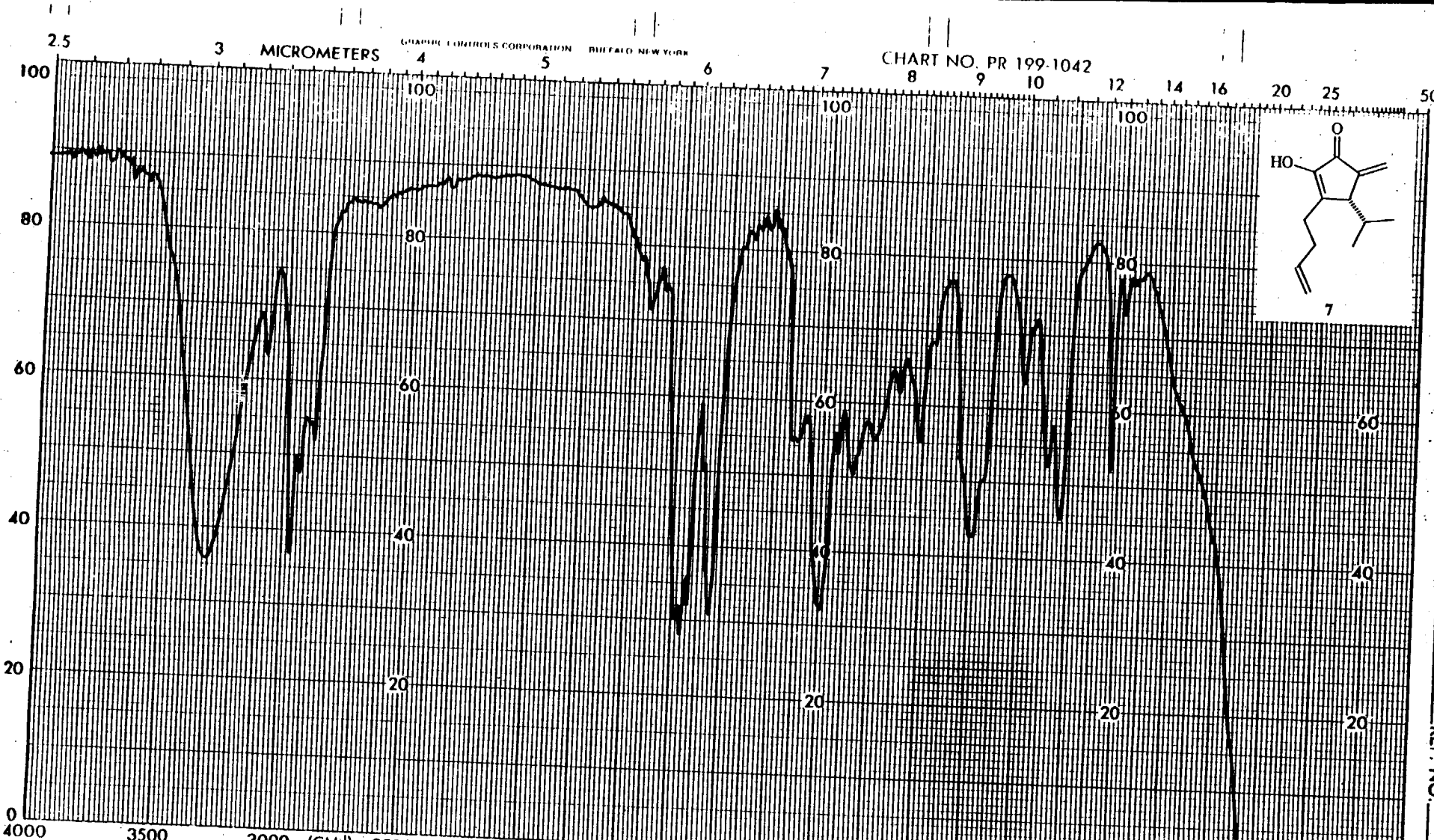
33 **29**

A mixture of alkyne **33** (871 mg, 3.18 mmol) and potassium *tert*-butoxide (ca. 50 mg) was heated to 70°C for 1 h, cooled to room temperature, and purified directly by flash column chromatography on silica (5% to 10% EtOAc in hexanes). Allene **29** (430 mg, 49% yield) was isolated as a colorless oil: R_f = 0.35 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.71 (t, *J* = 6.0 Hz, 1H), 5.45 (dd, *J* = 8.8, 6.1 Hz, 1H), 5.38 (dd, *J* = 8.8, 6.1 Hz, 1H), 4.48 (d, *J* = 7.1 Hz, 1H), 3.65-3.10 (m, 6H), 3.62 (s, 3H), 3.57 (s, 3H), 3.52 (s, 3H), 3.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.0, 119.2, 101.0, 89.9, 86.3, 83.1, 79.1, 74.7, 71.1, 60.5, 60.2, 60.1, 59.1; IR (neat) 2940, 2900, 2840, 1970, 1450, 1385, 1340, 1310, 1100, 995, 940, 890 cm^{-1}; mass spectrum m/z 187 (56), 111 (40), 101 (100), 89 (30), 88 (67), 75 (42), 73 (33), 71 (51); exact mass calcd for $C_{13}H_{22}O_6$ 274.1416, found 274.1465; optical rotation $[\alpha]^{27}_D$ -7° (*c* 0.024, $CHCl_3$).

