

Organic Process Research & Development

Org. Process Res. Dev., 1998, 2(3), 175-185, DOI:[10.1021/op970121s](https://doi.org/10.1021/op970121s)

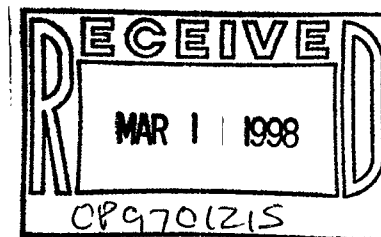
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Supplementary Material For

Novel Stereoselective Syntheses of the Fused Benzazepine Dopamine D₁ Antagonist (6a*S*,13b*R*)-11-chloro-6,6a,7,8,9,13b-hexahydro-7- methyl-5H-benzo[d] naphth[2,1-b]azepin-12-ol (Sch 39166): Part I: Aziridinium Salt Based Syntheses

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Chemical Development Department

Werthenstein Chemie AG

6105 Schachen, Switzerland

Capillary GC Conditions:

Compound 22:

Column: Supelco SPB 5, 30 m x 0.25 mm

Temperature Method: 200°C (hold for 5 min), up 5°C/min to 250°C (hold for 10 min).

Detection: Flame Ionization Detector

Internal Standard: pyrene

Injection volume: 1 µL

Split ratio: 100:1

Flow rate: 1.5 mL/min (Helium)

Retention Times: **22** - 21.1 min; pyrene - 9.75 min

Compound 25:

Column: Supelco SPB 5, 30 m x 0.25 mm

Temperature Method: 100°C (hold for 5 min), up 5°C/min to 150°C (hold for 10 min).

Detection: Flame Ionization Detector

Internal Standard: dodecane

Injection volume: 1 µL

Split ratio: 100:1

Flow rate: 1.5 mL/min (Helium)

Retention Times: epoxide **25** - 9.69 min; naphthalene - 5.21 min; dodecane - 5.57 min

Chiral HPLC Conditions¹

Compound	Column	Solvent System	Flow Rate	Detector	Conc.	Retention Times
9	Chiracel OD	93:7 hexanes/ <i>i</i> -PrOH	0.7 mL/min	220 nm	0.5 mg/mL	(-): 9.2 min (+): 11.3 min
22	Chiralcel OD-R	60:40 (0.75M NaClO ₄ , 0.02M KH ₂ PO ₄ , pH 4.2)/ CH ₃ CN	1 mL/min	210 nm	0.5 mg/mL	(-): 17.9 min (+): 20.6 min
23	Chiralcel OD-R	60:40 (0.75M NaClO ₄ , 0.02M KH ₂ PO ₄ , pH 4.2)/ CH ₃ CN	1 mL/min	210 nm	0.5 mg/mL	(-): 15.6 min (+): 18.5 min
25	Chiralcel OB	95:5 <i>i</i> -PrOH/ hexanes	1 mL/min	210 nm	0.5 mg/mL	(+): 23.6 min (-): 28.4 min
27	Chiralcel OD-R	20:80 CH ₃ CN/ 0.75M NaClO ₄ , 0.02 M KHPO ₄ , pH=4.2 (adjusted with H ₃ PO ₄)	1 mL/min	210 nm	1.0 mg/mL	(-) <i>trans</i> : 5.0 min (+) <i>trans</i> : 6.3 min
32	Chiralcel OD-R (30°C)	25:75 CH ₃ CN/ 0.5M NaClO ₄ , pH=2.1 (adjusted with HClO ₄)	0.5 mL/min	210 nm	0.1 mg/mL	(<i>R, R</i>): 7.9 min (<i>S, S</i>): 8.9 min

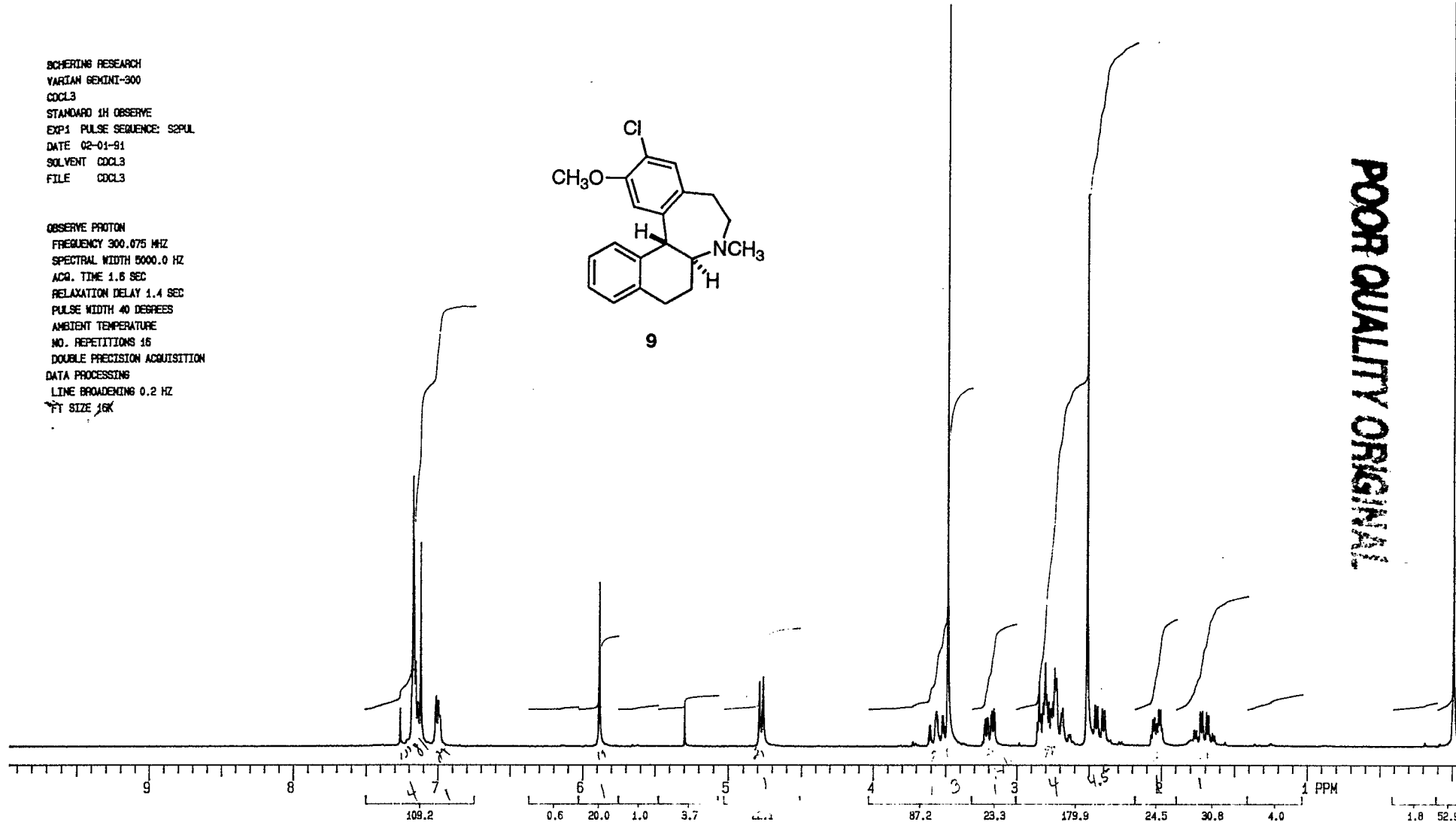
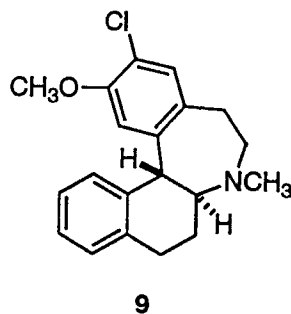
1. All samples were dissolved in the mobile phase. Injection volumes were 20 μ L.

¹H NMR Spectra for the following compounds:

¹H NMR spectra for **9**, **18-20**, **22-27**, **29**, **30**, **32** and **35**; SINEPT and APT ¹H NMR experiments for **24** and COSY ¹H NMR experiment for **26** follows.