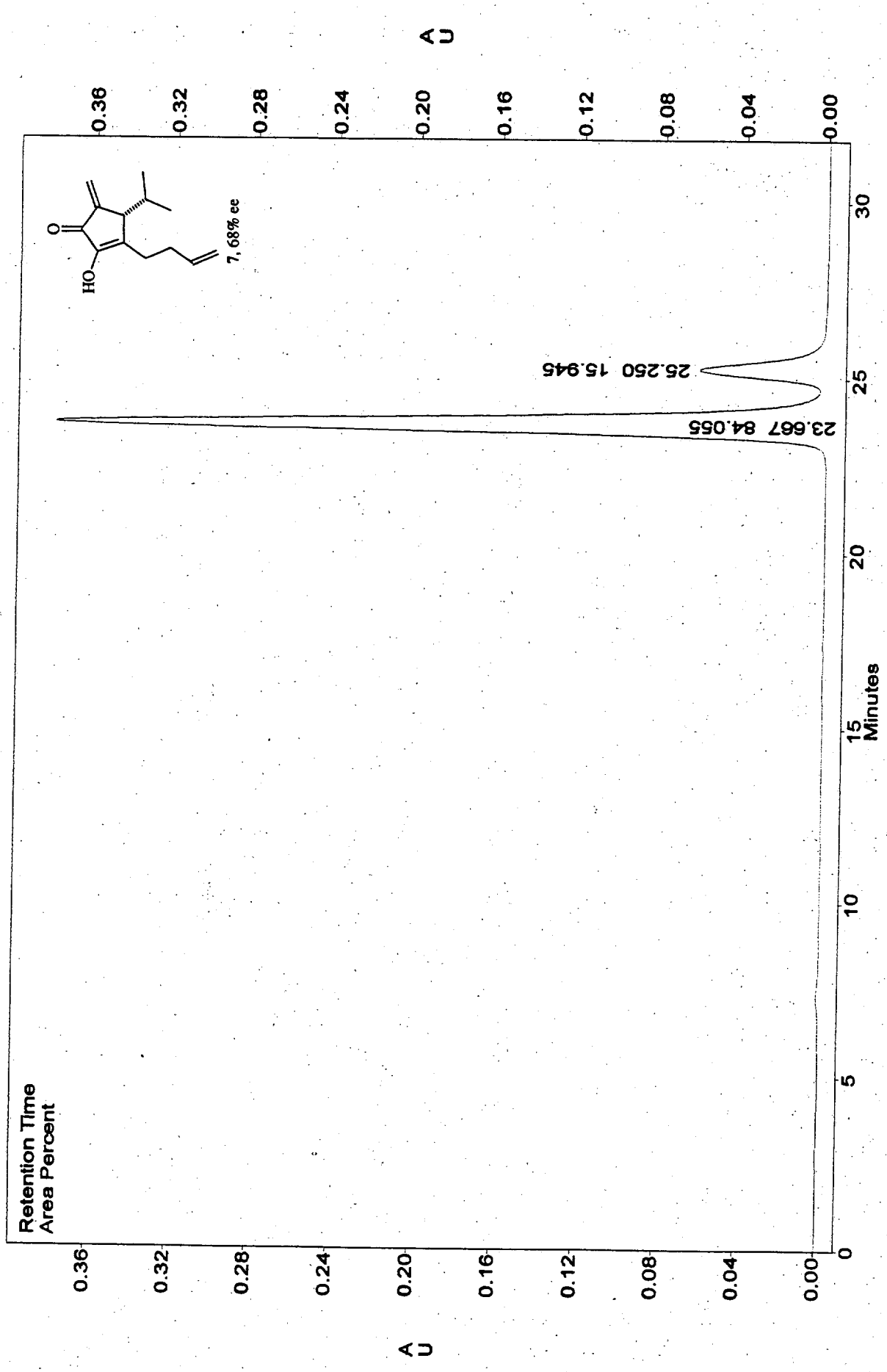

Nucleus H1
Scans 1D 16
Scan Count 8
SW +/- 2000.0
Dwell 1D 250u
Points 1D 16384
Acq. Points 16384
F1 freq 300.1655920
F2 freq 300.1650000
RCVR gain 970
TX Power 0
DEC Power 2850
DEC Scheme WALTZ 16
DEC BW 63
PW01
Last Delay 600m
Dummy scan 0
FILTER 2000
Sequence single
Field 7.0509500
Acq. Time 4.096s
LB 1D 0.30
Phase 0 97.86
Phase 1 167.53
GN set -600
lock freq 0.000
Solvent Chloroform
USER User
Filename PH7-189-01
Date 5/3/0
O
HO
7
7.00
6.00
5.00
4.00
3.00
2.00
1.00
ppm