BIOHERING RESEARCH
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SOLVENT CDCL3
FILE CDCL3

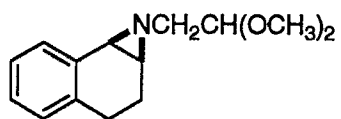
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RELAXATION DELAY 1.4 SEC
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DOUBLE PRECISION ACQUISITION
DATA PROCESSING
LINE BROADENING 0.2 HZ
FT SIZE 16K



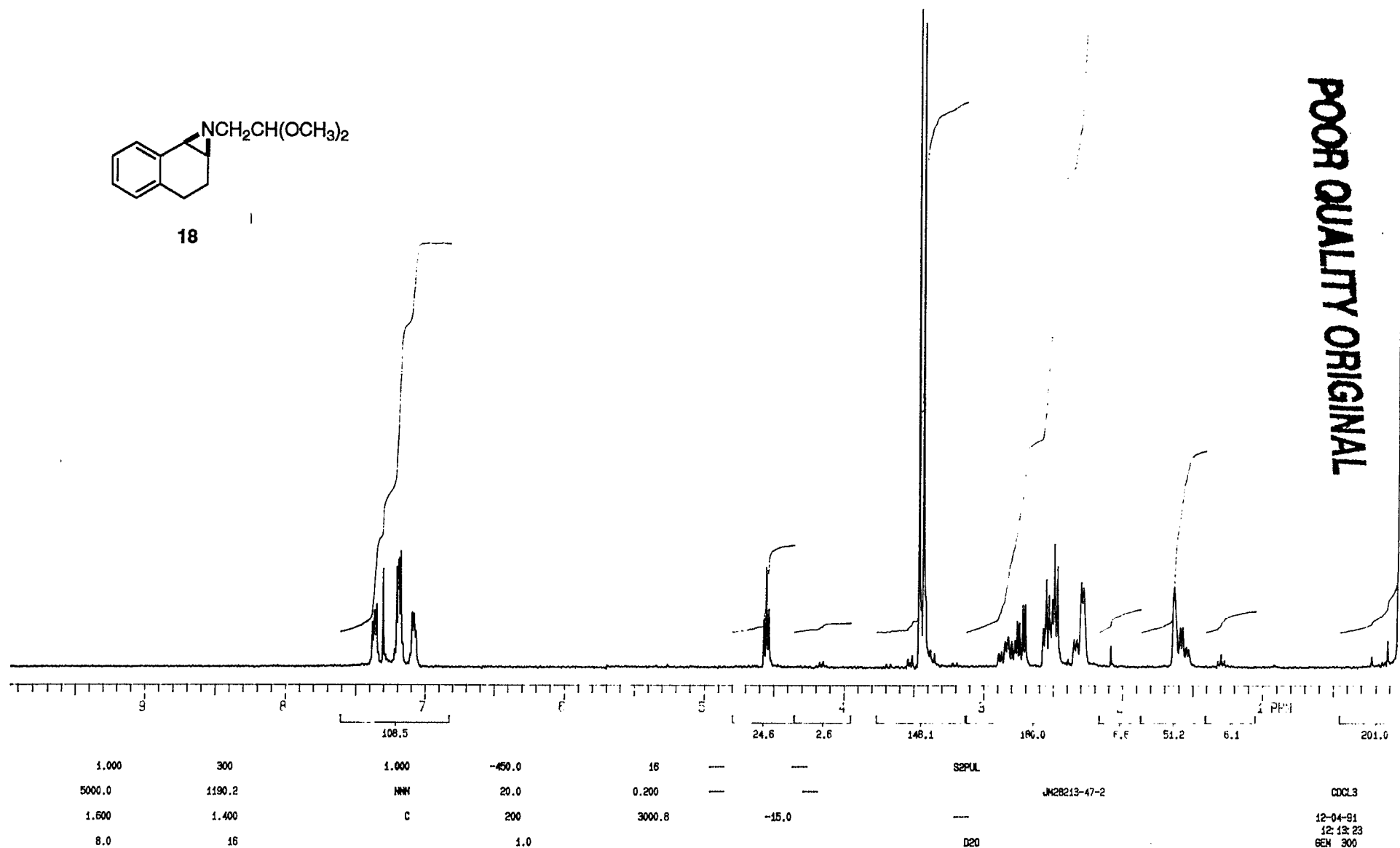
JM26963-26-1

POOR QUALITY ORIGINAL

POOR QUALITY ORIGINAL



18



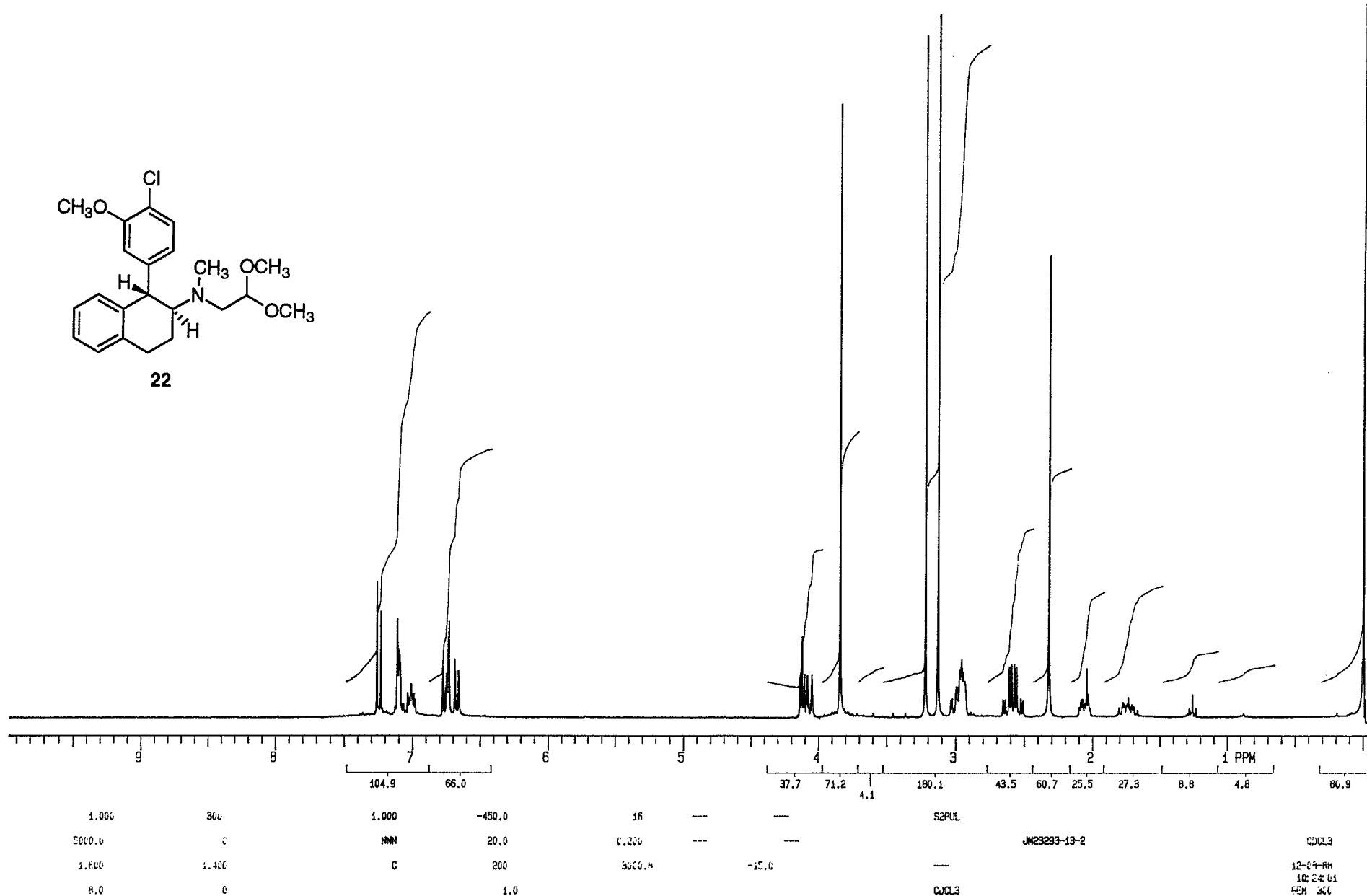
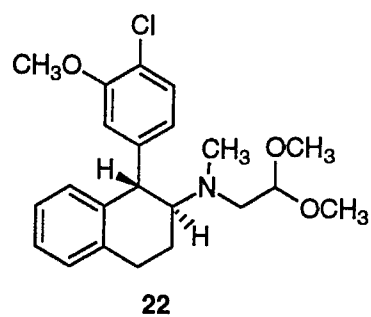


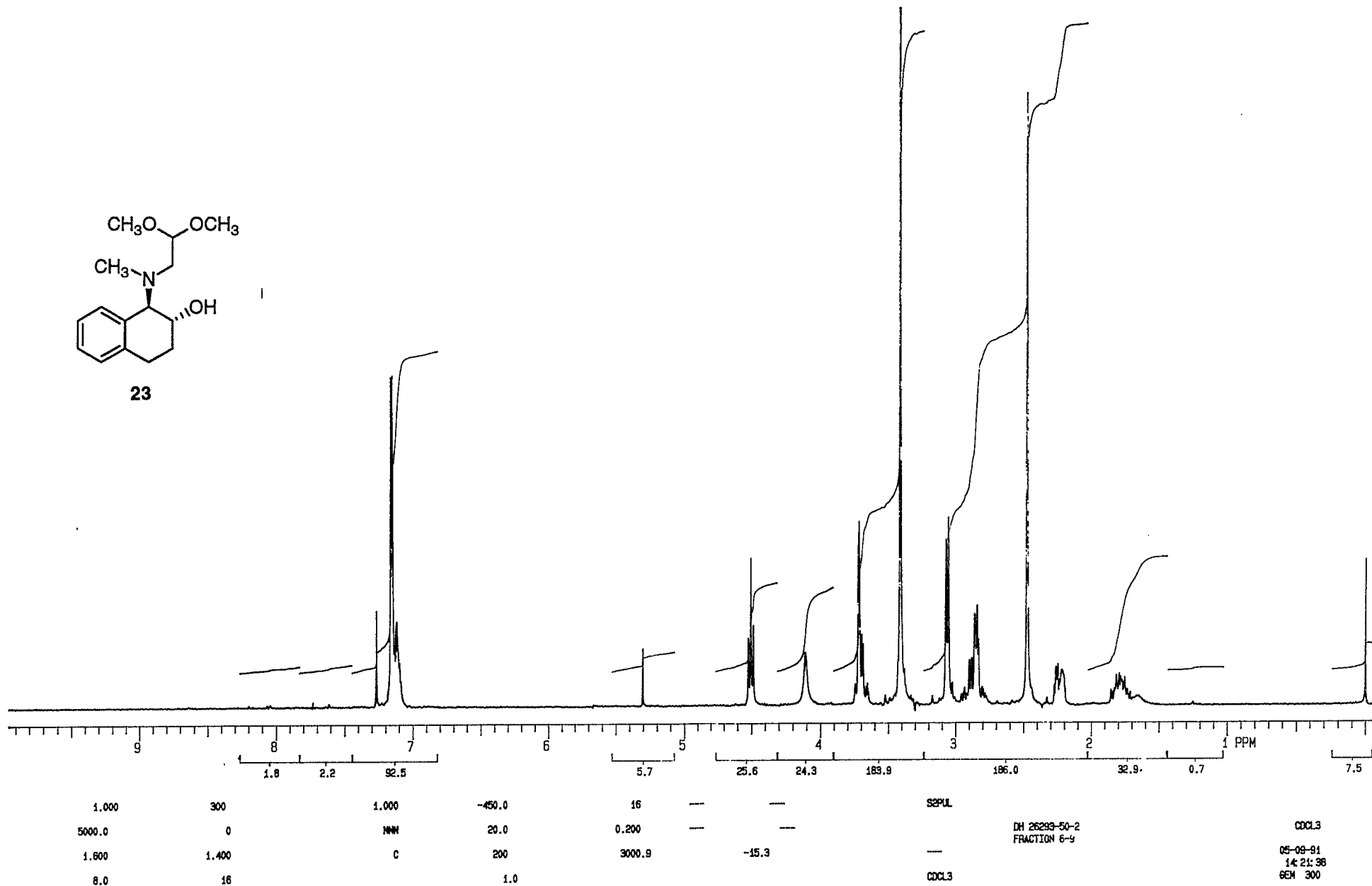
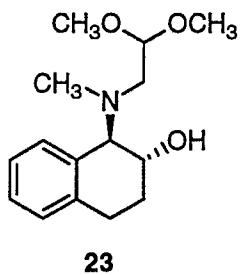


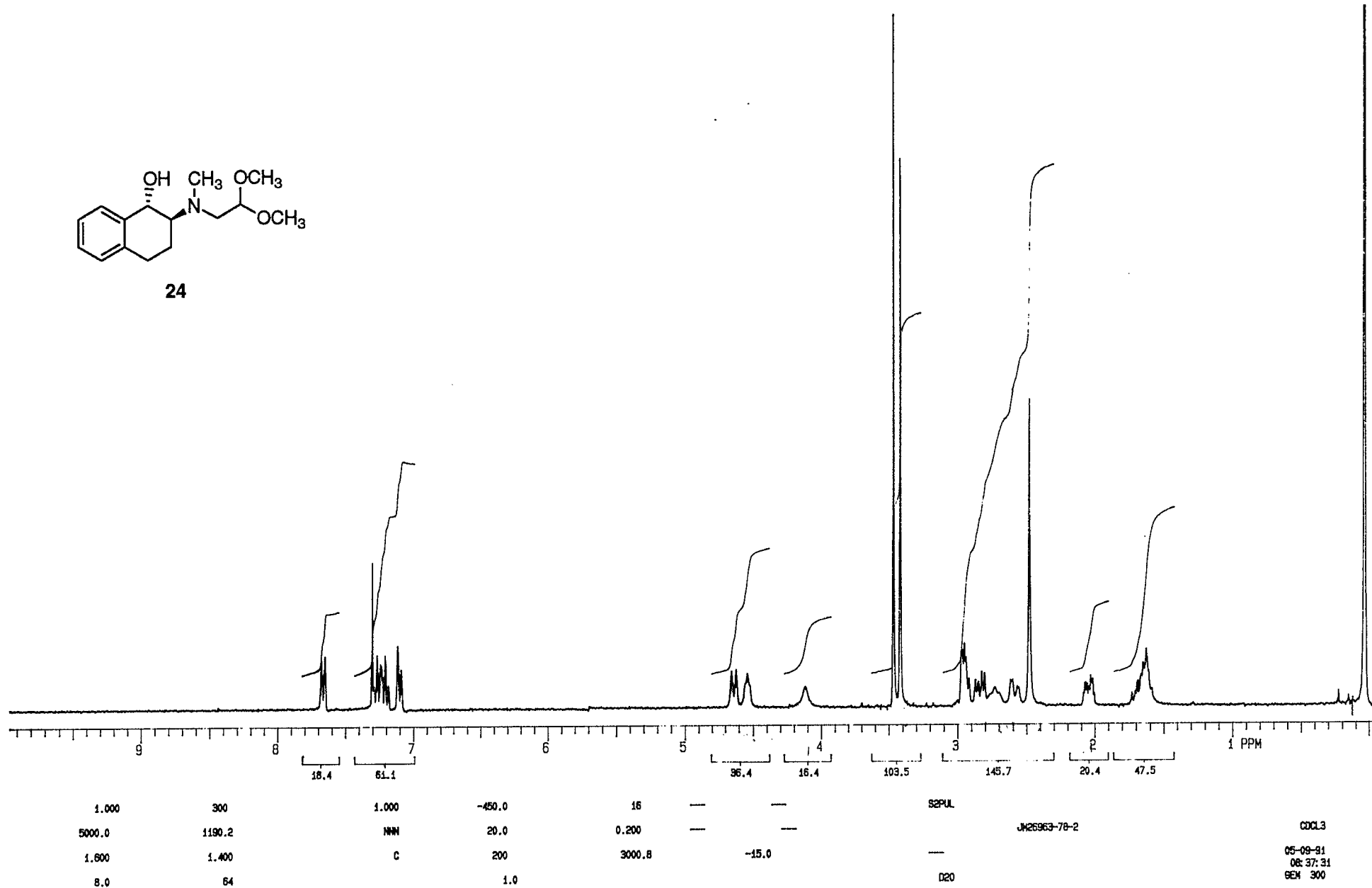
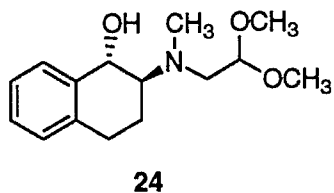
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OFFSET - LEER

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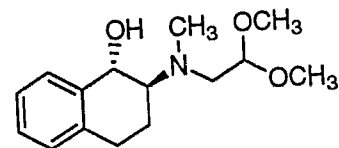
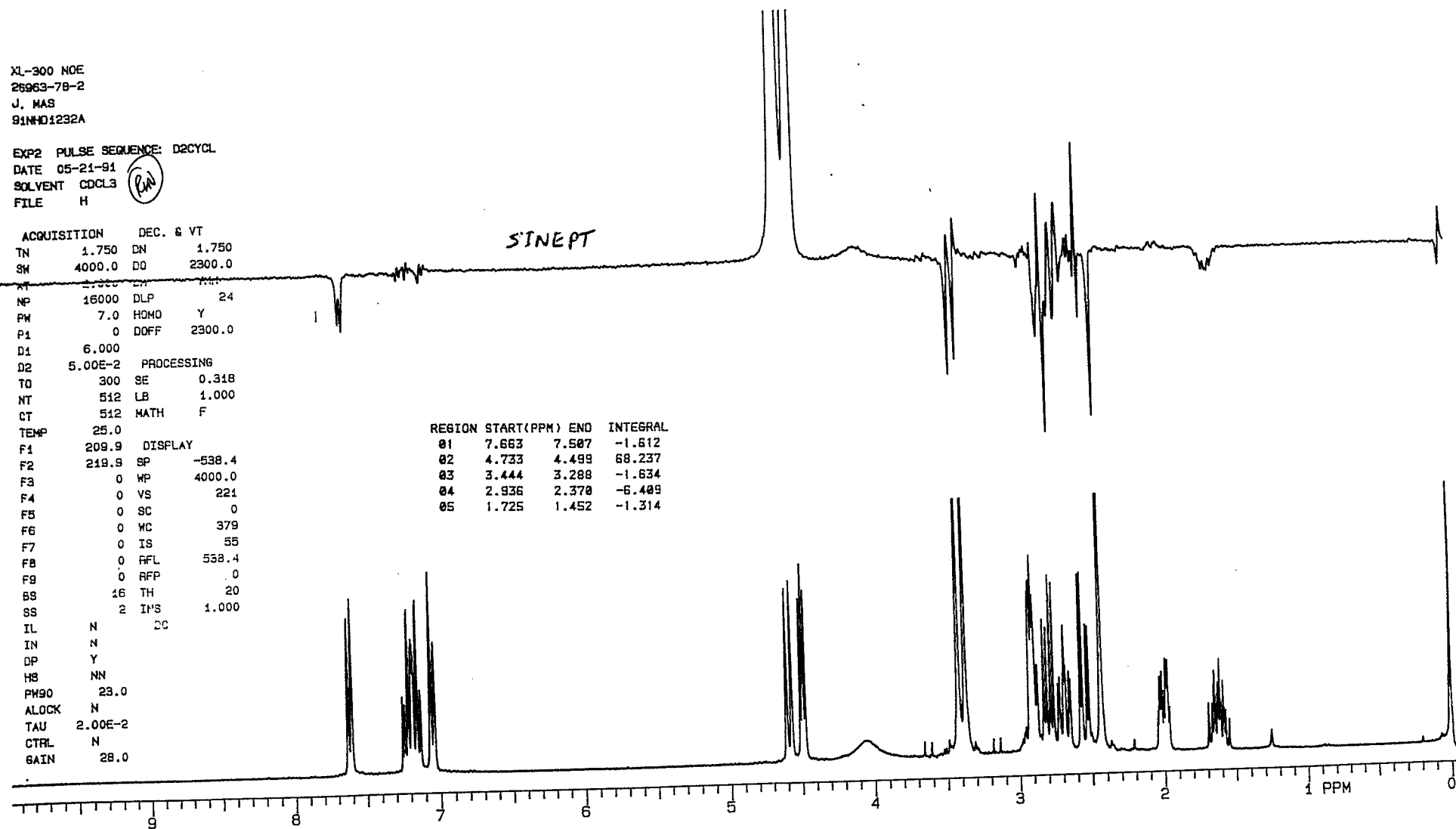
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XL-300 NOE
26963-78-2
J. MAS
91NH01232A