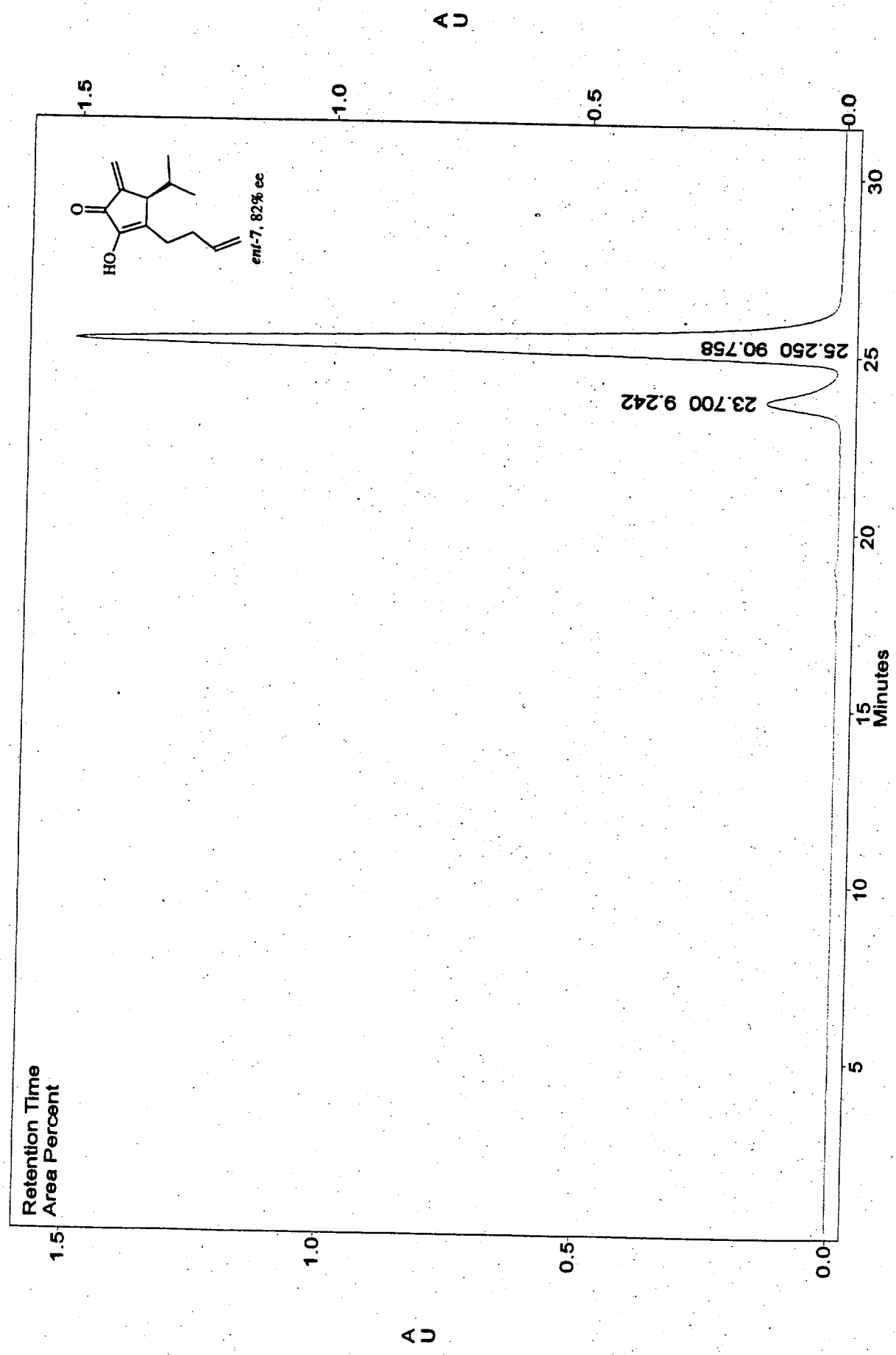

Nucleus C13
Scans 1D 32000
Scan Count 1120
SW +/- 9000.0
Dwell 1D 55.556u
Points 1D 16384
Acq. Points 16384
F1 freq 75.4843969
F2 freq 300.1650000
RCVR gain 1562
TX Power 0
DEC Power 2700
DEC Scheme •WALTZ 16
DEC BW 63
PW01
Last Delay 2s
Dummy scan 2
FILTER 9000
Sequence single
Field 7.0509500
Acq. Time 910.222m
LB 1D 1.00
Phase 0 87.83
Phase 1 64.57
GN set -600
lock freq 0.000
Solvent Chloroform
User
Filename C13-PH7-189-01
Date 5/3/0
O
HO
7
150.00
100.00
50.00
ppm





ABSCISSA	ORDINATE		
EXPANSION PH7-189-01	EXPANSION	SCAN TIME	REP. SCAN SINGLE BEAM
	% T ABS	MULTIPLIER	TIME DRIVE
SAMPLE	REMARKS	SLIT PROGRAM	OPERATOR DATE
ORIGIN		SOLVENT	CELL PATH
		CONCENTRATION	REFERENCE


Retention Time
Area Percent
23.667 84.055
25.250 15.945
7, 68% ee
HO
O
AU
Minutes
0.00
0.04
0.08
0.12
0.16
0.20
0.24
0.28
0.32
0.36
0
5
10
15
20
25
30


AU
1.5
1.0
0.5
0.0
ent-7, 82% ee
HO
O
25.250 90.758
23.700 9.242
5
10
15
20
25
30
Minutes
Retention Time
Area Percent
AU