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DATE 05-21-91
SOLVENT CDCL3
FILE H

ACQUISITION DEC. & VT
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SM 4000.0 DO 2300.0
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PW 7.0 HOMO Y
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D1 6.000
D2 5.00E-2 PROCESSING
T0 300 SE 0.318
NT 512 LB 1.000
CT 512 MATH F
TEMP 25.0
F1 209.9 DISPLAY
F2 219.9 SP -538.4
F3 0 WP 4000.0
F4 0 VS 221
F5 0 SC 0
F6 0 WC 379
F7 0 IS 55
F8 0 RFL 538.4
F9 0 RFP 0
BS 16 TH 20
SS 2 IMS 1.000
IL N DC
IN N
DP Y
HS NN
PW90 23.0
ALOCK N
TAU 2.00E-2
CTRL N
GAIN 28.0

REGION START(PPM) END INTEGRAL
01 7.663 7.507 -1.612
02 4.733 4.499 68.237
03 3.444 3.288 -1.634
04 2.936 2.378 -6.489
05 1.725 1.452 -1.314



24

XL-300 CMR
26963-78-2
J.MAS
91NCD1227

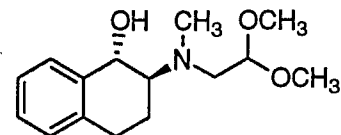
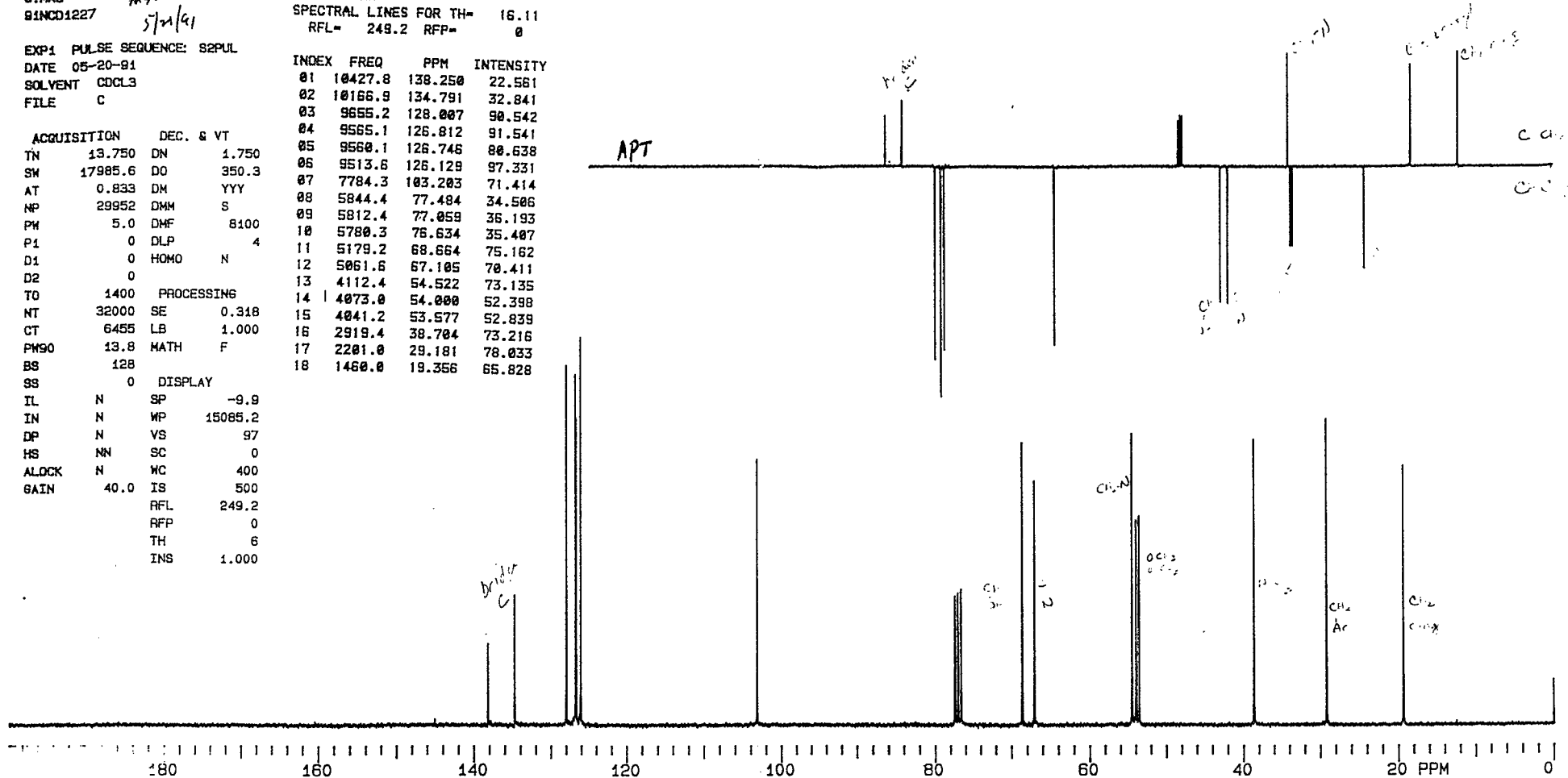
ms
5/21/91

XL-300 CMR
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RFL- 249.2 RFP- 0

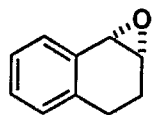
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DATE 05-20-91
SOLVENT CDCL3
FILE C

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D1 0 HOMO N	
D2 0	
TO 1400 PROCESSING	
NT 32000 SE 0.318	
CT 6455 LB 1.000	
PM90 13.8 MATH F	
BS 128	
SS 0 DISPLAY	
IL N SP -9.9	
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	RFP 0
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	INS 1.000

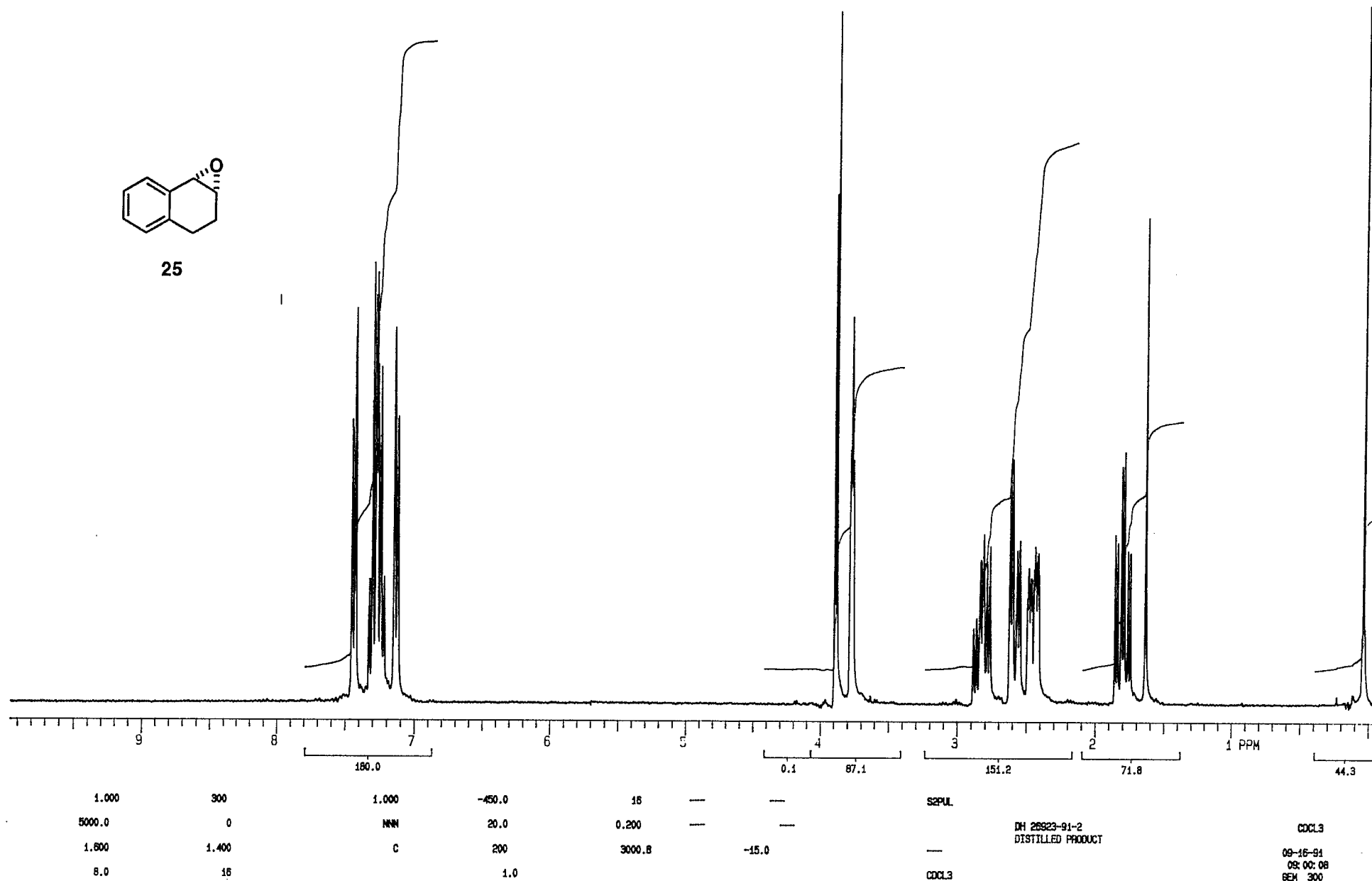
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06	9513.6	126.129	97.331
07	7784.3	103.203	71.414
08	5844.4	77.484	34.506
09	5812.4	77.059	36.193
10	5780.3	76.634	35.407
11	5179.2	68.664	75.162
12	5061.6	67.105	70.411
13	4112.4	54.522	73.135
14	4073.0	54.000	52.398
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24



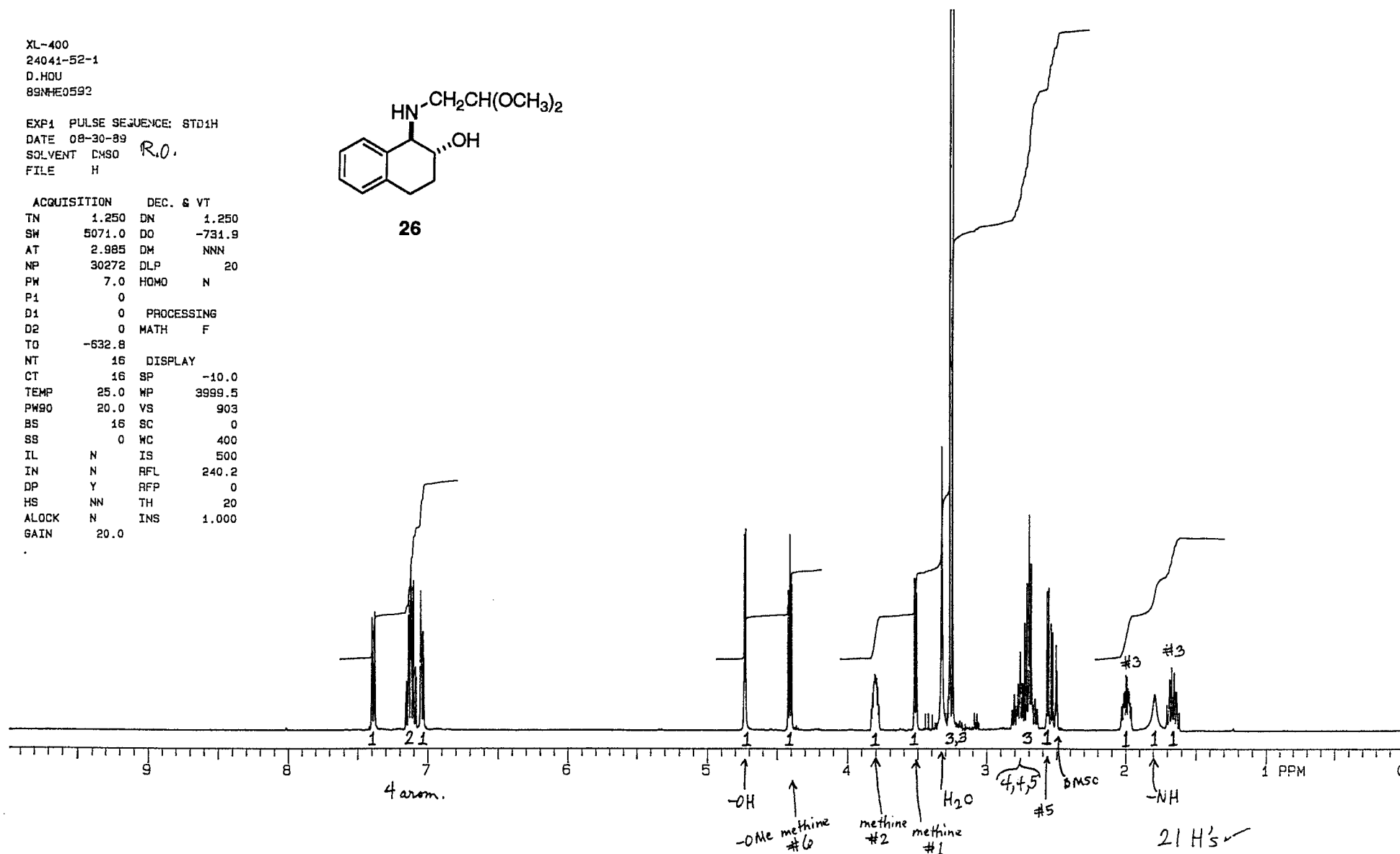
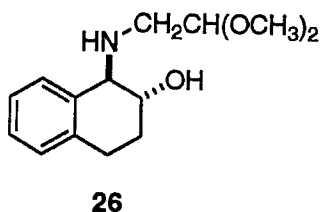
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XL-400
24041-52-1
D.HOU
89NHE0592

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DATE 08-30-89
SOLVENT CDMSO
FILE H

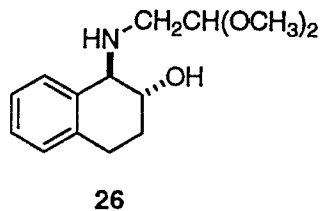
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D2	0	MATH	F
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NT	16	DISPLAY	
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SS	0	WC	400
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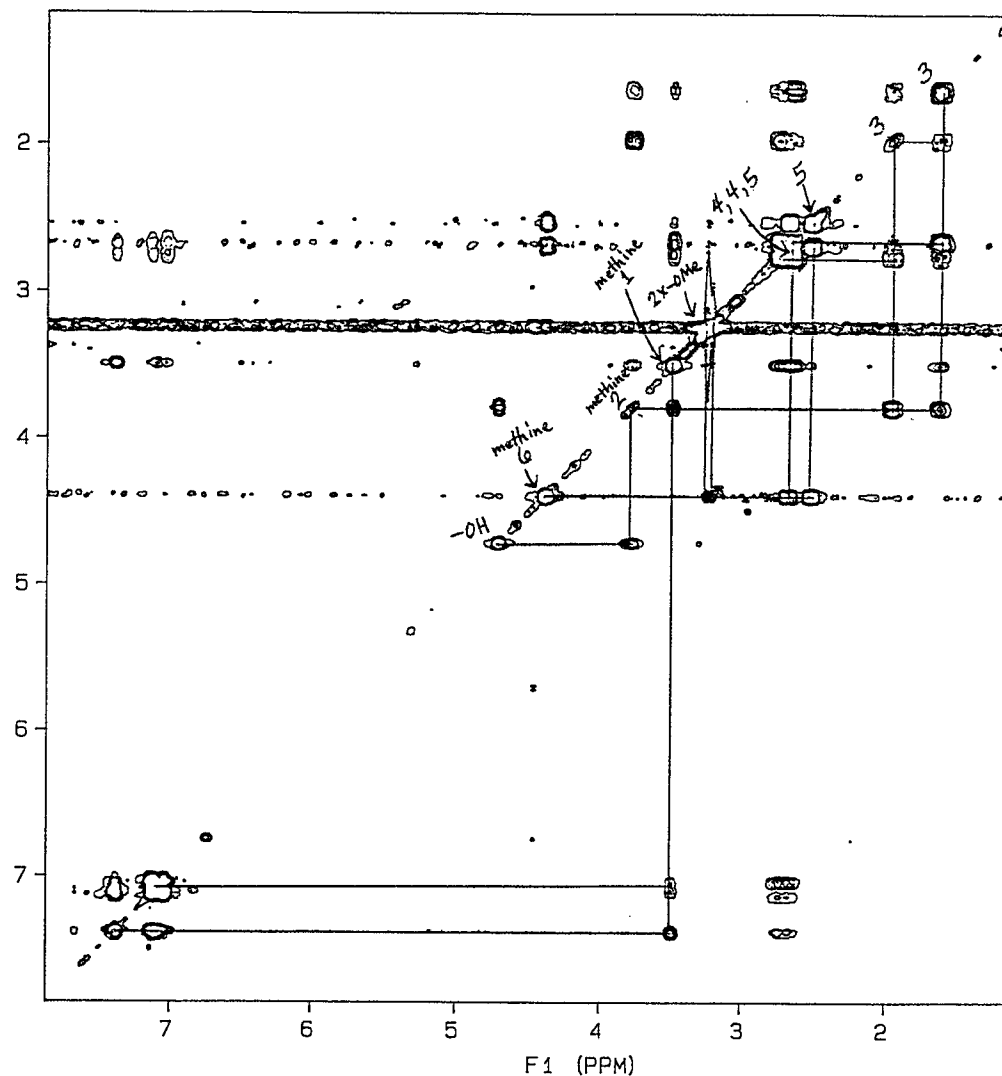
XL-400
24041-52-1
D.HOU
89NHE05923

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DATE 08-30-89 R.O.
SOLVENT DMSO
FILE COSY

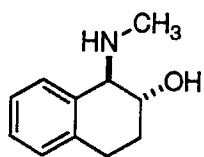
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P1	18.0		
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CT	4	MATH	F
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NI	400		
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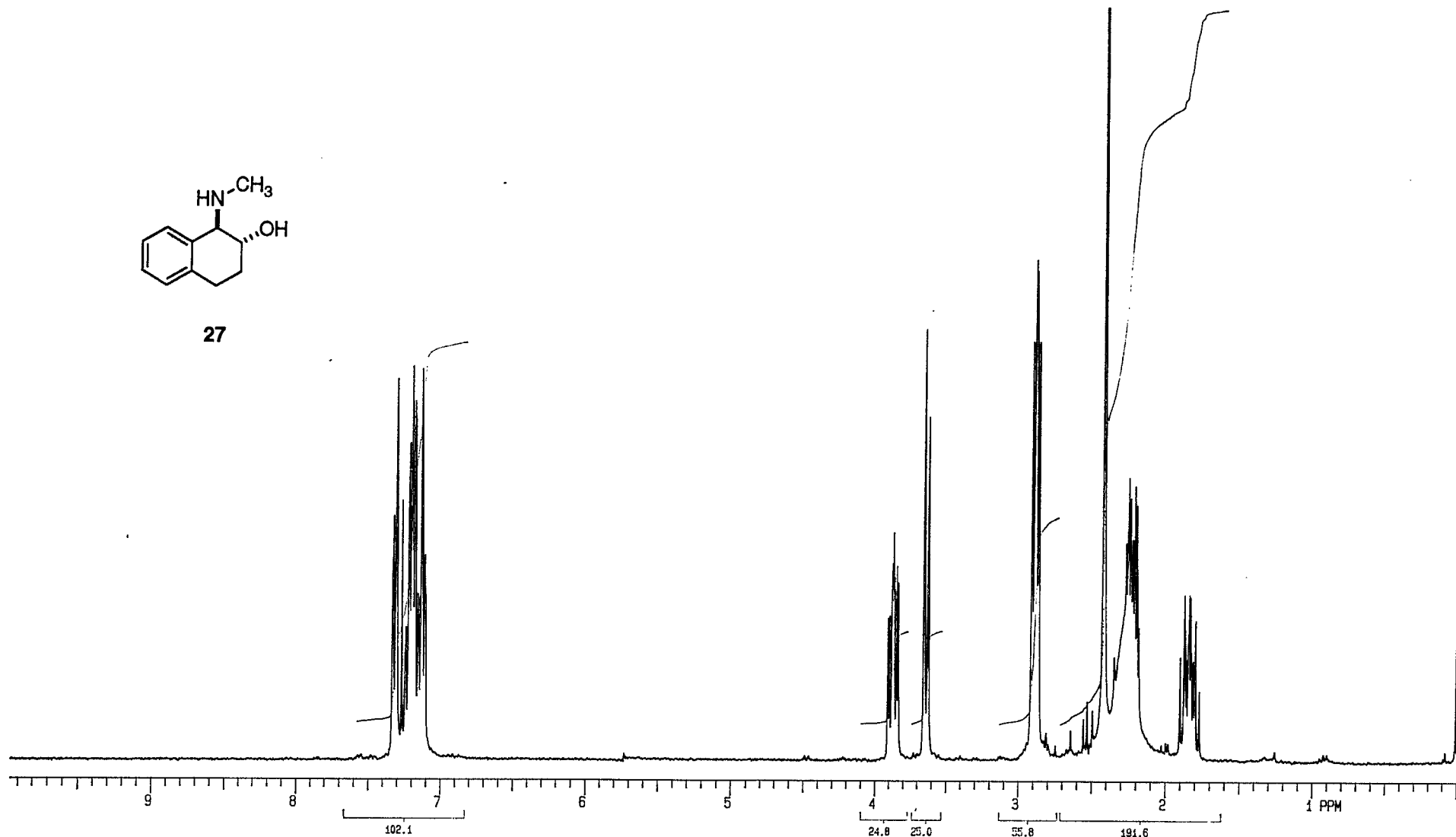
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24041-52-1E
redwood



27



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S2PUL

DH 24041-74-3
KUGELROHR DISTILL

CDCL3

CDCL3

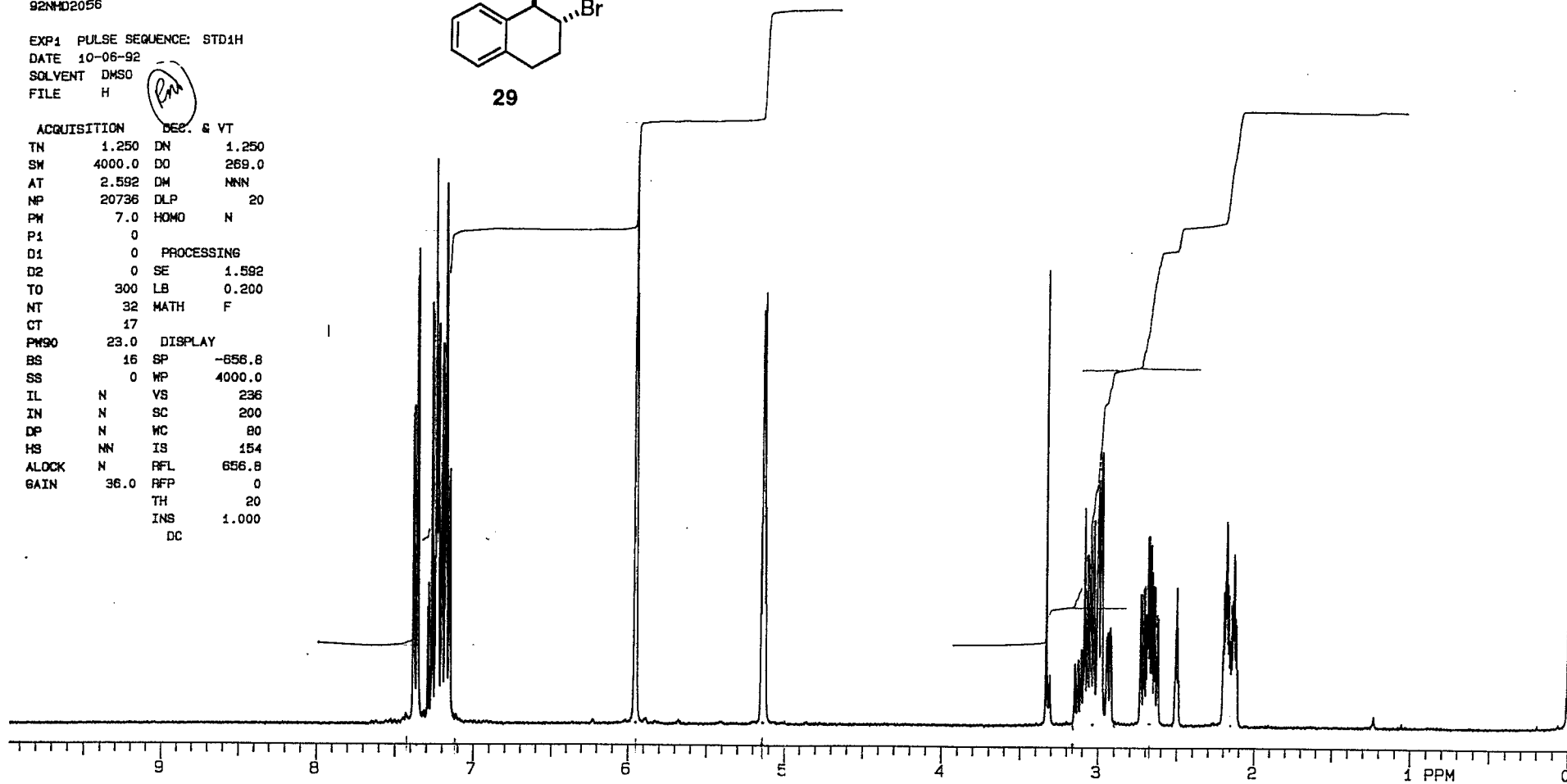
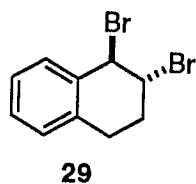
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XL-300
30164-4A
R. DRAPER
92NHD2056

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DATE 10-06-92
SOLVENT DMSO
FILE H

Em

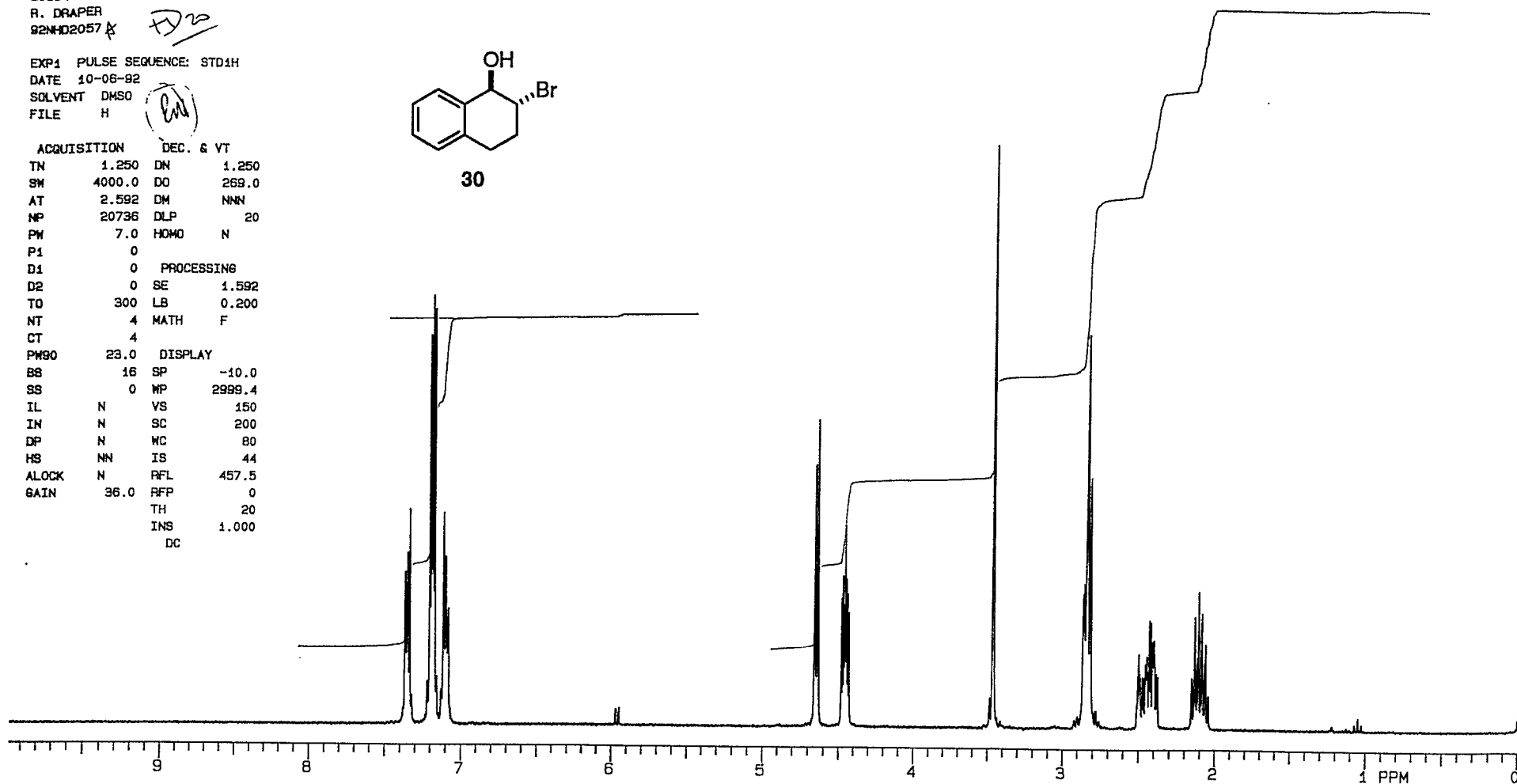
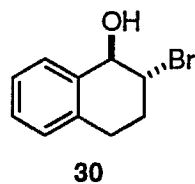
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D2	0	SE	1.592
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CT	17		
PH90	23.0	DISPLAY	
BS	16	SP	-656.8
SS	0	WP	4000.0
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IN	N	SC	200
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ALOCK	N	RFL	656.8
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XL-300
30164-5A
R. DRAPER
92NHD2057

EXP1 PULSE SEQUENCE: STD1H
DATE 10-06-92
SOLVENT DMSO
FILE H

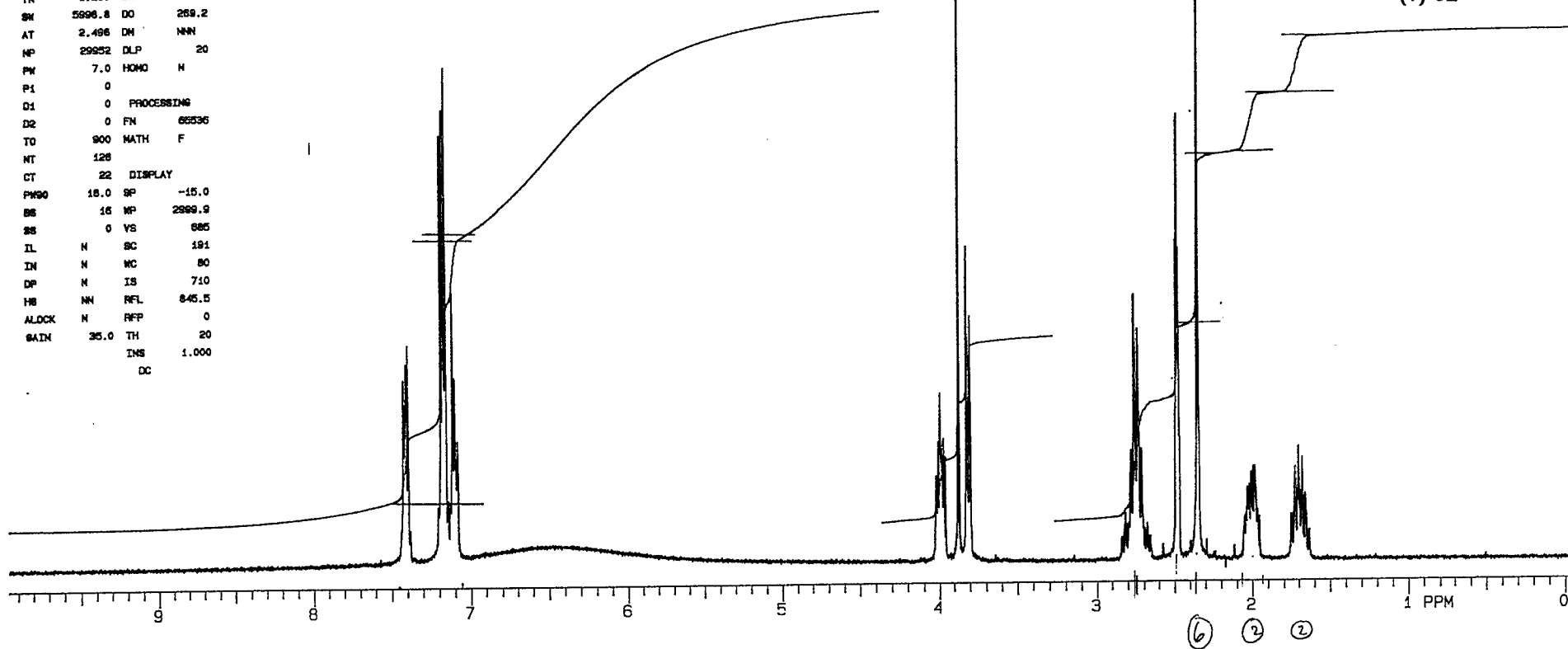
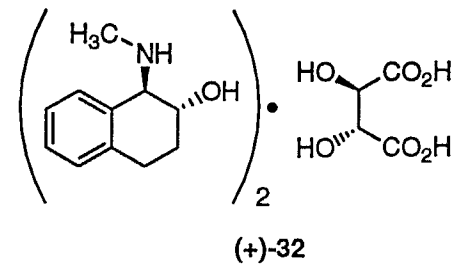
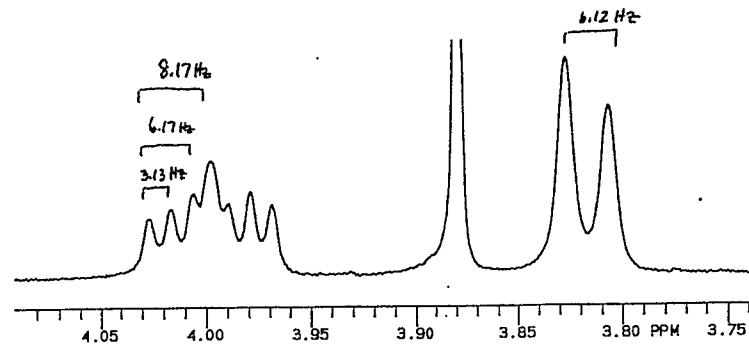
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CT 4
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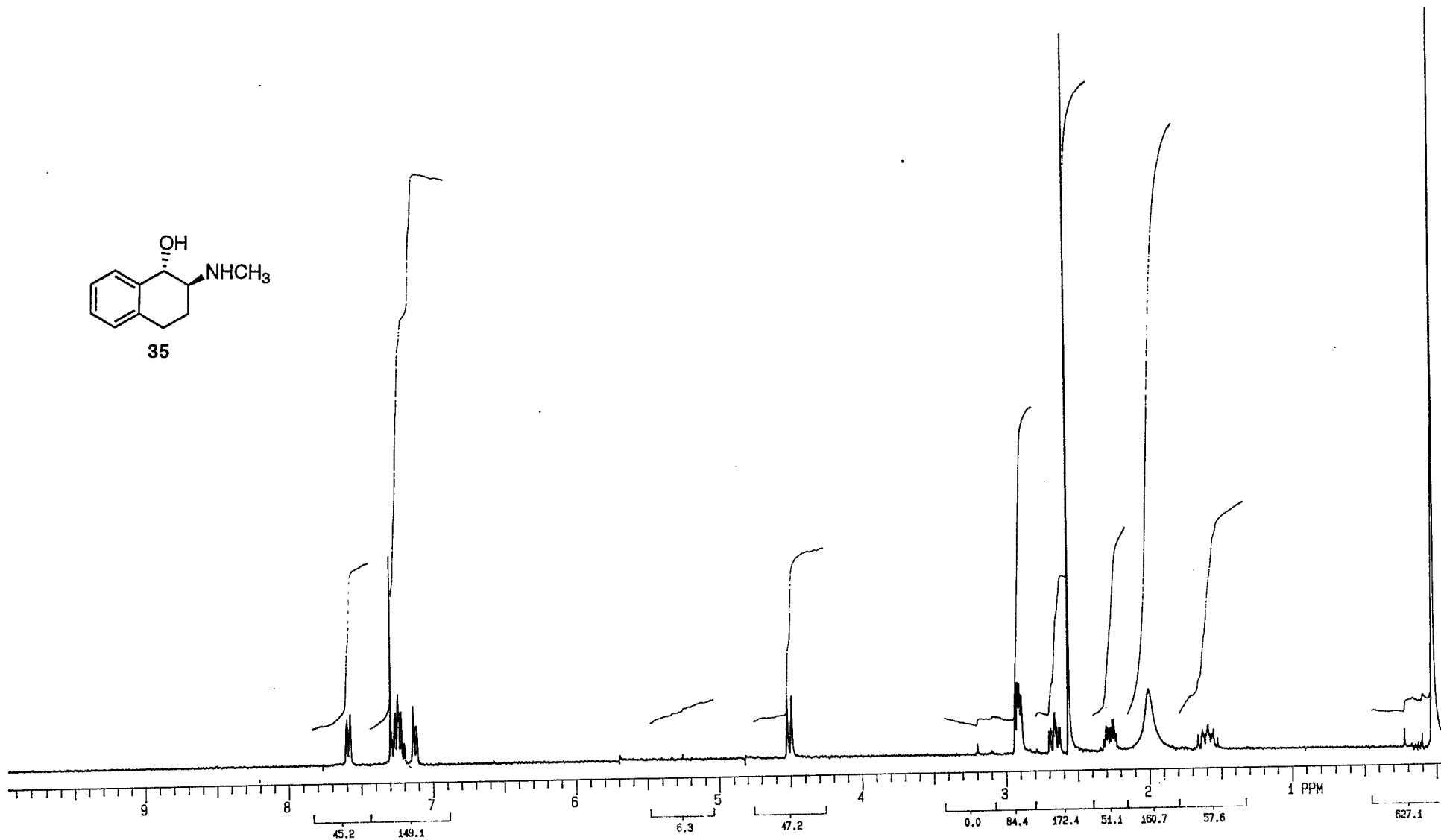
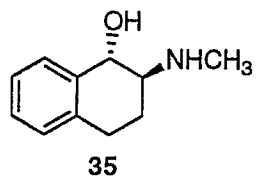


87N01746 36078-117-A
 R. DRAPER
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 1H OBSERVE

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 DATE 07-29-97
 SOLVENT DMSO
 FILE DMSO

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D2 0 FM 65336	
TO 900 MATH F	
NT 128	
CT 22 DISPLAY	
PK90 15.0 SP -15.0	
BS 16 MP 2899.9	
SS 0 VS 885	
IL N SC 191	
IN N MC 80	
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HB NN REL 845.5	
ALOCK N RFP 0	
GAIN 35.0 TH 20	
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	DC





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 8.0

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 16

1.000
 NNN
 C

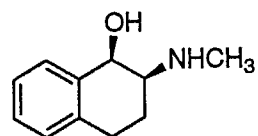
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S2PUL
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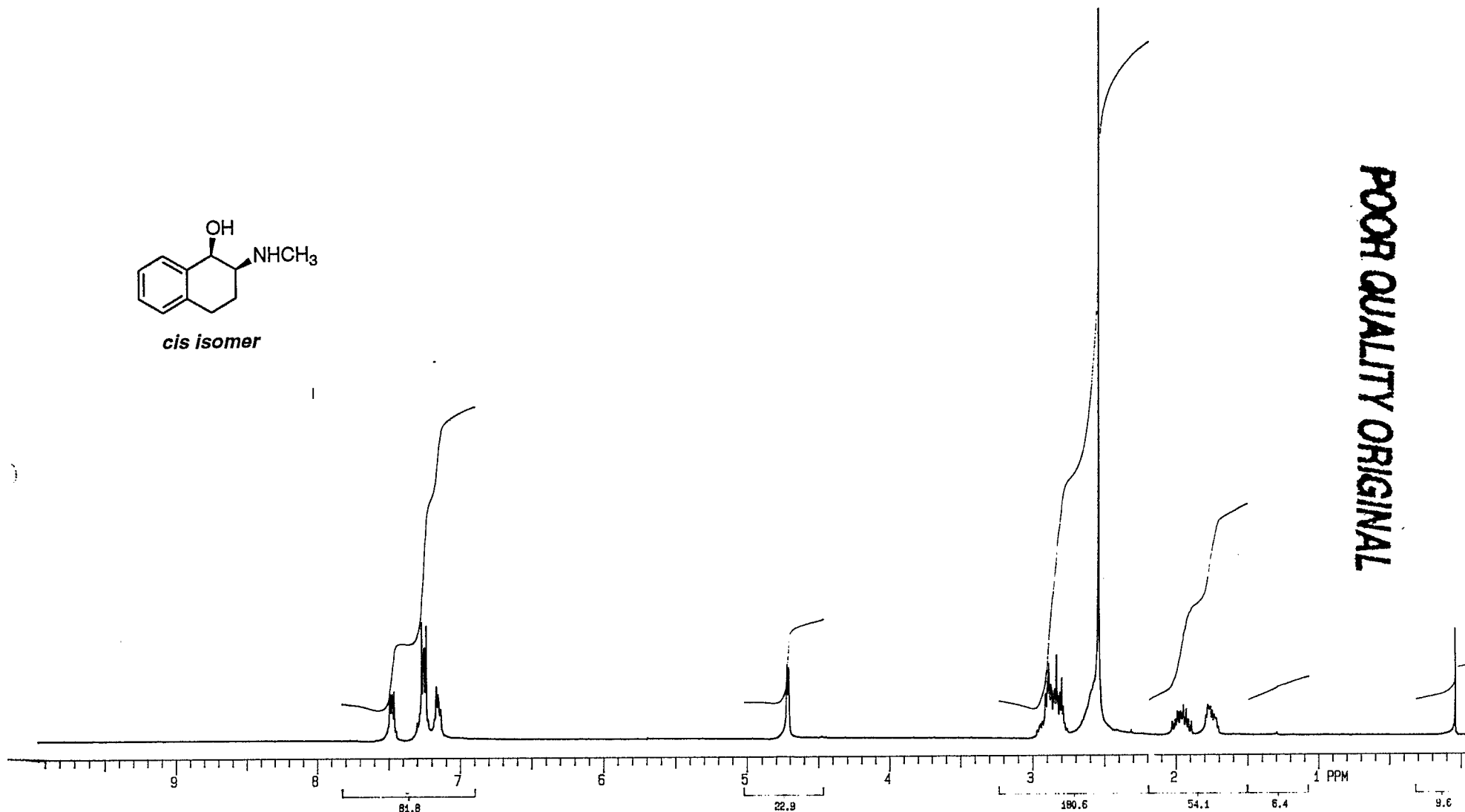
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cis isomer

POOR QUALITY ORIGINAL



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S2PUL
CDCL3

JN26963-R3-1

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